NGA

Version 1.0

Cerebral palsy: diagnosis and management in children and young people under 25

Full Guideline

Clinical Guideline <…>

Methods, evidence and recommendations

August 2016

Draft for consultation

Commissioned by the National Institute for Health and Care Excellence

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

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Contents

1 Introduction

Cerebral palsy is the most common cause of physical disability in children and young people in the developed world, with a prevalence of around 2–2.5 per 1000 live births. The term describes a group of permanent, non-progressive abnormalities of the developing fetal or infant brain leading primarily to disorders of movement and posture, causing 'activity limitation' and 'functional impact'. These constructs of body structure, function and participation were developed within the International Classification of Disability and Health – the ICF; and as such guide all areas of clinical and social interaction. Modern classification systems focus on the individual's level of functional ability (for example Gross Motor Functional Classification System, Manual Ability Classification System) as well as body topography (unilateral / bilateral) and the different patterns of motor types observed in the individual (spastic / dystonic / ataxic).

As well as outlining the intrinsic neurologically derived movement disorder, the formal definition of cerebral palsy also recognises the fact that there are often a variety of other associated clinical and developmental comorbidities. These include 'disturbances of sensation, perception, cognition, communication and behaviour, epilepsy, and secondary musculoskeletal problems'. Cerebral palsy is not curable and the wide variety of comorbidity observed can have tremendous impact on many areas of participation and quality of life for individuals of all ages, particularly eating and drinking, comfort and sleep.

The interaction of primary neurological and secondary physiological factors leads to challenges in terms of both early recognition of cerebral palsy and lifelong management for the person and their families. Infants with cerebral palsy generally present to services in 1 of 2 ways: either identification of atypical motor patterns in those considered at high risk because of antenatal or perinatal complications, or because of atypical motor development picked up during background population assessment.

Recognition of clinical risk and management for people with cerebral palsy change throughout their lives. Understanding the aetiology of the condition, and so minimising the risk and early impact on the brain, may directly affect lifelong outcomes. Throughout growth and development, the assessment and management of complex comorbidity can change the trajectory of patient pathways. With increased longevity, there are now probably at least 3 times as many adults as children with cerebral palsy and as such it presents a considerable challenge for health and social services in the 21st century.

The management of cerebral palsy is a two-pronged approach, and is provided by a variety of multidisciplinary services with a focus on maximising individual function, choice and independence. The first of these is optimising movement and posture for optimal activity and participation while minimising potential secondary musculoskeletal deformity. The second is recognising and intervening to address the many developmental and clinical comorbidities that are associated with cerebral palsy. The former is dealt with by the NICE guideline on Spasticity in under 19s, which concentrates on the motor disorder of cerebral palsy.

This guideline focuses on the second of these aspects, particularly where there may be variation in practice and in patient and family experience across England and Wales. It looks at practical areas of management that are important to children and young people with cerebral palsy, their families and carers, and a wide variety of healthcare and other professionals; These include causation, recognition and prognosis, as well as the associated developmental and clinical comorbidities.

1 Guideline summary

1.1 Committee membership, National Guideline Alliance (NGA) staff and acknowledgements

Table 1: Committee members

Name	Role
Charlie Fairhurst (Chair)	Consultant in Paediatric Neurodisability Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust
Helen Cockerill	Senior Consultant speech and Language Therapist, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust
Zoe Connor	Paediatric Dietitian, Lewisham and Greenwich, NHS Trust Senior Lecturer in Dietetics and Nutrition, London Metropolitan University, London Freelance Dietitian, Nutrition Ltd, Warwickshire
Elspeth Dixon	Patient or carer representative
Wendy Doyle	Neurosciences Social Worker, Great Ormond Street Hospital, London
Paul Eunson	Consultant Paediatric Neurologist, Royal Hospital For Sick Children, Edinburgh
Elizabeth (Liz) Keenan	Clinical Nurse Specialist In Spasticity Management (Adults) National Hospital for Neurology and Neurosurgery, UCLH NHS Foundation Trust
Bidisha Lahoti	Consultant Community Paediatrician, Community Children's Services Sunshine House Children's and Young People's Development Centre, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust
Athena Logothetis	Specialist Occupational Therapist, The Bobath Centre
Margaret Mayston	Clinical Specialist Physiotherapist, The Portland Hospital, London, and Principal Teaching Fellow, Div. Biosciences, University College London
Laura Middleton	General Practitioner, The Parks Medical Practice, Northamptonshire and Speciality Doctor, Helen and Douglas House Hospice Oxford.
Neil Wimalasundera	Consultant in Paediatric Neurodisability, Wolfson Neurodisability Service, Great Ormond Street Hospital, London
Cheryl Newton (nee Davis)	Consultant Paediatric Neuropsychologist, Sheffield Children's NHS Foundation Trust
Valerie Stevenson	Consultant Neurologist, National Hospital for Neurology and Neurosurgery, UCLH NHS Foundation Trust
Duncan Walsh	Patient or carer representative
Co-opted members	
Russel Peek	Consultant Paediatrician and Neonatologist, Gloucestershire Hospitals NHS Foundation Trust
Lindsay Pennington	Senior Lecturer and Speech and Language Therapist, Institute of Health and Society, Newcastle University, Newcastle-upon-Tyne
Neil Stoodley	Consultant Neuroradiologist, Southmead Hospital Bristol and Bristol Royal Hospital for Children

Table 2: NGA staff

Name	Role
Omnia Abdulrazeg	Research Fellow (until January 2016)
Zosia Beckles	Information Scientist (until April 2016)
Kate Coles	Project Manager
Vanessa Delgado Nunes	Senior Research Fellow and Guideline Lead
Eva Gonzalez-Viana	Research Assistant (from January 2016)
Paul Jacklin	Senior Research Fellow- Health Economics
Gemma Marceniuk	Health Economist (from June 2015)
Stephen Murphy	Clinical Advisor (child health)
Valentina Ricci	Interim Senior Research Fellow

Additional support was received from Ebenezer Ademisoye, Taryn Krause, Katie Webster and Rachel Wheeler.

1.2 Care pathway/Algorithm

Figure 1: Cerebral palsy algorithm – identification

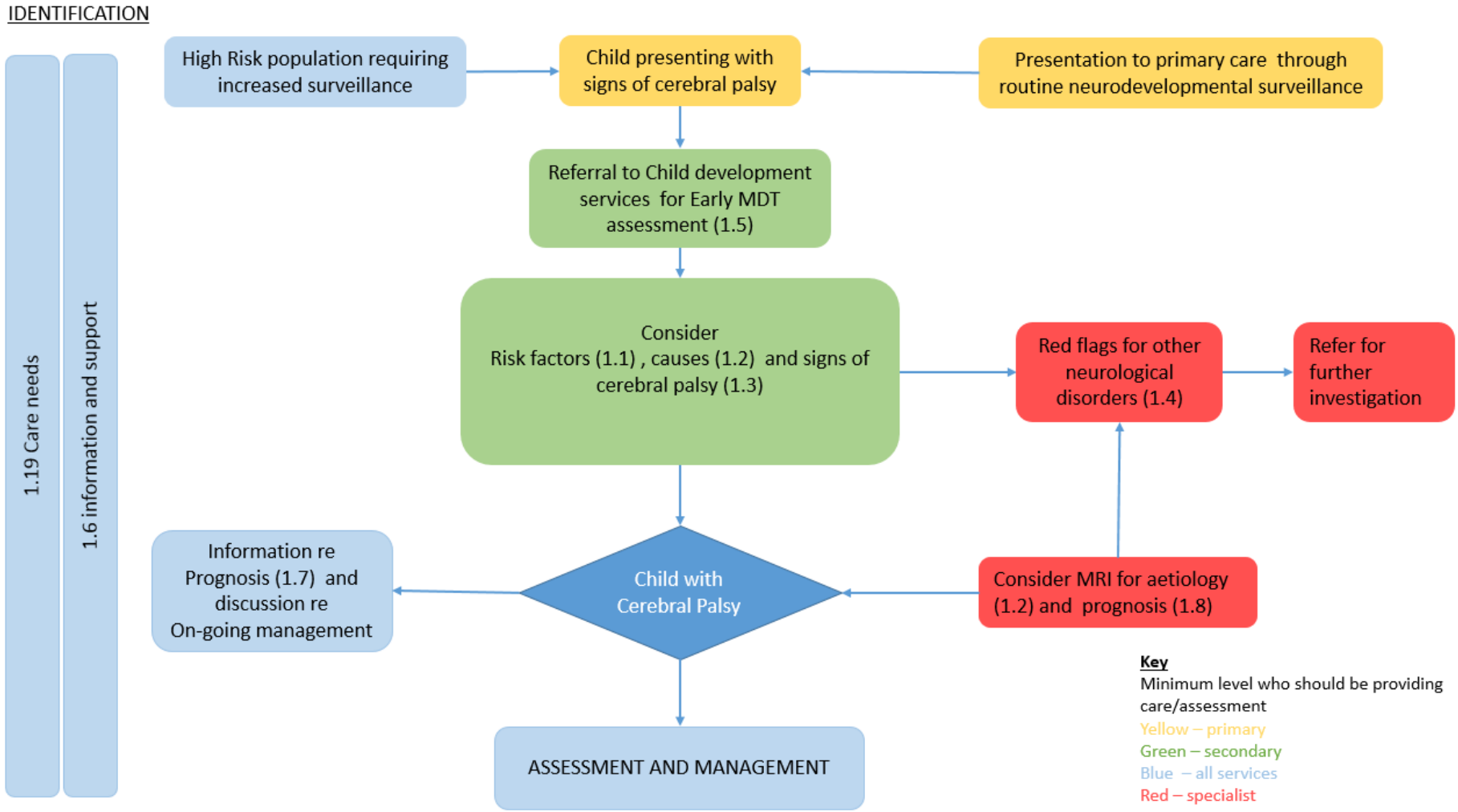
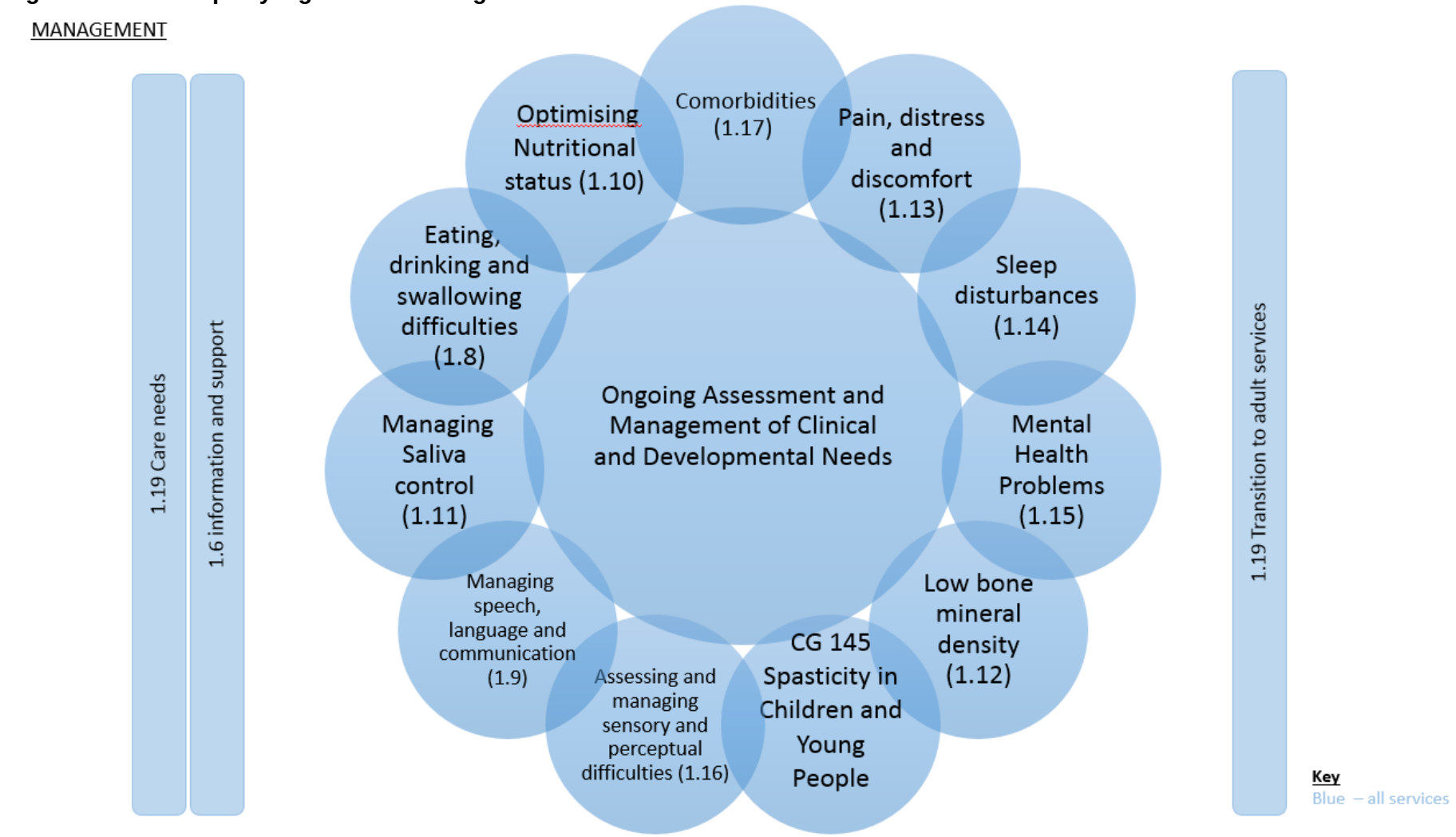


Figure 2: Cerebral palsy algorithm – management



1.3 Other versions of the guideline

NICE produce a number of versions of this guideline:

- The 'short guideline' lists the recommendations, context and recommendations for research.
- 'Information for the public' is written using suitable language for people without specialist medical knowledge.
- NICE Pathways brings together all connected NICE guidance.

1.4 Schedule for updating the guideline

For the most up-to-date information about guideline reviews, please see the latest version of the NICE guidelines manual available from the NICE website.

1.5 Recommendations

Risk Factors

1. Recognise the following as independent risk factors for cerebral palsy:
    - antenatal factors:
        - preterm birth (with risk increasing with decreasing gestational age)[a]
        - chorioamnionitis
        - maternal respiratory tract or genito-urinary infection treated in hospital
    - perinatal factors:
        - low birth weight
        - chorioamnionitis
        - neonatal encephalopathy
        - neonatal sepsis (particularly with a birth weight below 1.5 kg)
        - maternal respiratory tract or genito-urinary infection treated in hospital
    - postnatal factors:
        - meningitis.
2. Provide an enhanced clinical and developmental follow-up programme (see recommendation 12) for infants who have any of the risk factors listed in recommendation 1.

Causes of cerebral palsy

3. When assessing the likely cause of cerebral palsy in a child, recognise that a number of MRI-identified brain abnormalities have been reported at the following approximate prevalences in children with cerebral palsy:
    - white matter damage: 45%
    - basal ganglia or deep grey matter damage: 13%

[a] The NICE guideline on developmental follow-up of preterm babies (publication expected August 2017) will contain more information about risk factors specific to preterm birth.

- congenital malformation: 10%
- focal infarcts: 7%.

4. When assessing the likely cause of cerebral palsy, recognise that white matter damage, including periventricular leukomalacia shown on neuroimaging:
    - is more common in children born preterm than in those born at term
    - may occur in children with any functional level or motor subtype, but is more common in spastic than in dyskinetic cerebral palsy
5. When assessing the likely cause of cerebral palsy recognise that basal ganglia or deep grey matter damage is mostly associated with dyskinetic cerebral palsy.
6. When assessing the likely cause of cerebral palsy, recognise that congenital malformations as a cause of cerebral palsy:
    - are more common in children born at term than in those born preterm
    - may occur in children with any functional level or motor subtype
    - are associated with higher levels of functional impairment than other causes.
7. Recognise that the clinical syndrome of neonatal encephalopathy can result from various pathological events, such as a hypoxic–ischaemic brain injury or sepsis, and if there has been more than one such event they may interact to damage the developing brain.
8. When assessing the likely cause of cerebral palsy, recognise that neonatal encephalopathy has been reported at the following approximate prevalences in children with cerebral palsy born after 35 weeks:
    - attributed to a perinatal hypoxic–ischaemic injury: 20%
    - not attributed to a perinatal hypoxic–ischaemic injury: 12%.
9. Recognise that for cerebral palsy associated with a perinatal hypoxic–ischaemic injury:
    - the extent of long-term functional impairment is often related to the severity of the initial encephalopathy
    - the dyskinetic motor subtype is more common than other subtypes.
10. Recognise that for cerebral palsy acquired after the neonatal period, the following causes and approximate prevalences have been reported:
    - meningitis: 20%
    - other infections: 30%
    - head injury: 12%.
11. When assessing the likely cause of cerebral palsy, recognise that independent risk factors:
    - can have a cumulative impact, adversely affecting the developing brain and resulting in cerebral palsy
    - may have an impact at any stage of development, including the antenatal, perinatal and postnatal periods.

Clinical and developmental manifestations of cerebral palsy

12. Provide an enhanced clinical and developmental follow-up programme for infants and children who are at increased risk of developing cerebral palsy (see recommendation 1):

- From 0–6 months: consider using the General Movement Assessment (GMA) during routine neonatal follow-up assessments.
- From 6–24 months: use a multidisciplinary neurological assessment if continued follow-up assessments are needed.

13. Recognise the following as possible early motor features in the presentation of cerebral palsy:
    - unusual fidgety movements or other abnormalities of movement, including asymmetry or paucity of movement
    - abnormalities of tone, including hypotonia (floppiness), spasticity (stiffness) or dystonia (fluctuating tone)
    - abnormal motor development, including late sitting, crawling or walking, or problems with feeding.
14. Recognise that the most common delayed motor milestones in infants and children with cerebral palsy are:
    - late sitting (after 8 months)
    - late walking (after 18 months)
    - early asymmetry of hand function (hand preference before 1 year).
15. Refer all infants and children with delayed motor milestones to a child development service for further assessment.
16. Refer children who have obvious and persistent toe walking to a child development service for further assessment.
17. If there are concerns that an infant or child may have cerebral palsy but a definitive diagnosis cannot be made, discuss this with their parents or carers and explain that an enhanced clinical and developmental follow-up programme will be necessary to try to reach a definite conclusion.
18. Refer all infants and children with suspected cerebral palsy immediately to a child development service for a multidisciplinary assessment, in order to facilitate early diagnosis and intervention.
19. Recognise that ongoing communication between all levels of service provision in the care of children and young people with cerebral palsy is crucial, particularly involvement of primary care from diagnosis onwards.
20. Review a diagnosis of cerebral palsy if clinical signs or the child's development over time do not follow the patterns expected for cerebral palsy, taking into account that the functional and neurological manifestations of cerebral palsy change over time.

Red flags for other neurological disorders

21. Recognise the following as red flags for neurological disorders other than cerebral palsy, and refer the child or young person to a specialist in paediatric neurology if any of these are observed:
    - absence of known risk factors (see recommendation 1)
    - family history of a progressive neurological disorder
    - loss of already attained cognitive or developmental abilities
    - development of unexpected focal neurological signs
    - MRI findings suggestive of a progressive neurological disorder
    - MRI findings not in keeping with clinical signs of cerebral palsy.

MRI and identification of other causes of cerebral palsy

22. Offer MRI for a child or young person with suspected or known cerebral palsy if the aetiology is not clear after consideration of:
    - antenatal, perinatal and postnatal history
    - their ongoing developmental and medical history
    - the findings on clinical examination
    - early cranial ultrasound examination.
23. Recognise that MRI will not accurately establish the timing of a hypoxic-ischaemic brain injury in a child with cerebral palsy.
24. When deciding the best age to perform an MRI scan for a child with cerebral palsy, take account of the following:
    - Subtle neuro-anatomical changes that could explain the aetiology of cerebral palsy may not be apparent until 2 years of age.
    - The presence of any red flags for a progressive neurological disorder (see section 7.7).
    - That a general anaesthetic is usually needed for young children having MRI.
    - The views of the child or young person and their parents or carers.
25. Consider repeating the MRI scan if:
    - there is a change in the expected clinical and developmental profile **or**
    - any red flags for a progressive neurological disorder appear (see section 7.7).
26. Discuss with the child or young person and their parents or carers the reasons for performing MRI in each individual circumstance.
27. Take account of the likely cause of cerebral palsy and the findings from MRI (if performed) when discussing prognosis with the child or young person and their parents or carers.

MRI and prognosis of cerebral palsy

28. Do not rely on MRI alone for predicting prognosis in infants and children with cerebral palsy.

Prognosis for walking, talking and life expectancy

29. Provide the following information to parents or carers about the prognosis for walking for a child with cerebral palsy:
    - The more severe the child's physical, functional or cognitive impairment, the greater the possibility of difficulties with walking.
    - If a child can sit at 2 years of age it is likely, but not certain, that they will be able to walk unaided by age 6.
    - If a child cannot sit but can roll at 2 years of age, there is a possibility that they may be able to walk unaided by age 6.
    - If a child cannot sit or roll at 2 years of age, they are unlikely to be able to walk unaided.
30. Recognise the following in relation to prognosis for speech development in a child with cerebral palsy, and discuss this with parents or carers as appropriate:

- Around 1 in 2 children with cerebral palsy have some difficulty with elements of communication (see recommendation 125).
- Around 1 in 3 children have specific difficulties with speech and language.
- The more severe the child's physical, functional or cognitive impairment, the greater the likelihood of difficulties with speech and language.
- Uncontrolled epilepsy may be associated with difficulties with all forms of communication, including speech.
- A child with bilateral spastic, dyskinetic or ataxic cerebral palsy is more likely to have difficulties with speech and language than a child with unilateral spastic cerebral palsy.

31. Provide the following information to parents or carers, as appropriate, about prognosis for life expectancy for a child with cerebral palsy:
    - The more severe the child's physical, functional or cognitive impairment, the greater the likelihood of reduced life expectancy.
    - There is an association between reduced life expectancy and the need for enteral tube feeding, but this reflects the severity of swallowing difficulties and is not because of the intervention.

Information and support

32. Ensure that information and support focuses as much on the functional abilities of the child or young person with cerebral palsy as on any functional impairment.
33. Provide clear, timely and up-to-date information to parents or carers on the following topics:
    - diagnosis (see section 6.7)
    - aetiology (see section 5.6)
    - prognosis (see section 10.7)
    - natural history
    - comorbidities (see section 27.20)
    - specialist equipment that is available
    - resources available and access to financial, respite, social care and other support for children and young people and their parents, carers and siblings (see also recommendations 139 and 143)
    - educational placement
    - transition (see section 29.6).
34. Ensure that clear information about the 'patient pathway' is shared with the child or young person and their parents or carers (for example, by providing them with copies of correspondence). Follow the principles in the recommendations about communication, information and shared decision-making in the NICE guideline on patient experience in adult NHS services.
35. Provide information to the child or young person with cerebral palsy, and their parents or carers, on an ongoing basis. Adapt the communication methods and information resources to take account of the needs and understanding of the child or young person and their parents or carers. For example, think about using 1 or more of the following:
    - oral explanations
    - written information and leaflets

- mobile technology, including apps
- augmentative and alternative communication systems (see section 16.7).

36. Work with the child or young person and their parents or carers to develop and maintain a personal 'folder' in their preferred format containing relevant information that can be shared with their extended family and friends and used in health, social care, educational and transition settings. Information could include:
    - early history
    - motor subtype and limb involvement
    - functional abilities
    - interventions
    - medication
    - comorbidities
    - preferred methods of communication
    - any specialist equipment that is used or needed
    - care plans
    - emergency contact details.
37. Ensure that the child or young person and their parents or carers are given personalised information from a specialist about the following topics as appropriate:
    - menstruation
    - fertility
    - contraception
    - sex
    - sexuality
    - parenting.
38. Provide information to the child or young person and their parents or carers, and to all relevant teams around the child and young person, about the local and regional services available for children and young people with cerebral palsy, and how to access them.
39. Provide information about local support and advocacy groups to the child or young person and their parents or carers.

Assessment of eating, drinking and swallowing difficulties

40. If eating, drinking and swallowing difficulties are suspected in a child or young person with cerebral palsy, carry out a clinical assessment as first-line investigation to determine the safety, efficiency and enjoyment of eating and drinking. This should include:
    - taking a relevant clinical history, including asking about any previous chest infections
    - observation of eating and drinking in a normal mealtime environment by a speech and language therapist with training in assessing and treating dysphagia.
41. Refer the child or young person to a local specialist multidisciplinary team with training in assessing and treating dysphagia if there are clinical concerns about eating, drinking and swallowing, such as:

- coughing
- choking
- gagging
- change in colour during eating
- recurrent chest infection
- prolonged meal duration.

42. Do not use videofluoroscopy or fibroscopic endoscopy for the initial assessment of eating, drinking and swallowing difficulties in children and young people with cerebral palsy.

43. The specialist multidisciplinary team should consider videofluoroscopy if any of the following apply:

    - There is uncertainty about the safety of eating, drinking and swallowing after specialist clinical assessment.
    - The child or young person has recurrent chest infection without overt clinical signs of aspiration.
    - There is deterioration in eating, drinking and swallowing ability with increasing age (particularly after adolescence).
    - There is uncertainty about the impact of modifying food textures (for example, use of thickeners or pureeing).
    - Parents or carers need support to understand eating, drinking and swallowing difficulties, to help with decision-making.

44. Videofluoroscopy should only be performed in a centre with a specialist multidisciplinary team who have experience and competence in using it with children and young people with cerebral palsy.

45. Do not routinely perform videofluoroscopy when considering starting enteral tube feeding in children and young people with cerebral palsy.

46. Ensure that children and young people with ongoing eating, drinking and swallowing difficulties have access to regional tertiary specialist assessment.

Management of eating, drinking and swallowing difficulties

47. Develop strategies and goals in partnership with the child or young person with cerebral palsy and their parents, carers and other family members for interventions to improve eating, drinking and swallowing.

48. Create an individualised plan for managing eating, drinking and swallowing difficulties in children and young people with cerebral palsy, taking into account the understanding, knowledge and skills of parents, carers and any other people involved in feeding the child or young person. Assess the role of the following:

    - postural management and positioning when eating
    - modifying fluid and food textures and flavours
    - feeding techniques, such as pacing and spoon placement
    - equipment, such as specialised feeding utensils
    - optimising the mealtime environment
    - strategies for managing behavioural problems associated with eating and drinking
    - strategies for developing oral motor skills

- communication strategies
- modifications to accommodate visual or other sensory impairments that affect eating, drinking and swallowing
- the training needs of the people who care for the child or young person particularly outside the home.

49. Advise parents or carers that intra-oral devices have not been shown to improve eating, drinking and swallowing in children and young people with cerebral palsy.
50. Use outcome measures important to the child or young person and their parents or carers to review:
    - whether individualised goals have been achieved
    - the clinical and functional impact of interventions to improve eating, drinking and swallowing.

Optimising nutritional status

51. Regularly review the nutritional status of children and young people with cerebral palsy, including taking anthropometric measurements.
52. Provide timely access to assessment and nutritional interventional support from a dietitian if there are concerns about oral intake, growth or nutritional status.
53. If oral intake is still insufficient to provide adequate nutrition after assessment and nutritional interventions, refer the child or young person to be assessed for enteral tube feeding by a multidisciplinary team with relevant expertise.
54. For guidance on nutritional interventions and enteral tube feeding in over 18s, see the NICE guideline on nutrition support for adults.
55. Regularly assess children and young people with cerebral palsy during routine reviews to identify concerns about speech, language and communication, including speech intelligibility.
56. Refer children and young people with cerebral palsy for specialist assessment if there are concerns about speech, language and communication, including speech intelligibility.
57. Specialist assessment of the communication skills, including speech intelligibility, of children and young people with cerebral palsy should be conducted by a multidisciplinary team that includes a speech and language therapist.
58. Offer interventions to improve speech intelligibility, for example targeting posture, breath control, voice production and rate of speech, to children and young people with cerebral palsy:
    - who have a motor speech disorder and some intelligible speech **and**
    - for whom speech is the primary means of communication **and**
    - who can engage with the intervention.

Improving speech language and communication: communication systems

59. Consider augmentative and alternative communication systems for children and young people with cerebral palsy who need support in the understanding and producing speech. These may include pictures, objects, symbols and signs, and speech-generating devices.
60. If there are ongoing problems with using augmentative and alternative communication systems, refer the child or young person to a specialist service in order to tailor interventions to their individual needs, taking account of their cognitive, linguistic, motor, hearing and visual abilities.

61. Regularly review children and young people who are using augmentative and alternative communication systems, to monitor their progress and ensure that interventions continue to be appropriate for their needs.

62. Provide individualised training in communication techniques for families, carers, school staff and other people involved in the care of a child or young person with cerebral palsy.

Managing saliva control

63. Assess factors that may affect drooling in children and young people with cerebral palsy, such as positioning, medication history, reflux and dental issues, before starting drug therapy.

64. To reduce the severity and frequency of drooling in children and young people with cerebral palsy, consider transdermal hyoscine hydrobromide[b].

65. If transdermal hyoscine hydrobromide is contraindicated, not tolerated or not effective, consider:

    - glycopyrrolate[c] (oral or by enteral tube) **or**
    - other anticholinergic drugs, such as trihexyphenidyl hydrochloride[d] for children with dyskinetic cerebral palsy, but only with input from specialist services.

66. Regularly review the effectiveness, tolerability and side effects of all drug treatments used for saliva control.

67. Refer the child or young person to a specialist service if the anticholinergic drug treatments outlined in recommendations 65 and 66 are contraindicated, not tolerated or not effective, to consider other treatments for saliva control.

68. Consider specialist assessment and use of botulinum toxin A injections to the salivary glands with ultrasound guidance to reduce the severity and frequency of drooling if anticholinergic drugs provide insufficient benefit or are not tolerated.

69. Advise children and young people and their parents or carers that high-dose botulinum toxin A injection[e] to the salivary glands can rarely cause swallowing difficulties, and so they should return to hospital immediately if breathing or swallowing difficulties occur.

70. Consider referring young people for a surgical opinion, after an assessment confirming clinically safe swallow, if there is:

[b] At the time of consultation (August 2016), transdermal hyoscine hydrobromide (scopolamine hydrobromide) did not have a UK marketing authorisation for use in children and young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[c] At the time of consultation (August 2016), glycopyrrolate did not have a UK marketing authorisation for use in children and young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[d] At the time of consultation (August 2016), trihexyphenidyl hydrochloride did not have a UK marketing authorisation for use in children and young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[e] At the time of consultation (August 2016), some botulinum toxin A products had a UK marketing authorisation for use in the treatment of focal spasticity in children, young people and adults, including the treatment of dynamic equinus foot deformity due to spasticity in ambulant paediatric cerebral palsy patients, 2 years of age or older. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

- a potential need for lifelong drug treatment or
- insufficient benefit or non-tolerance of anticholinergic drugs and botulinum toxin A injections[e].

Risk factors for low bone mineral density

71. Recognise that in children and young people with cerebral palsy the following are independent risk factors for low bone mineral density:
    - non-ambulant (GMFCS level IV or V)
    - vitamin D deficiency
    - presence of eating drinking and swallowing difficulties or concerns about nutritional status
    - low weight for age (below the 2nd centile).
    - history of low-impact fracture
    - use of anticonvulsant medication
72. Recognise that there is an increased risk of low-impact fractures in children and young people with cerebral palsy who are non-ambulant or have low bone mineral density.
73. Inform children and young people with cerebral palsy and their parents or carers if they are at an increased risk of low-impact fractures.

Prevention of reduced bone mineral density

74. If a child and young person with cerebral palsy has 1 or more risk factors for low bone mineral density (see recommendation 71):
    - assess their dietary intake of calcium and vitamin D **and**
    - consider the following laboratory investigations of calcium and vitamin D status:
        - serum calcium, phosphate and alkaline phosphatase
        - serum vitamin D
        - urinary calcium/creatinine ratio.
75. Create an individualised care plan for children and young people with cerebral palsy who have one or more risk factors for low bone mineral density (see recommendation 71).
76. Consider the following as possible interventions to reduce the risk of reduced bone mineral density and low-impact fractures:
    - an active movement programme
    - active weight bearing
    - dietetic interventions as appropriate, including nutritional support and calcium and vitamin D supplementation
    - minimising risks associated with movement and handling.
77. Consider a DEXA scan under specialist guidance for children and young people with cerebral palsy who have had low-impact fracture.
78. Refer children and young people with cerebral palsy with reduced bone density and a history of low-impact fracture to a specialist centre for consideration of bisphosphonate therapy.

79. Do not offer standing frames solely to prevent low bone mineral density in children and young people with cerebral palsy.
80. Do not offer vibration therapy solely to prevent low bone mineral density in children and young people with cerebral palsy.

Causes of pain, discomfort, distress, and sleep disturbances

Pain, discomfort and distress

81. Explain that most children and young people with cerebral palsy experience pain regularly, and that the prevalence of pain increases with increasing severity of motor impairment.
82. Recognise that common causes of pain in all children and young people also affect those with cerebral palsy, and that difficulties with communication and perception may make identifying the cause more challenging. Common types of pain in children and young people include:
    - non-specific back pain
    - headache
    - non-specific abdominal pain
    - dental pain
    - dysmenorrhea.
83. Recognise that the most common condition-specific causes of pain in children and young people with cerebral palsy include:
    - musculoskeletal problems (for example, scoliosis, hip subluxation and dislocation)
    - increased muscle tone (including dystonia and spasticity)
    - constipation
    - vomiting and gastro-oesophageal reflux.

Sleep disturbances

84. Explain to parents or carers that, in children and young people with cerebral palsy sleep disturbances (for example, difficulties with falling asleep and staying asleep and with daytime sleepiness):
    - are common
    - may be caused by factors such as environment, hunger and thirst.
85. Recognise that the most common condition-specific causes of sleep disturbances in children and young people with cerebral palsy include:
    - sleep-induced breathing disorders, such as obstructive sleep apnoea
    - seizures
    - pain and discomfort
    - need for repositioning because of immobility
    - poor sleep hygiene (poor night-time routine and environment)
    - night-time interventions, including overnight tube feeding or the use of orthoses
    - comorbidities, including adverse effects of medication.

Assessment of pain, distress, discomfort and sleep disturbances

86. Refer the child or young person for a specialist multidisciplinary team assessment of pain, distress and sleep if the cause of pain or distress is not clear after routine assessment.

Pain, discomfort and distress

87. Take into account that parents and familiar carers have a key role in recognising and assessing pain and discomfort in children and young people with cerebral palsy.
88. When assessing pain in children and young people with cerebral palsy:
    - recognise that assessing the presence and degree of pain can be challenging, especially if there are communication difficulties or learning disabilities
    - ask about signs of distress and sleep disturbances at every contact
    - recognise that pain-related behaviour can present differently compared with that in the wider population.
89. Assess for other possible causes of distress in the absence of identifiable physical causes of pain and discomfort, such as:
    - psychological and emotional distress
    - increased sensitivity to environmental triggers
    - thirst or hunger.
90. Consider using tools to identify pain or assess severity of pain in children and young people with cerebral palsy, for example:
    - For children and young people with communication difficulties:
        - Paediatric Pain Profile
        - Non-communicating Children's Pain Checklist – postoperative version
    - For children and young people without communication difficulties:
        - Numeric pain rating scale.

Sleep disturbances

91. When identifying and assessing sleep disturbances in children and young people with cerebral palsy:
    - recognise that parents and familiar carers have the primary role in this
    - consider using sleep questionnaires or diaries.
92. Always ask about pain, sleep and distress as part of any clinical consultation.
93. For reversible causes of pain identified in children and young people with cerebral palsy, treat the cause where appropriate using targeted interventions in line with the following NICE guidelines:
    - spasticity in under 19s
    - constipation in children and young people
    - gastro-oesophageal reflux disease in children and young people and gastro-oesophageal reflux disease and dyspepsia in adults
    - headaches in over 12s

- low back pain in adults
- urinary tract infection in under 16s.

Management of pain, distress and discomfort

94. For common interventions used in the management of cerebral palsy (such as physical therapies, botulinum toxin A injections and surgery) that can cause acute pain:
    - advise the child or young person and their parents or carers that these interventions may reduce discomfort in the long term
    - minimise discomfort during these procedures.
95. In the absence of an identifiable cause of pain, discomfort or distress in a child or young person with cerebral palsy:
    - consider a 'stepped approach' trial of simple analgesia (such as paracetamol and/or ibuprofen) for mild to moderate pain
    - monitor the duration, pattern and severity of symptoms.
96. Refer the child or young person to a specialist pain multidisciplinary team for a more detailed assessment if a trial of analgesia is unsuccessful.

Management of sleep disturbances

97. Optimise sleep hygiene for children and young people with cerebral palsy.
98. Manage treatable causes of sleep disturbances that are identified in children and young people with cerebral palsy.
99. If no treatable cause is found, consider a trial of melatonin[f] to manage sleep disturbances for children and young people with cerebral palsy, particularly for problems with falling asleep.
100. Do not offer regular sedative medication to manage primary sleep disorders in children with cerebral palsy without seeking specialist advice.
101. Do not offer sleep positioning systems solely to manage primary sleep disorders in children and young people with cerebral palsy.
102. Refer the child or young person to specialist sleep services for multidisciplinary team assessment and management if there are ongoing sleep disturbances.
103. Follow the relevant NICE guidelines when identifying and managing mental health problems and psychological and neurodevelopmental disorders in children and young people with cerebral palsy:
    - depression in children and young people.
    - depression in adults
    - generalised anxiety disorder and panic disorder in adults
    - Antisocial behaviour and conduct disorders in children and young people
    - challenging behaviour and learning disabilities
    - antisocial behaviour and conduct disorders in children and young people
    - mental health problems in people with learning disabilities[g]

[f] At the time of consultation (August 2016), melatonin did not have a UK marketing authorisation for use in children and young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

- autism in under 19s and autism in adults.
- attention deficit hyperactivity disorder.

Assessment of mental health problems

104. Take into account that parents and familiar carers have a central role in recognising and assessing emotional difficulties and mental health problems in children and young people with cerebral palsy.

105. Recognise that children and young people with cerebral palsy have an increased prevalence of:

- mental health and psychological problems, including depression, anxiety and conduct disorders
- behaviours that challenge, which may be triggered by pain, discomfort or sleep disturbances
- neurodevelopmental disorders, including autism spectrum disorders (ASD) and attention deficit hyperactivity disorder (ADHD).

106. Recognise that emotional and behavioural difficulties (for example, low self-esteem) are reported in up to 1 in 4 children and young people with cerebral palsy.

107. Any multidisciplinary team should:

- recognise that mental health problems and emotional difficulties can be as important as physical health problems for children and young people with cerebral palsy
- explore such difficulties during consultations
- recognise that assessing psychological problems can be challenging in children and young people with communication difficulties or learning disabilities.

108. Think about and address the following contributory factors if a change in emotional state occurs in a child or young person with cerebral palsy:

- pain or discomfort (see sections 20.6, 21.6 and 22.6)
- frustration associated with communication difficulties
- social factors, such as a change in home circumstances or care provision.

109. Use validated tools, such as the Child Health Questionnaire and the Strengths and Difficulties Questionnaire, to assess mental health problems in children and young people with cerebral palsy.

Management of mental health problems

110. Refer the child or young person for specialist psychological assessment and ongoing management if emotional and behavioural difficulties persist or there are concerns about their mental health.

111. Work in partnership with the child or young person with cerebral palsy, and their parents and primary carers, when assessing and managing mental health problems and setting goals.

[g] Publication expected September 2016; the consultation draft of the guideline can be viewed here

112. When making an individual management plan to address the mental health needs of a child or young person with cerebral palsy, take into account ways of providing support to parents or carers.

113. Recognise that there are specific challenges in managing and minimising the impact of mental health problems in children and young people with cerebral palsy. These include:

- communication difficulties
- comorbidities, particularly epilepsy and pain
- side effects and drug interactions of multiple medications (polypharmacy)
- specific social care needs.

Management of sensory and perceptual difficulties

114. Explain to children and young people with cerebral palsy and their parents or carers that difficulties with learning and movement may be exacerbated by difficulties with registering or processing sensory information. These may include:

- primary sensory disorders, such as the way visual or hearing information is processed
- complex disorders of sensory processing and perception, such as planning movements.

115. For children and young people with cerebral palsy who have difficulties with processing sensory and perceptual information:

- agree a functional, goal-orientated, individualised programme in partnership with parents or carers
- explain to parents or carers that there is a lack of evidence to support specific interventions.

Other comorbidities in cerebral palsy

116. Assess children and young people with cerebral palsy regularly for developmental and clinical comorbidities, and recognise that these can have an important impact on wellbeing, function and participation.

117. Manage comorbidities, and refer the child or young person for further specialist care if necessary (for example, if a management programme is unsuccessful).

118. Ensure that the child or young person has access to a multidisciplinary team that:

- is able to meet their individual needs
- can provide the following expertise, through a local network of care:
  - paediatric medicine
  - adult medicine (as appropriate)
  - nursing care
  - physiotherapy and occupational therapy
  - orthotics and rehabilitation (as appropriate)
  - speech and language therapy
  - dietetics
  - psychology
  - social care.

119. Ensure that routes for accessing specialist teams involved in managing comorbidities associated with cerebral palsy are clearly defined on a regional basis.

120. Talk to children and young people and their parents or carers about visual impairment that can be associated with cerebral palsy. Information that may be useful to discuss includes the following:

- visual impairment occurs in around 1 in 2 children and young people with cerebral palsy
- it may occur in children and young people with any functional level or motor subtype, but prevalence increases with increasing severity of motor impairment
- it may include impairment of control of eye movements, ocular function and cerebral visual processing
- regular ongoing visual assessment is necessary.

121. Regularly assess children and young people with cerebral palsy for signs of cortical visual impairment, bearing in mind that this:

- occurs in around 1 in 5 children and young people with cerebral palsy
- may occur in children and young people with any functional level or motor subtype but prevalence increases with increasing severity of motor impairment
- may be difficult to recognise in the early stages.

122. Talk to children and young people and their parents or carers about hearing impairment that can be associated with cerebral palsy. Information that may be useful to discuss includes the following:

- hearing impairment occurs in around 1 in 10 children and young people with cerebral palsy
- it may occur in children and young people with any functional level or motor subtype but prevalence increases with increasing severity of motor impairment
- it is more common in people with dyskinetic or ataxic cerebral palsy than in those with spastic cerebral palsy
- regular ongoing hearing assessment is necessary.

123. Talk to children and young people and their parents or carers about learning disabilities that can be associated with cerebral palsy (for example, problems with knowledge acquisition, memory and understanding and use of language). Information that may be useful to discuss includes the following:

- learning disabilities occur in around 1 in 2 children and young people with cerebral palsy
- severe learning disabilities (IQ below 50) occur in around 1 in 2 of these
- learning disabilities can be associated with any functional level, but prevalence increases with increasing severity of motor impairment:
  - GMFCS level I or II: around 1 in 3 have an IQ below 70
  - GMFCS level III, IV or V: around 2 in 3 have an IQ below 70.

124. Talk to children and young people and their parents or carers about communication difficulties that can be associated with cerebral palsy. Information that may be useful to discuss includes the following:

- communication difficulties occur in around 1 in 2 children and young people with cerebral palsy
- at least 1 in 10 need augmentative and alternative communication (signs, symbols and speech generating devices)
- around 1 in 10 children and young people cannot If there are ongoing problems with using augmentative and alternative communication systems, refer the child or young person to a specialist service use formal methods of augmentative and alternative communication because of cognitive and sensory impairments communication difficulties
- communication difficulties may occur with any functional level or motor subtype, but are more common in children and young people with dyskinetic or severe bilateral spastic cerebral palsy
- communication difficulties do not necessarily correlate with learning disabilities.

125. Talk to children and young people and their parents or carers about behavioural difficulties that can be associated with cerebral palsy. Information that may be useful to discuss includes that around 2–3 in 10 children and young people with cerebral palsy have 1 or more of the following:
    - emotional and behavioural difficulties that have an effect on the child or young person's function and participation
    - problems with peer relationships
    - difficulties with attention, concentration and hyperactivity
    - conduct behavioural difficulties.
126. Support children and young people with cerebral palsy and their families and carers to recognise behavioural problems.
127. Manage routine behavioural problems within the multidisciplinary team, and refer the child or young person to specialist services if problems persist.
128. Advise parents or carers that vomiting, regurgitation and gastro-oesophageal reflux are common in infants, children and young people with cerebral palsy. If there is a marked change in the pattern of vomiting, assess for a clinical cause.
129. For guidance on identifying and managing gastro-oesophageal reflux disease, see the NICE guidelines on gastro-oesophageal reflux disease in children and young people and gastro-oesophageal reflux disease and dyspepsia in adults.
130. Recognise that around 3 in 5 children and young people with cerebral palsy have chronic constipation, and:
    - discuss this with children and young people and their parents or carers
    - carry out regular clinical assessments for constipation.
131. For guidance on identifying and managing constipation in under 18s, see the NICE guideline on constipation in children and young people.
132. Advise children and their parents or carers that epilepsy may be associated with cerebral palsy. Information that may be useful to discuss includes the following:
    - epilepsy occurs in around 1 in 3 children with cerebral palsy
    - it may occur in children and young people with any functional level or motor subtype but prevalence increases with increasing severity of motor impairment
    - it is reported in around 1 in 2 children with dyskinetic cerebral palsy.

133. Ensure that dyskinetic movements are not misinterpreted as epilepsy in children with cerebral palsy.

134. For guidance on identifying and managing epilepsy, see the NICE guideline on epilepsies: diagnosis and management.

135 For guidance on managing problems with movement and posture in children and young people with cerebral palsy, see the NICE guideline on spasticity in under 19s.

Social care needs

136. Recognise the importance of social care needs in facilitating participation and independent living for children and young people with cerebral palsy.

137. Assess the care needs of every child with cerebral palsy, and of their parents or carers, at diagnosis and reassess regularly if appropriate.

138. Provide information on the following areas of care at diagnosis of cerebral palsy and as appropriate thereafter:

- social care services
- financial support, welfare rights and charities
- support groups (including emotional support for the child or young person and their families and carers, including siblings).

139. Address and review the specific needs of the child or young person with cerebral palsy in relation to accessing their physical environment (for example, home, school, healthcare, workplace, community), in order to optimise their functional participation. Think about the following aspects:

- mobility
- equipment, particularly wheelchairs and hoists
- transport
- toileting and changing facilities.

140. Ensure effective communication and integrated team working between health and social care providers.

141. When assessing care needs, take into account the role of any social, cultural, spiritual or religious networks that support the child or young person with cerebral palsy and their family.

142. Take into account that English may not be the first language of children and young people with cerebral palsy or their parents or carers. Provide an interpreter if necessary. Follow the principles in the NICE guideline on patient experience in adult NHS services.

143. Explore with the child or young person and their parents or carers the value of respite services, such as carer support either at home or in another setting.

144. Ensure that individual, tailored care pathways (including pain management, rehabilitation and equipment) are in place after any major surgical intervention for children and young people with cerebral palsy (see also the NICE guideline on spasticity in under 19s).

Transition to adult services

145. Follow the NICE guideline on transition from children's to adults' services for young people using health or social care services.

146. Recognise that challenges for young people with cerebral palsy continue into adulthood, and ensure that their individual developmental, social and health needs, particularly those relating to learning and communication, are addressed when planning and delivering transition.

147. Recognise that for young people with cerebral palsy there may be more than one transition period in health and social care settings; for example, college, resident educational and adult home settings.

148. Develop clear pathways for transition that involve:

- the young person's GPs and
- named paediatricians and named clinicians in adults' services, both locally and regionally, who have an interest in the management of cerebral palsy.

149. Ensure that professionals involved in providing future care for young people with cerebral palsy have sufficient training in order to address all their health and social care needs.

150. As a minimum standard of care, ensure that the young person has access to adults' services both locally and regionally that include healthcare professionals with an understanding of managing cerebral palsy.

151. Ensure that all relevant information is communicated at each point of transition; for example, using a personal 'folder' containing relevant information as described in recommendation 36 (see also recommendations about support before transfer in the NICE guideline on transition from children's to adults' services).

152. Recognise that functional challenges (including those involving eating, drinking and swallowing, communication and mobility) and physical problems (including pain and discomfort) may change over time for people with cerebral palsy, and take this into account in transition planning.

153. Provide a named worker to facilitate timely and effective transition, and recognise the importance of continuity of care (see also recommendations about transition planning in the NICE guideline on transition from children's to adults' services) and about continuity of care and relationships in the NICE guideline on patient experience in adult NHS services).

1.6 Key research recommendations

- What is the association between different antibiotic regimes to treat genito-urinary and respiratory tract infections in pregnant women and subsequent rates of cerebral palsy in children?
- What is the clinical and cost effectiveness of early interventions for optimising protein, energy and micronutrient nutritional status in children with cerebral palsy?
- What is the clinical and cost effectiveness of interventions for managing communication difficulties in children with cerebral palsy?
- Does use of pain assessment tools by parents and carers improve the recognition and early management of pain in children and young people with cerebral palsy in a community setting?
- What is the prevalence of mental health problems in young people (up to the age of 25) with cerebral palsy?

1.7 Research recommendations

1. What is the association between different antibiotic regimes to treat genito-urinary and respiratory tract infections in pregnant women and subsequent rates of cerebral palsy in children?
2. Can epidemiological recording in the UK of the burden of care of cerebral palsy improve equity of access to care?
3. What is the clinical and cost effectiveness and safety profile of interventions to improve eating, drinking and swallowing in children and young people with cerebral palsy?
4. What is the clinical and cost effectiveness of early interventions for optimising protein, energy and micronutrient nutritional status in children with cerebral palsy?
5. What is the clinical and cost effectiveness of interventions for managing communication difficulties in children with cerebral palsy?
6. Does use of pain assessment tools by parents and carers improve the recognition and early management of pain in children and young people with cerebral palsy in a community setting?
7. What is the clinical and cost effectiveness of interventions (sleep hygiene, sedatives, melatonin) to improve sleep disturbance in children and young people with cerebral palsy?
8. What is the prevalence of mental health problems in young people (up to the age of 25) with cerebral palsy?
9. What is the clinical and cost effectiveness of interventions to manage specific sensory and perceptual difficulties?
10. What is the clinical and cost effectiveness of early interventions to improve cognitive learning/ability in children and young people with cerebral palsy?

2 Development of the guideline

2.1 What is a NICE clinical guideline?

National Institute for Health and Care Excellence (NICE) clinical guidelines are recommendations for the care of individuals in specific clinical conditions or circumstances within the NHS – from prevention and self-care through primary and secondary care to more specialised services. We base our clinical guidelines on the best available research evidence, with the aim of improving the quality of healthcare. We use predetermined and systematic methods to identify and evaluate the evidence relating to specific review questions.

NICE clinical guidelines can:

- provide recommendations for the treatment and care of people by healthcare professionals
- be used to develop standards to assess the clinical practice of individual healthcare professionals
- be used in the education and training of healthcare professionals
- help patients to make informed decisions
- improve communication between patients and healthcare professionals.

While guidelines assist the practice of healthcare professionals, they do not replace their knowledge and skills.

We produce our guidelines using the following steps:

- The guideline topic is referred to NICE from the Department of Health.
- Stakeholders register an interest in the guideline and are consulted throughout the development process.
- The scope is prepared by the National Guideline Alliance (NGA)
- The NGA establishes a guideline Committee.
- A draft guideline is produced after the Committee assesses the available evidence and makes recommendations.
- There is a consultation on the draft guideline.
- The final guideline is produced.

The NGA and NICE produce a number of versions of this guideline:

- The ‘full guideline’ contains all the recommendations, together with details of the methods used and the underpinning evidence.
- The ‘short guideline’ lists the recommendations, context and recommendations for research.
- ‘Information for the public’ is written using suitable language for people without specialist medical knowledge.
- NICE Pathways brings together all connected NICE guidance.

2.2 Remit

NICE received the remit for this guideline from the Department of Health. It commissioned the NGA to produce the guideline.

The remit for this guideline is to develop a clinical guideline on the diagnosis and management of cerebral palsy in children and young people.

2.3 Who developed this guideline?

A multidisciplinary Committee comprising healthcare professionals and researchers as well as lay members developed this guideline (see the list of Committee members and acknowledgements).

NICE funds the NGA and thus supported the development of this guideline. The Committee was convened by the NGA and chaired by Dr Charlie Fairhurst in accordance with guidance from NICE.

The Committee met every 6 weeks during the development of the guideline. At the start of the guideline development process all Committee members declared interests including consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry. At all subsequent Committee meetings, members declared arising conflicts of interest.

Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix C.

Staff from the NGA provided methodological support and guidance for the development process. The team working on the guideline included a guideline lead, a project manager, systematic reviewers, health economists and information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate and drafted the guideline in collaboration with the Committee.

2.4 What this guideline covers

2.4.1 Groups that will be covered

This guideline covers the following groups:

- Children and young people from birth up to their 25th birthday who have cerebral palsy.
- Subgroups to be considered:
  - recognised subgroups within the cerebral palsy population, depending on level of cognitive disability and functional disability (for example, Gross Motor Function Classification System levels I to V), and age ranges will be considered where appropriate.

2.4.2 Key clinical issues that will be covered

The following clinical issues are covered in this guideline:

Diagnosis and assessment

- Determining the key clinical and developmental manifestations of cerebral palsy at first presentation in order to help with early recognition.
- Identifying risk factors for cerebral palsy that may:
  - inform the need for enhanced surveillance
  - help in diagnosing the underlying cause of cerebral palsy
  - facilitate early intervention.
- Identifying the key information to be obtained from history and examination, including developmental screening to help in determining the underlying cause of cerebral palsy.

- Identifying 'red flags' that might suggest a neurodevelopmental disorder other than cerebral palsy, such as progressive neurological or neuromuscular disorders.
- Determining the potential value of MRI of the brain in cerebral palsy.
- The prognosis for children and young people with cerebral palsy in relation to:
  - ability to walk
  - ability to talk
  - life expectancy.
- Identifying common and important comorbidities associated with cerebral palsy and the subgroups most at risk of these comorbidities.
- Determining an effective approach to investigating difficulties with eating, drinking and swallowing in children and young people with cerebral palsy, including:
  - clinical observation
  - videofluoroscopic swallow studies and fibroscopic endoscopy.

Interventions

- Managing mental health problems in children and young people with cerebral palsy.
- Determining the effectiveness of interventions in tackling communication difficulties in children and young people with cerebral palsy.
- Determining the effective management of difficulties with eating, drinking and swallowing in children and young people with cerebral palsy.
- Determining the effective management of difficulties with saliva control (drooling) in children and young people with cerebral palsy.
- Nutritional management in children and young people with cerebral palsy.
- Assessing and managing pain, discomfort, distress and sleep disturbance in children and young people with cerebral palsy.
- Interventions to reduce the risk of reduced bone mineral density and low-impact fractures in children and young people with cerebral palsy.
- Managing difficulties associated with the processing of sensory and perceptual information in children and young people with cerebral palsy.
- Identifying social care needs that are specific to children and young people with cerebral palsy and their family members and carers.
- Communication, information and support needs that are specific to children and young people with cerebral palsy and their family members and carers.
- The role of the multidisciplinary team in the care of children and young people with cerebral palsy.
- Aspects of the transition from paediatric to adult health services that are specific to the needs of young people with cerebral palsy and their family members and carers.

Note that guideline recommendations will normally fall within licensed indications. Exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. This guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

For further details please refer to the scope in Appendix A and review questions in Appendix D.

2.5 What this guideline does not cover

2.5.1 Groups that will not be covered

This guideline does not cover:

- Adults 25 years and older.
- Children and young people with a progressive neurological or neuromuscular disorder.

2.5.2 Clinical issues that will not be covered

This guideline does not cover:

- Management of spasticity and co-existing motor disorders.
- Skin care, including management of pressure ulcers.
- Laboratory investigations for progressive neurological and neuromuscular disorders.
- Management of cognitive impairment and learning difficulties.
- Management of bladder dysfunction (urinary retention and incontinence) and bowel dysfunction (constipation and soiling).
- Management of gastro-oesophageal reflux disease.
- Management of respiratory complications such as pulmonary aspiration.
- Management of visual and hearing impairment.
- Management of epilepsy.

2.6 Relationships between the guideline and other NICE guidance

2.6.1 Related NICE guidance

2.6.1.1 Published

- Transition from children's to adult services (2016) NICE guideline NG43
- Challenging behaviour and learning disabilities (2015) NICE guideline NG11
- Gastro-oesophageal reflux disease in children and young people (2015) NICE guideline NG1
- Pressure ulcers (2014) NICE guideline CG179
- Intrapartum care (2014) NICE guideline CG190
- Gastro-oesophageal reflux disease and dyspepsia in adults (2014) NICE guideline CG184
- Obesity (2014) NICE guideline CG189
- Vitamin D: increasing supplement use in at-risk groups (2014) NICE public health guidance PH56
- Autism in under 19s (2013) NICE guideline CG170
- Antisocial behaviour and conduct disorders in children and young people (2013) NICE guideline CG158
- Headaches in over 12s (2012) NICE guideline CG150
- Urinary incontinence in neurological disease (2012) NICE guideline CG148
- Osteoporosis in adults (2012) NICE guideline CG146
- Spasticity in under 19s (2012) NICE guideline CG145
- Autism in adults (2012) NICE guideline CG142

- Patient experience in adult NHS services (2012) Nice guideline GC 138
- Epilepsies (2012) NICE guideline CG137
- Autism in under 19s (2011) NICE guideline CG128
- Common mental health problems (2011) NICE guideline CG123
- Generalised anxiety disorder and panic disorder in adults (2011) NICE guideline CG113
- Selective dorsal rhizotomy for spasticity in cerebral palsy (2010) NICE interventional procedure guidance 373
- Constipation in children and young people (2009) NICE guideline CG99
- Depression in adults (2009) NICE guideline CG90
- Low back pain in adults (2009) NICE guideline CG88
- Attention deficit hyperactivity disorder (2008) Nice guideline CG72
- Urinary tract infection in under 16s (2007) NICE guideline CG54
- Obesity prevention (2006) NICE guideline CG43
- Postnatal care up to 8 weeks after birth (2006) NICE guideline CG37
- Nutrition support for adults (2006) NICE guideline CG32
- Depression in children and young people (2005) NICE guideline CG28

2.6.1.27 In development

- Mental health problems in people with learning disabilities. NICE guideline. Publication due September 2016
- Developmental follow-up of pre-term babies. NICE guideline. Publication due August 2017.
- Faltering growth. NICE guideline. Publication due October 2017.

3 Guideline development methodology

This section sets out in detail the methods used to review the evidence and to generate the recommendations that are presented in subsequent sections. This guidance was developed in accordance with the methods outlined in the NICE guidelines manual 2012 for the stages up to guideline development and then in accordance with the updated NICE guidelines manual 2014 from the consultation stage.

Table 3: Summary of manuals used during the guideline development

Phase of development	Manual
Scoping phase	2012 NICE Manual
Development phase	2012 NICE Manual
Consultation phase	2014 NICE Manual
Validation phase	2014 NICE Manual

3.1 Developing the review questions and protocols

Review questions were developed according to the type of question:

- intervention reviews – in a PICO framework (patient, intervention, comparison and outcome)
- reviews of diagnostic test accuracy – in a framework of population, index tests, reference standard and target condition
- qualitative reviews – using population, area of interest and outcomes.

These frameworks guided the literature searching process, critical appraisal and synthesis of evidence and facilitated the development of recommendations by the Committee. The review questions were drafted by the NGA technical team and refined and validated by the Committee. The questions were based on the key clinical areas identified in the scope (Appendix A).

A total of 27 review questions were identified (see Table 4).

Full literature searches, critical appraisals and evidence reviews were completed for all the specified review questions.

Table 4: Description of review questions

Section	Type of review	Review questions	Outcomes
17	Intervention	In children and young people with cerebral palsy, what interventions are effective in optimising saliva control?	• Reduction of frequency and severity of drooling (including specific rating scales and volume) • Health-related quality of life. • Psychological wellbeing (for example, depression or anxiety). • Adverse effects: ○ Pharmacological treatment: visual disturbance and constipation.

Section	Type of review	Review questions	Outcomes
			○ Botulinum: swallowing problems and breathing problems. ○ Surgery: ranulae and chest infection.
14	Intervention	In children and young people with cerebral palsy, what interventions are effective at optimising nutritional status?	• Anthropometric measures: • Weight • Growth percentile • Adverse events: o complications of feeding tubes o complications of antiemetics o vomiting frequency • Dietary intake - food offered and consumed. • Health related quality of life: using Child Health Questionnaire
6	Clinical prediction	What are the key clinical and developmental manifestations that are predictive of cerebral palsy at first presentation? What are the best tools to identify clinical and developmental manifestations of cerebral palsy at first presentation?	Question 1 • Risk of cerebral palsy (RRs, ORs, aRRs, aORs) Question 2 • Sensitivity: the proportion of true positives of all cases diagnosed with CP in the population • Specificity: the proportion of true negatives of all cases not-diagnosed with CP in the population. • Positive Predictive Value (PPV): the proportion of patients with positive test results who are correctly diagnosed. • Negative Predictive Value (NPV): the proportion of patients with negative test results who are correctly diagnosed. • Area under the Curve (AUC): are constructed by plotting the true positive rate as a function of the false positive rate for each threshold. • Likelihood ratios • Prevalence of true positives
7	Clinical prediction	What clinical manifestations should be recognised as 'red flags' that suggest a progressive disorder rather than cerebral palsy?	Differential diagnosis of: • Neurometabolic (leukodystrophy;

Section	Type of review	Review questions	Outcomes
			mitochondrial disorder) • Neuromuscular (SMA, muscular dystrophy) • Tumours (benign and malignant) • Genetic disorders (hereditary spastic paraparesis, primary dystonia, Rett syndrome) • Spinal cord disorders
15	Intervention	In children and young people with cerebral palsy, what interventions are effective in improving speech intelligibility?	• Quality of life • Speech intelligibility (for example percentage intelligibility) • Participation (including communication) • Self-confidence • Family stress and coping • Satisfaction of patient and family with treatment
16	Intervention	In children and young people with cerebral palsy, which communication systems (alternative or augmentative) are effective in improving communication?	• Communication production • Change in communication production • Change in sign/symbol production • Impact on family: stress, coping • Parental satisfaction • Participation • Quality of life
4	Clinical prediction	What are the most important risk factors for developing cerebral palsy with a view to informing more frequent assessment and early recognition?	• Prevalence/proportion of risk factors
10	Prognostic	In infants, children and young people with cerebral palsy, what are the clinical and developmental prognostic indicators in relation to: • the ability to walk • the ability to talk • life expectancy?	• Survival • Ability to walk (including independent community walking/functional walking) • Ability to talk
27	Prevalence	In infants, children and young people with cerebral palsy what is the prevalence of important comorbidities with a view to informing early identification?	• Percentage/proportion of comorbidities
13	Interventions	In children and young people with cerebral palsy, what interventions are effective in managing difficulties with eating,	• physiological function of the oropharyngeal mechanism (Determined by clinical evaluation, VF or fibreoptic

Section	Type of review	Review questions	Outcomes
		drinking and swallowing?	endoscopic evaluation of swallowing) • change in diet consistency a child is able to consume (developmentally appropriate oral diet; texture/consistency of foods and fluids must be modified; supplementary feeding required) • Respiratory health - presence of a history of confirmed aspiration pneumonia or recurrent chest infection (with or without pneumonia with suspected prandial aspiration aetiology) • nutritional status/changes in growth (weight and height percentiles) • child's level of participation in mealtime routine/length of meal times(time taken to feed). • psychological wellbeing of parents/carers • acceptability of programme • survival
12	Diagnostic	In infants, children and young people with cerebral palsy, what is the value of videofluoroscopy or fibreoptic endoscopic evaluation of swallowing in addition to clinical assessment in assessing difficulties with eating, drinking and swallowing?	The diagnostic accuracy in identifying the oropharyngeal mechanisms underlying difficulties with eating, drinking and swallowing, including: -[oral] motor difficulties (tongue movement, chewing, transfer to posterior pharynx, initiation of swallow etc.) • Vocal cord function -aspiration or risk of aspiration • Post-swallow pooling/residue - Nasopharyngeal reflux/regurgitation - oesophageal obstruction/dysmotility • Sensitivity • Specificity • Positive Likelihood Ratios • Negative Likelihood Ratios
18	Clinical prediction	In children and young people with cerebral palsy, what are the risk factors for reduced bone mineral density and low-impact fractures?	• Risk of low volume bone mineral density- adjusted for the key confounders • Risk of low impact fractures-

Section	Type of review	Review questions	Outcomes
			adjusted for the key confounders (As adjusted HR/ORs)
19	Intervention	In children and young people with cerebral palsy, what interventions are effective in preventing reduced bone mineral density and low-impact fractures?	• Alteration on DEXA score (levels of bone mineral density) • Change in frequency of minimally traumatic fractures • Patients satisfaction/acceptability • QoL • Pain • Adverse effects (drugs) for example: • Bone fragility • Gastric/oesophageal irritation/ulceration
8	Clinical prediction	Does MRI in addition to routine clinical assessment (including neonatal ultrasound) help determine the aetiology in children and young people with suspected or confirmed cerebral palsy and if so in which subgroups is it most important?	Proportion of participants with each neuroimaging pattern against aetiology: • Considered aetiology changed after MRI performed • Recognition of the following patterns of abnormality for aetiology: • Periventricular leukomalacia/ white matter injury • Deep grey matter / basal ganglia lesions (typical of Hypoxic ischaemic injury) • Diffuse encephalopathy • Brain Malformations (for example mal-development of brain folding [gyri and sulci] and non-genetic conditions such as congenital infections) • Focal ischaemic infarct or haemorrhagic lesions (Confirmation/ruling out of genetic or progressive movement disorders [as per study]
9	Clinical prediction	Does MRI undertaken at the following ages: • before 1 month (corrected for gestation) • 1 month to 2 years	Binary outcomes: • Proportion of CYP with epilepsy • Proportion of CYP with feeding problems

Section	Type of review	Review questions	Outcomes
		• 2-4 years help to predict the prognosis of children and young people with cerebral palsy?	• Severity of functional disability using: ○ Gross Motor System Classification ○ The Manual Ability Classification System • communication problems • cognitive problems • changes in health-related quality of life (for example Lifestyle Assessment Questionnaire - Cerebral Palsy [LAQ-CP]) Time to event outcomes: • mortality
21	Validity and reliability	What is the validity and reliability of published tools to identify and aid understanding of discomfort, pain and/or distress in children and young people with cerebral palsy?	• reliability • validity • sensitivity • specificity
20	Prevalence	In children and young people with cerebral palsy, what are the common causes of pain, discomfort, distress and sleep disturbance?	• prevalence of pain, discomfort, distress and sleep disturbance
22	Intervention	In children and young people with cerebral palsy, which interventions are effective in managing discomfort and/or pain and distress with no identifiable cause?	• pain control • distress • physical function (Multidimensional Pain Inventory Interference Scale / Brief Pain Inventory interference items) • emotional function (for example, depression or anxiety using Beck's depression inventory) • adverse events, including withdrawal • health-related quality of life (for example, Peds-QL, Pediatric QOL-CP module or EQ-5D) • Parent/carer outcomes (for example)
23	Intervention	In children and young people with cerebral palsy, which interventions are effective in managing sleep disturbance arising from no identifiable cause?	• sleep quality, measured for example, by polysomnography (gold standard) or by other methods such as wrist actigraphy, sleep diaries, Sleep Habits Questionnaire

Section	Type of review	Review questions	Outcomes
			• adverse events, including withdrawal • day time emotional wellbeing/lability • health-related quality of life (for example, Peds-QL, Pediatric QOL-CP module or EQ-5D)
5	Prevalence	What are the most common causes of cerebral palsy in resource-rich countries with a view to informing relevant investigation and change in management?	• Proportion/percentage of causes in cerebral palsy
28	Qualitative	What are the specific social care needs of children and young people with cerebral palsy and their family members and carers?	Thematic analysis
24	Diagnostic	In children and young people with cerebral palsy, what assessments are effective in identifying the presence of mental health problems?	• Sensitivity • Specificity • Positive predictive value • Negative predictive value • Area under the curve • Reliability/validity
25	Intervention	What is the clinical and cost effectiveness of interventions to manage mental health problems in children and young people with moderate to severe cerebral palsy (GMFCS III-V)	• Health related quality of life of children and young people with CP as well as parents/carers (for example, KIDSCREEN-10, PedsQL, CHQ, European generic HRQOL, CPQOL-child, CPQOL-teen) • Social participation • Emotional health (for example, SDQ) • Improvement in behaviour (for example, Behaviour Problems Inventory/index) Child Behaviour Checklist • Psychological wellbeing (for example, Beck Youth Inventory) • Parent/carer impression of change (for example, Kiddie-SAD PL (at school starting age)) • Adverse effects (side effects of medications - sedation, drowsiness, change in movement, worsening of seizure) • Suicide risk • Sleep quality

Section	Type of review	Review questions	Outcomes
29	Qualitative	What are the specific elements of the process of transition from paediatric to adult services that are important for young people with cerebral palsy and their family members and carers?	Thematic analysis
11	Qualitative	What information and information types (written or verbal) are perceived as helpful and supportive by children and young people with cerebral palsy and their family members and carers?	Thematic analysis
26	Intervention	In children and young people with cerebral palsy, what interventions are effective for managing problems associated with difficulties in processing of sensory and perceptual information?	• Improvement in processing sensory and perceptual information (for example, improvement in learning, cognitive function, emotional well-being, physical function, socialising and making friends) • Health related quality of life (Child health questionnaire, CPQOL) • Improvement in psychological wellbeing (anxiety and depression) (for example, HADS, Becks Depression Inventory) • Wellbeing of parents/carers (for example, Becks Depression inventory) • Goal attainment scales

3.2 Searching for evidence

3.2.1 Clinical literature search

Systematic literature searches were undertaken to identify all published clinical evidence relevant to the review questions.

Databases were searched using relevant medical subject headings, free-text terms and study type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to retrieve only articles published in English. All searches were conducted in MEDLINE, Embase and The Cochrane Library as a minimum and for certain topics additional databases were used including CINAHL, AMED, PsycINFO, PEDro, OTSeeker and SpeechBITE. All searches were updated on 11 May 2016. Any studies added to the databases after this date (even those published prior to this date) were not included unless specifically stated in the text.

Search strategies were quality assured by cross-checking reference lists of highly relevant papers, analysing search strategies in other systematic reviews and asking the Committee

members to highlight any additional studies. The questions, the study type filters applied, the databases searched and the years covered can be found in Appendix E.

The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were assessed against the inclusion criteria.

During the scoping stage, searches were conducted for guidelines, health technology assessments, systematic reviews, economic evaluations and reports on biomedical databases and websites of organisations relevant to the topic. Searching for grey literature or unpublished literature was not undertaken. Searches for electronic, ahead-of-print publications were not routinely undertaken unless indicated by the Committee. All references suggested by stakeholders at the scoping consultation were initially considered.

3.2.2 Health economic literature search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting a broad search relating to cerebral palsy in the NHS Economic Evaluation Database (NHS EED), the Health Economic Evaluations Database (HEED) and Health Technology Assessment (HTA) databases with no date restrictions. Additionally, the search was run in Medline and Embase using a specific economic filter to ensure recent publications that had not yet been indexed by the economic databases were identified. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English.

The search strategies for the health economic literature search are included in Appendix E. All searches were updated in 11 May 2016. No papers published after this date were considered.

3.3 Reviewing and synthesising the evidence

The evidence was reviewed following these steps:

- Potentially relevant studies were identified for each review question from the relevant search results by reviewing titles and abstracts. Full papers were then obtained.
- Full papers were reviewed against pre-specified inclusion and exclusion criteria to identify studies that addressed the review question in the appropriate population and reported on outcomes of interest (review protocols are included in Appendix D).
- Relevant studies were critically appraised using the appropriate checklist as specified in the NICE guidelines manual 2012. For diagnostic questions the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) checklist was followed. For prevalence questions the quality of the evidence was assessed by using the tool developed and published by Munn et al. 2014. For validity and reliability review questions, the quality of each study was assessed using the checklist reported by Jerosch-Herold et al., 2005.
- Key information was extracted on the study's methods, PICO factors and results. These were presented in summary tables in each section and evidence tables (in Appendix J).
- Summaries of evidence were generated by outcome and were presented in committee meetings:
  - randomised studies – data were meta-analysed where appropriate and reported in the Grading of Recommendations Assessment, Development and Evaluation (GRADE) profiles (for interventional reviews)
  - diagnostic/predictive accuracy studies – presented as measures of diagnostic/predictive test accuracy (sensitivity, specificity, positive and negative predictive value); a meta-analysis was only conducted when the included studies were not heterogeneous

- qualitative studies – the themes of the studies were organised in a modified version of a GRADE profile, where possible, along with quality assessment otherwise presented in a narrative form.

- Of all data extracted, 50% was quality assured by a second reviewer and 50% of the GRADE quality assessment was quality assured by a second reviewer to minimise any potential risk of reviewer bias or error.

3.3.17 Methods of combining clinical studies

3.3.1.18 Data synthesis for intervention reviews

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software or STATA. Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for the binary outcomes.

For the continuous outcomes, measures of central tendency (mean) and variation (standard deviation) were required for meta-analysis. A generic inverse variance option in RevMan5 was used if any studies reported solely the summary statistics and 95% confidence interval (95% CI) or standard error; this included any hazard ratios reported. However, in cases where standard deviations were not reported per intervention group, the standard error (SE) for the mean difference was calculated from other reported statistics (probability [p] values or 95% CIs) if available: meta-analysis was then undertaken for the mean difference and SE using the generic inverse variance method in RevMan5. When the only evidence was based on studies that summarised results by presenting medians (and interquartile ranges), or only p values were given, this information was assessed in terms of the study's sample size and was included in the GRADE tables as a narrative summary. Consequently, aspects of quality assessment such as imprecision of effect could not be assessed for this evidence and this has been recorded in the footnotes of the GRADE tables.

In instances where multiple scales were reported for a single outcome, mean differences were standardised (divided by their SD) before pooling, giving meta-analysed results that were reported as standardised mean differences (SMD), with a standard deviation of 1.

Where reported, time-to-event data were presented as a hazard ratio or results from a Cox hazard proportion model were given as a result from a multivariate analysis.

Stratified analyses were predefined for some review questions at the protocol stage when the Committee identified these strata to be different in terms of clinical characteristics and the interventions were expected to have a different effect, for example on the management of short-term symptoms. We stratified our analysis for women with a uterus, women without a uterus and women with a history of or at risk of breast cancer. Statistical heterogeneity was assessed by visually examining the forest plots, and by considering the chi-squared test for significance at $p<0.1$ or an I-squared inconsistency statistic (with an I-squared value of 50–74.99% indicating serious inconsistency and I-squared value of over 75% indicating very serious inconsistency). If the heterogeneity still remained, a random effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect. For meta-analyses with serious heterogeneity, but no pre-defined strata for stratified analysis, basic sensitivity analyses on features like age, gender, study types was carried out.

3.3.1.24 Data synthesis for diagnostic test accuracy review

For diagnostic test accuracy studies, the following outcomes were reported:

- sensitivity

- specificity
- positive and negative likelihood ratio
- area under the curve (AUC).

3.3.1.3 Data synthesis for qualitative review

For the qualitative review in the guideline, results were reported narratively either by individual study or by summarising the range of values as reported across similar studies, following basic thematic analysis. A summary evidence table was used when data allowed for this.

3.3.2 Type of studies

Systematic reviews (SRs) with or without meta-analyses were considered the highest quality evidence to be selected for inclusion.

Randomised trials and observational studies were included in the evidence reviews as appropriate.

Literature reviews, posters, letters, editorials, comment articles, conference abstracts, unpublished studies and studies not in English were excluded.

For intervention reviews in this guideline, randomised controlled trials (RCTs) were included because they are considered the most robust study design for unbiased estimation of intervention effects. No restrictions on RCT sample size were applied.

Based on their judgement, if the Committee believed RCT data were not appropriate or there was limited evidence from RCTs, they agreed to include prospective observational studies with N>30 participants for evidence reviews looking at the effectiveness of interventions.

For clinical prediction, diagnostic and prognostic reviews, the Committee prioritised observational studies (prospective studies were preferred) of N>50 participants. This is based on the sample size suggested by Green (1991) $N \geq 50 + 8k$ (k=no. of variables/predictors).

For prevalence reviews, the Committee prioritised cross-sectional studies (national registries were preferred) of N> 250 participants. Based on the Committee's judgement, they agreed that a larger sample size was required for a prevalence review.

The sample size thresholds were agreed with the Committee as pragmatic cut-offs to identify best available evidence. These were agreed during the development of the protocols with the Committee and are based on their knowledge of the published evidence on the topic.

Please refer to Appendix D for full details on the study design of studies selected for each review question.

3.3.3 Appraising the quality of evidence by outcomes

The evidence for outcomes from the included RCTs and, where appropriate, observational studies was evaluated and presented using an adaptation of the GRADE toolbox developed by the international GRADE working group. The software developed by the GRADE working group (GRADEpro) was used to assess the quality of each outcome, taking into account individual study quality factors and the meta-analysis results. The clinical/economic evidence profile tables include details of the quality assessment and pooled outcome data, where appropriate, an absolute measure of intervention effect and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate summary measures of effect and measures of dispersion (such as mean and standard deviation or median and range) for continuous outcomes and frequency of events (n/N: the

sum across studies of the number of patients with events divided by sum of the number of completers) for binary outcomes. Reporting or publication bias was only taken into consideration in the quality assessment and included in the clinical evidence profile tables if it was apparent.

The selection of outcomes for each review question was decided when each review protocol was discussed with the Committee. However, given the nature of most of the review questions included in this guideline (driven by short- or long-term outcomes), the categorisation of outcomes as critical and important did not follow the standard GRADE approach. The outcomes selected for a review question were critical for decision-making in a specific context.

The evidence for each outcome in interventional reviews was examined separately for the quality elements listed and defined in Table 5. Each element was graded using the quality levels listed in Table 6.

The main criteria considered in the rating of these elements are discussed below. Footnotes were used to describe reasons for grading a quality element as having serious or very serious limitations. The ratings for each component were summed to obtain an overall assessment for each outcome (Table 7).

The GRADE toolbox is designed only for RCTs and observational studies but we adapted the quality assessment elements and outcome presentation for diagnostic accuracy and qualitative studies, subject to data availability. For example, for diagnostic accuracy studies, the GRADE tables were modified to include the most appropriate measures of diagnostic accuracy (sensitivity, specificity, positive and negative likelihood ratio) whereas qualitative studies were presented in summary evidence tables around themes identified or direct participants' quotations. Quality of the evidence in the qualitative reviews was assessed per study level.

Table 5: Description of quality elements in GRADE for intervention studies

Quality element	Description
Risk of bias (study limitations)	Limitations in the study design and implementation may bias the estimates of the treatment effect. High risk of bias for the majority of the evidence decreases confidence in the estimate of the effect.
Inconsistency	Inconsistency refers to an unexplained heterogeneity of results.
Indirectness	Indirectness refers to differences in study population, intervention, comparator and outcomes between the available evidence and the review question, or recommendation made, such that the effect estimate is changed.
Imprecision	Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of the effect. Imprecision results if the confidence interval includes the clinically important threshold.
Publication bias	Publication bias is a systematic underestimate or an overestimate of the underlying beneficial or harmful effect due to the selective publication of studies.

Table 6: Levels of quality elements in GRADE level

Levels of quality elements in GRADE level	Description
None	There are no serious issues with the evidence.
Serious	The issues are serious enough to downgrade the outcome evidence by 1 level.
Very serious	The issues are serious enough to downgrade the outcome evidence by 2 levels.

Table 7: Overall quality of outcome evidence in GRADE Level

Overall quality of outcome evidence in GRADE level	Description
High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

3.3.3.12 Grading the quality of clinical evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using the GRADE approach:

- A quality rating was assigned based on the study design. RCTs start as high, observational studies as low and uncontrolled case series as low or very low.
- The rating was then downgraded for the specified criteria: risk of bias (study limitations); inconsistency; indirectness; imprecision; and publication bias. These criteria are detailed below. Evidence from observational studies (which had not previously been downgraded) was upgraded if there was a large magnitude of effect or a dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have 'serious' or 'very serious' risk of bias was rated down by 1 or 2 points respectively.
- The downgraded/upgraded ratings were then summed and the overall quality rating was revised. For example, all RCTs started as high and the overall quality became moderate, low or very low if 1, 2 or 3 points were deducted respectively.
- The reasons or criteria used for downgrading were specified in the footnotes.

The details of the criteria used for each of the main quality elements are discussed further in Sections 3.3.3.2 to 3.3.3.6.

3.3.3.20 Risk of bias

Bias can be defined as anything that causes a consistent deviation from the truth. Bias can be perceived as a systematic error; for example, if a study was carried out several times and there was a consistently wrong answer, the results would be inaccurate.

The risk of bias for a given study and outcome is associated with the risk of over- or underestimation of the true effect.

The risks of bias are listed in Table 8.

A study with a poor methodological design does not automatically imply high risk of bias; the bias is considered individually for each outcome and it is assessed whether this poor design will impact on the estimation of the intervention effect.

Table 8: Risk of bias in randomised controlled trials

Risk of bias	Explanation
Allocation concealment	Those enrolling patients are aware of the group to which the next enrolled patient will be allocated (this is a major problem in 'pseudo' or 'quasi' randomised trials with allocation by, for example, day of week, birth date, chart number).

Risk of bias	Explanation
Lack of blinding	Patient, caregivers, those recording outcomes, those adjudicating outcomes or data analysts are aware of the arm to which patients are allocated.
Incomplete accounting of patients and outcome events	Missing data not accounted for and failure of the trialists to adhere to the intention to treat principle when indicated.
Selective outcome reporting	Reporting of some outcomes and not others on the basis of the results.
Other risks of bias	For example: • stopping early for benefit observed in randomised trials, in particular in the absence of adequate stopping rules • use of unvalidated patient-reported outcomes • recruitment bias in cluster randomised trials.

3.3.3.3 Diagnostic studies

For diagnostic accuracy studies, the Quality Assessment of Diagnostic Accuracy Studies version 2 (QUADAS-2) checklist was used. Risk of bias and applicability in primary diagnostic accuracy studies in QUADAS-2 consists of 4 domains (see Figure 3):

- patient selection
- index test
- reference standard
- flow and timing.

Figure 3: Summary of QUADAS-2 with a reference to quality domains

DOMAIN	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING
Description	Describe methods of patient selection: Describe included patients (prior testing, presentation, intended use of index test and setting):	Describe the index test and how it was conducted and interpreted:	Describe the reference standard and how it was conducted and interpreted:	Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2x2 table (refer to flow diagram): Describe the time interval and any interventions between index test(s) and reference standard:
Signalling questions (yes/no/unclear)	Was a consecutive or random sample of patients enrolled?	Were the index test results interpreted without knowledge of the results of the reference standard?	Is the reference standard likely to correctly classify the target condition?	Was there an appropriate interval between index test(s) and reference standard?
	Was a case-control design avoided?	If a threshold was used, was it pre-specified?	Were the reference standard results interpreted without knowledge of the results of the index test?	Did all patients receive a reference standard?
	Did the study avoid inappropriate exclusions?			Did all patients receive the same reference standard?
				Were all patients included in the analysis?
Risk of bias: High/low/unclear	Could the selection of patients have introduced bias?	Could the conduct or interpretation of the index test have introduced bias?	Could the reference standard, its conduct, or its interpretation have introduced bias?	Could the patient flow have introduced bias?
Concerns regarding applicability: High/low/unclear	Are there concerns that the included patients do not match the review question?	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	

3.3.3.4 Inconsistency

Inconsistency refers to an unexplained heterogeneity of results. When estimates of the treatment effect across studies differ widely (that is, when there is heterogeneity or variability in results), this suggests true differences in underlying treatment effect.

Heterogeneity in meta-analyses was examined and sensitivity and subgroup analyses performed as pre-specified in the protocols (Appendix D).

When heterogeneity existed (chi-squared p less than 0.1, I-squared inconsistency statistic of between 50% and 74.99% or I-squared greater than 50% or evidence from examining forest plots), but no plausible explanation was found (for example duration of intervention or different follow-up periods) the quality of evidence was downgraded by 1 or 2 levels, depending on the extent of uncertainty to the results contributed by the inconsistency in the results. In addition to the I-squared and chi-squared values, the decision for downgrading was also dependent on factors such as whether the intervention is associated with benefit in all other outcomes or whether the uncertainty about the magnitude of benefit (or harm) of the outcome showing heterogeneity would influence the overall judgment about net benefit or harm (across all outcomes).

When outcomes are derived from a single trial, inconsistency is not an issue for downgrading the quality of evidence. However, ‘no inconsistency’ is nevertheless used to describe this quality assessment in the GRADE tables.

3.3.3.5 Indirectness

Directness refers to the extent to which the populations, intervention, comparisons and outcome measures are similar to those defined in the inclusion criteria for the reviews. Indirectness is important when these differences are expected to contribute to a difference in effect size or may affect the balance of harms and benefits considered for an intervention.

3.3.3.6 Imprecision

Imprecision in guideline development concerns whether the uncertainty (confidence interval) around the effect estimate means that it is not clear whether there is a clinically important difference between interventions or not. Therefore, imprecision differs from the other aspects of evidence quality in that it is not really concerned with whether the point estimate is accurate or correct (has internal or external validity) but instead is concerned with the uncertainty about what the point estimate is. This uncertainty is reflected in the width of the confidence interval.

The 95% confidence interval (95% CI) is defined as the range of values that contain the population value with 95% probability. The larger the trial, the smaller the 95% CI and the more certain the effect estimate.

Imprecision in the evidence reviews was assessed by considering whether the width of the 95% CI of the effect estimate was relevant to decision-making, considering each outcome in isolation.

When the confidence interval of the effect estimate is wholly contained in 1 of the 3 zones (clinically important benefit, clinically important harm, no clinically important benefit or harm) we are not uncertain about the size and direction of effect (whether there is a clinically important benefit, or the effect is not clinically important, or there is a clinically important harm), so there is no imprecision.

When a wide confidence interval lies partly in each of 2 zones, it is uncertain in which zone the true value of effect estimate lies and therefore there is uncertainty over which decision to make (based on this outcome alone). The confidence interval is consistent with 2 decisions

and so this is considered to be imprecise in the GRADE analysis and the evidence is downgraded by 1 level ('serious imprecision').

If the confidence interval of the effect estimate crosses into 3 zones, this is considered to be very imprecise evidence because the confidence interval is consistent with 3 clinical decisions and there is a considerable lack of confidence in the results. The evidence is therefore downgraded by 2 levels in the GRADE analysis ('very serious imprecision').

Implicitly, assessing whether the confidence interval is in, or partially in, a clinically important zone requires the Committee to estimate a minimally important difference (MID) or to say whether they would make different decisions for the 2 confidence limits.

Originally, the Committee was asked about MIDs in the literature or well-established MIDs in the clinical community (for example international consensus documents) for the relevant outcomes of interest.

For the following review, the Committee agreed and used established MID:

Table 9: MIDs agreed by the Committee

Review question	Thresholds agreed
In children and young people with cerebral palsy, what interventions are effective in optimising saliva control?	• Thomas-Stonell and Greenberg scale: 2-points reduction (1 point for each section of the scale) • Teacher Drooling scale: 3-points reduction difference • Drooling Impact score: 10-points reduction

<Insert Note here>

Due to the lack of well-established and widely accepted MIDs in the literature around cerebral palsy, the Committee agreed to use the GRADE default MIDs.

The Committee therefore considered it clinically acceptable to use the GRADE default MID to assess imprecision: a 25% relative risk reduction or relative risk increase was used, which corresponds to clinically important thresholds for a risk ratio of 0.75 and 1.25 respectively. This default MID was used for all the dichotomous outcomes in the interventions evidence reviews and for outcomes reported as ratios of means (RoM). For continuous outcomes, a MID was calculated by adding or subtracting 0.5 times standard deviations. For outcomes that were meta-analysed using the standardised mean difference approach (SMD), the MID was calculated by adding or subtracting 0.5 (given SD equals 1).

For the diagnostic questions, we assessed imprecision on the outcome of positive likelihood ratio because this was prioritised by the Committee as the most important diagnostic outcome for their decision-making. The assessment of imprecision for the results on positive likelihood ratio followed the same concept as used in interventional reviews. For example, if the 95% CI of the positive likelihood ratio crossed 2 zones (from moderately useful [5 to 10] to very useful [more than 10]) then imprecision was downgraded by 1, or if crossed 3 zones (not useful [less than 5], moderately useful [5 to 10] and very useful [more than 10] then imprecision was downgraded by 2. These values have been used in previous guidelines developed in the NGA and the Committee agreed to using them. The specific use of a diagnostic test and which measures were to be of most interest (e.g. for rule in / rule out) were discussed with the Committee and recommendations were made accordingly.

3.3.3.7 Quality assessment of qualitative studies

Quality of qualitative studies (at study level) was assessed following the NICE checklists. The main quality assessment domains are organised across the definition of population included,

the appropriateness of methods used and the completeness of data analysis and the overall relevance of the study participants to the population of interest for the guideline.

Individual studies were assessed for methodological limitations using an adapted Critical Appraisal Skills Programme (CASP, 2006) checklist for qualitative studies, where items in the original CASP checklist were adapted and fitted into 5 main quality appraisal areas according to the following criteria:

- aim (description of aims and appropriateness of the study design)
- sample (clear description, role of the researcher, data saturation, critical review of the researchers' influence on the data collection)
- rigour of data selection (method of selection, independence of participants from the researchers, appropriateness of participants)
- data collection analysis (clear description, how are categories or themes derived, sufficiency of presented findings, saturation in terms of analysis, the role of the researcher in the analysis, validation)
- results / findings (clearly described, applicable and comprehensible, theory production)

An adapted GRADE approach was then used to then assess the evidence by themes across different included studies. Similar to GRADE in effectiveness reviews this includes 4 domains of assessment and an overall rating:

- limitations across studies for a particular finding or theme (using the criteria described above)
- coherence of findings (equivalent to heterogeneity but related to unexplained differences or incoherence of descriptions)
- applicability of evidence (equivalent to directness, i.e. how much the finding applies to our review protocol)
- saturation or sufficiency (this related particularly to interview data and refers to whether all possible themes have been extracted or explored)

3.3.4 Use of absolute effect in decision-making

The Committee assessed the evidence by outcome in order to determine if there was, or potentially was, a clinically important benefit, a clinically important harm or no clinically important difference between interventions. To facilitate this, binary outcomes were converted into absolute risk differences (ARDs) using GRADEpro software: the median control group risk across studies was used to calculate the ARD and its 95% CI from the pooled risk ratio.

3.3.5 Evidence statements

Evidence statements are summary statements that are presented after the GRADE profiles, summarising the key features of the clinical evidence presented. The wording of the evidence statements reflects the certainty or uncertainty in the estimate of effect. The evidence statements are presented by comparison (for interventional reviews) or by description of outcome where appropriate and encompass the following key features of the evidence:

- the number of studies and the number of participants for a particular outcome
- a brief description of the participants
- an indication of the direction of effect (if 1 treatment is beneficial or harmful compared with the other, or whether there is no difference between the 2 tested treatments)
- a description of the overall quality of evidence (GRADE overall quality).

3.3.6 Evidence of cost effectiveness

The aims of the health economic input to the guideline were to inform the Committee of potential economic issues related to the diagnosis and management of cerebral palsy in children and young people to ensure that recommendations represented a cost-effective use of healthcare resources. Health economic evaluations aim to integrate data on benefits (ideally in terms of quality adjusted life years [QALYs]), harms and costs of different care options.

3.3.6.1 Literature review

The search strategy for existing economic evaluations combined terms capturing the target condition (cerebral palsy) and, for searches undertaken in MEDLINE, EMBASE and CCTR, terms to capture economic evaluations. No restrictions on language or setting were applied to any of the searches, but letters were excluded. Conference abstracts were considered for inclusion from January 2014, as high-quality studies reported in abstract form before this date were expected to have been published in a peer-reviewed journal. Full details of the search strategies are presented in Appendix E.

The Health Economist assessed the titles and abstracts of papers identified through the searches for inclusion using pre-defined eligibility criteria defined in Table 10.

Table 10: Inclusion and exclusion criteria for the systematic reviews of economic evaluations

Inclusion criteria
intervention or comparators according to the scope
study population according to the scope
full economic evaluations (cost-utility, cost-effectiveness, cost-benefit or cost-consequence analyses) that assess both costs and outcomes associated with the interventions of interest
Exclusion criteria
abstracts with insufficient methodological details
conference papers pre January 2014

Once the screening of titles and abstracts was complete, full versions of the selected papers were acquired for assessment. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for this search on economic evaluations is presented in Appendix F.

3.3.6.2 Undertaking new health economic analysis

As well as reviewing the published economic literature, as described above, new economic analysis was undertaken by the Health Economist in selected areas. The following priority areas for de novo economic analysis were agreed by the Committee after formation of the review questions and consideration of the available health economic evidence:

- determining the effective management of difficulties with saliva control (drooling) in children and young people with cerebral palsy;
- interventions to reduce the risk of reduced bone mineral density and low-impact fractures in children and young people with cerebral palsy.

The methods and results of de novo economic analyses are reported in Appendix G. When new economic analysis was not prioritised, the Committee made a qualitative judgement regarding cost effectiveness by considering expected differences in resource and cost use

between options, alongside clinical effectiveness evidence identified from the clinical evidence review.

3.3.6.3 Cost effectiveness criteria

NICE's report Social value judgements: principles for the development of NICE guidance sets out the principles that Committees should consider when judging whether an intervention offers good value for money. In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- the intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or;
- the intervention cost less than £20,000 per QALY gained compared with the next best strategy, or;
- the intervention provided clinically significant benefits at an acceptable additional cost when compared with the next best strategy.

The Committee's considerations of cost-effectiveness are discussed explicitly in the 'Consideration of economic benefits and harms' section of the relevant sections.

3.4 Developing recommendations

Over the course of the guideline development process, the Committee was presented with:

- evidence tables of the clinical and economic evidence reviewed from the literature: all evidence tables are in Appendix J
- summary of clinical and economic evidence and quality assessment (as presented in Sections 4 to 29)
- forest plots (Appendix I)
- a description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (Appendix G).

Recommendations were drafted on the basis of the Committee's interpretation of the available evidence, taking into account the balance of benefits, harms and costs between different courses of action. This was either done formally, in an economic model, or informally. Firstly, the net benefit over harm (clinical effectiveness) was considered, focusing on the critical outcomes, although most of the reviews in the guideline were outcome driven. When this was done informally, the Committee took into account the clinical benefits and harms when one intervention was compared with another. The assessment of net benefit was moderated by the importance placed on the outcomes (the Committee's values and preferences), and the confidence the Committee had in the evidence (evidence quality). Secondly, the Committee assessed whether the net benefit justified any differences in costs.

When clinical and economic evidence was of poor quality, conflicting or absent, the Committee drafted recommendations based on their expert opinion. The considerations for making consensus-based recommendations include the balance between potential harms and benefits, the economic costs or implications compared with the economic benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues. The Committee also considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation.

The wording of recommendations was agreed by the Committee and focused on the following factors:

- the actions healthcare professionals need to take

- the information readers need to know
- the strength of the recommendation (for example the word ‘offer’ was used for strong recommendations and ‘consider’ for weak recommendations)
- the involvement of patients (and their carers if needed) in decisions about treatment and care
- consistency with NICE’s standard advice on recommendations about drugs, waiting times and ineffective intervention.

The main considerations specific to each recommendation are outlined in the ‘Recommendations and link to evidence’ sections within each section.

3.4.1 Research recommendations

When areas were identified for which good evidence was lacking, the Committee considered making recommendations for future research. Decisions about inclusion were based on factors such as:

- the importance to patients or the population
- national priorities
- potential impact on the NHS and future NICE guidance
- ethical and technical feasibility.

3.4.2 Validation process

This guidance is subject to a 6-week public consultation and feedback as part of the quality assurance and peer review of the document. All comments received from registered stakeholders are responded to in turn and posted on the NICE website when the pre-publication check of the full guideline occurs.

3.4.3 Updating the guideline

Following publication, and in accordance with the NICE guidelines manual, NICE will undertake a review of whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an update.

3.4.4 Disclaimer

Healthcare providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by practitioners in light of individual patient circumstances, the wishes of the patient, clinical expertise and resources.

The National Guideline Alliance (NGA) disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.

3.4.5 Funding

The NGA was commissioned by the National Institute for Health and Care Excellence (NICE) to undertake the work on this guideline.

4 Risk factors

Review question: What are the most important risk factors for developing cerebral palsy with a view to informing more frequent assessment and early recognition?

4.1 Introduction

Risk factors are events or circumstances that increase the risk of brain injury or malformation which then results in cerebral palsy. A risk factor does not always mean that the child will develop cerebral palsy. It means that the chances are higher than if the risk factor was not present. The absence of risk factors does not ensure that the child will not develop cerebral palsy. Whilst many features can have associated risk of developing cerebral palsy it is important not to create unnecessary anxiety or increased surveillance for children who may develop typically.

Knowing the risk factors may help in preventing or effectively treating and managing risks.

The early identification and diagnosis of cerebral palsy is important for many reasons, not only to guide intervention but also to advise on prognosis and family planning.

The guideline has investigated the most important risk factors to target surveillance for those at risk of developing cerebral palsy. It focused on 3 specific timings of when the injury or dysfunction can occur in the developing brain, during the antenatal period (before birth), around the time of birth (perinatal factors) and after birth most commonly within the first year of life (postnatal factors). The list of potential risk factors can be very large including prematurity, infection and trauma so it was important to identify the most significant ones.

The aim of this evidence review was to identify the most important risk factors for developing cerebral palsy with the view to providing information for parents/carers and to inform the need for more frequent assessment and early intervention.

The Committee prioritised the risk factors that were most commonly seen in clinical practice as the view was that it was neither practical nor useful to assess all possible risk-factors. Only papers published after the year 2000 were included in the review to account for the changes in clinical practice and interventions available after this time.

Those prioritised were:

Antenatal factors

- Infections (for example rubella, toxoplasmosis, cytomegalovirus [CMV], herpes simples)
- Multiple pregnancy
- Intrauterine growth restriction
- Haemorrhagic events

Perinatal

- Hypoxic ischaemic events at term/post term
- neonatal encephalopathy
- Apgar score at 10 min (Low/very low below 4/3)
- Neonatal sepsis

Postnatal

- Extremely preterm 24 – 27 $^{+6}$ weeks gestational age
- Preterm 28 - 31 $^{+6}$ weeks gestational age
- Late preterm (32-37 weeks gestational age)

- Infections: meningitis and encephalitis
- Clotting disorders /hyper coagulation in mother
- Trauma/non-accidental injury

Individual systematic reviews were undertaken for each of these and the results are reported below grouped by antenatal, perinatal and postnatal factors.

4.26 Description of clinical evidence: antenatal risk factors

Nine observational studies have been identified for this review (Bear 2016; Streja 2013; Wu 2013; Miller 2013; Beaino 2010; Himpens 2010; Laptook 2005; Livinec 2005; Dammann 2001). Four were retrospective cohorts using national registries as data sources (Bear 2016; Streja 2013; Wu 2013; Miller 2013). Five studies were prospective cohorts, of which two were based on the EPIPAGE cohort (Beaino 2010; Livinec 2005), and included babies born between 22 and 32 weeks of gestational age; 1 study (Himpens 2010) included children assessed at 1 centre for developmental disorders and referred from NICU; 1 study (Laptook 2005) was multicentre, including 14 different centres participating to same network and it looked at very low birth weight babies; and 1 study included long-term survivors of a regional cohort of very low birth weight newborns (Dammann 2001).

Sample sizes ranged from 407 to 6,018,504 children.

Four studies reported on maternal infections as a risk factor for cerebral palsy: 1 study (Streja 2013) reported adjusted odds ratios for all infections, vaginal infections, and urinary infections; for vaginal infections, they also presented the data separately for at term and preterm babies. One study (Wu 2013) reported adjusted odds ratios for infections of the genitourinary system and for any other infections. One study (Miller 2013) reported adjusted estimates for any hospital reported maternal infection separately for preterm and at term babies; and 1 study (Bear 2016) presented adjusted odds ratios for genitourinary infections other than chorioamnionitis, and respiratory infections.

Three studies reported on multiple pregnancy as a risk factor for cerebral palsy (Beaino 2010; Himpens 2010; Laptook 2005).

One study reported results on haemorrhagic events as antenatal risk factor for developing cerebral palsy (Livinec 2005).

One study reported on fetal growth retardation as a risk factor for developing cerebral palsy (Dammann 2001).

Outcomes are reported as described in the original papers, so reflect the variation in reporting. Only studies presenting adjusted analyses have been considered for this review.

Studies were heterogeneous with regards to population and subgroups considered, risk factors studied and covariates included in the multivariate models. For these reasons, it was decided not to pool the data together. Therefore, forest plots presented in Appendix I do not report meta-analysed data but they have been produced to help the readers to visualise the direction of the effect sizes.

For this review, quality appraisal of the evidence has been conducted using the NICE manual methodology checklists. Quality appraisal has been conducted by study, and not by outcome. For full details see section 4.9.6 on quality of evidence.

The quality of each study was assessed using the NICE manual methodology checklists. Please see section 4.9.6 on quality of the evidence for more details.

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, forest plots in Appendix I, study evidence tables in Appendix J and exclusion list in Appendix K.

4.2.14 Summary of included studies and results

A summary of the studies that were included in this review and their results for antenatal factors are presented in Table 11.

1 **Table 11: Summary of included studies**

Study	Data source	Sample and population studied	Risk factor(s) studied	Adjustment for:	Results	Quality of the study
Beaino 2010	EPIPAGE cohort	N=2357 born 22-32 weeks of gestational age	• Multiple pregnancy	Gestational age, sex, small for GA, multiple pregnancy and PROM, neonatal factors (RDS).	aOR = 0.67 (0.43-1.03) • sub-group analysis for 30-34 weeks only (from Marret et al. 2007): aOR = 1.6 (0.7-3.8)	Moderate
Himpens 2010	children assessed at the 'centre for developmental disorders Ghent'	N=984 high-risk children (referred from NICU)	• Multiple pregnancy	GA, gender, MG, PA, MV, WM disease and DGM lesion	n=48/278 aOR = 1.3 (0.8-2.1)	High
Laptook 2005	14 centres of the National Institute of Child Health and Human Development Neonatal Research network	N=1473 VLBW babies	• Multiple pregnancy	prenatal variables, birth weight, gender, multiple births, pneumothorax, late-onset sepsis, ventilation	aOR = 1.6 (1.1-2.5	High
Livinec 2005	EPIPAGE cohort	N=2382 born 22-32 weeks of gestational age	• Maternal haemorrhagic events	for singletons = pregnancy complications, sex, GA, prenatal steroids; for twins = pregnancy complications, type of placentation, in utero vital status of co-twin, sex, GA, prenatal steroids	• In singletons: n=7/157 (4.3%); aOR = 1.1 (0.4-2.9) • In twins: n=2/23 (7.7%); aOR = 0.6 (0.1-3.7) • sub-group analysis for 30-34 weeks only (from Marret et al. 2007): Haemorrhage (singletons only) aOR = 0.4 (0.04-3.3)	High

Study	Data source	Sample and population studied	Risk factor(s) studied	Adjustment for:	Results	Quality of the study
Miller 2013	Danish National Birth Register (National Registry)	N=440,564 singletons born 1997-2003 and resided in Denmark up to Dec 2008	• Maternal infections	maternal age, smoking, parental income, calendar year	• Any hospital reported maternal infection • preterm delivery: n=20/1300 aHR = 1.4 (0.9-2.2) • term delivery: n=22/1363 aHR = 1.2 (0.9-1.8)	Very low
Streja 2013	Danish National Birth Cohort	N=81,066 singletons	• Maternal infections	maternal age, alcohol consumption, binge drinking, combined SES, season of birth, year of birth, number per household, smoking	• All infections n=119/139; aHR for CP = 0.98 (0.68-1.41) n=103/121; aHR for sCP = 1.00 (0.67-1.48) • Vaginal Infections n=130/139; aHR for CP = 1.52 (1.04-2.24) n=112/121; aHR for sCP = 1.73 (1.16-2.60) • Urinary Infections n=127/139; aHR for CP = 0.74 (0.40-1.38) n=110/121; aHR for sCP = 0.79 (0.41-1.50) Stratified analysis by GA • in children born at term vaginal infections = aHR 1.70 (1.08-2.67) for sCP • in children born preterm = aHR 1.59 (0.51-4.94)	Low

Study	Data source	Sample and population studied	Risk factor(s) studied	Adjustment for:	Results	Quality of the study
					for sCP	
Wu 2013	Danish Medical Birth Register (National Registry)	N=588,936 first-born singletons born 1982-2004.	• Maternal infections	maternal age, sex, maternal education, maternal marital status, birth year, family income, maternal infection before birth	• Infections of the genitourinary system n=105/14037 aOR = 1.61 (1.32-1.96) • Any other infections n=53/9556 aOR = 1.13 (0.86-1.49)	Moderate
Bear 2016	California Office of State-wide Health Planning an d Development,	N = 6,018,504 Californian births over an 11-year period	• Maternal infections	Maternal age, race, education, and socioeconomic status; maternal hospital diagnosis of obesity, and infant sex.	• GU infections OR = 1.4 (1.3-1.6) • Respiratory infections OR = 1.9 (1.5-2.2)	High
Dammann 2001	Regional cohort of VLBW babies	N=324 followed up until age 6 years.	• Fetal growth retardation (measured as SGA)	GA, foreign background, caesarean section, sepsis, and PROM	• Total sample (N=317): • aOR for bilateral spastic CP = 0.2 (0.03-0.96) • Subgroup 24-31 weeks GA (n=227 SGA only): • aOR for bilateral spastic CP = 1.2 (0.2-6.4) • Subgroup 28-31 weeks GA (n=160 SGA and AGA present): • aOR for bilateral spastic CP = 1.2 (0.2-6.4) • In matched sample (n=136) • aOR for bilateral spastic CP = 2.2 (0.3-15)	Moderate

1 *CP cerebral palsy, sCP spastic cerebral palsy, aOR adjusted odds ratio, aHR adjusted hazard ratio, GA gestational age, BW birth weight, VLBW very low birth weight, SES*
2 *socioeconomic status, RDS respiratory distress syndrome, BPD bronchopulmonary dysplasia, PDA patent ductus arteriosus, IVH intra-ventricular haemorrhage, PVL peri-*

ventricular haemorrhage, PROM premature rupture of membranes, NICU neonatal intensive care unit, HIE hypoxic ischaemic event, SGA small for gestational age, AGA appropriate birthweight for gestational age, EOS early onset sepsis, LOS late onset sepsis, MG multiple gestation, PA perinatal asphyxia, MV mechanical ventilation, WM disease white matter disease, DGM lesion deep grey matter lesion, RCT randomised controlled trial .

4.3 Evidence statements

4.3.1 Maternal infections

High quality evidence from 1 study with 6,018,504 participants (mother-infant dyads) reported an increased risk of cerebral palsy in children whose mothers had a hospital discharge diagnosis of genitourinary infection other than chorioamnionitis (OR = 1.4) and whose mothers had a hospital discharge diagnosis of respiratory infection (OR = 1.9).

Moderate evidence from 1 study with 588,936 singletons showed an increased risk for cerebral palsy in children whose mothers had infections of the genitourinary system during pregnancy, but not for those whose mothers had 'any other infections' during pregnancy.

Low quality evidence from 1 study with 81,066 singletons showed an increased risk for cerebral palsy in children whose mothers had vaginal infections during pregnancy; when looking at the risk of developing spastic cerebral palsy, an association was found for babies born at term but not for preterm babies. The same study reported no association between 'all infections', urinary infections and cerebral palsy.

Very low evidence from 1 study with 440,564 singletons showed no association between maternal infections and cerebral palsy in both preterm and at term babies.

4.3.2 Multiple pregnancy

High quality evidence from 1 study with 1473 very low birth weight babies showed an increased risk of cerebral palsy in babies born from multiple pregnancy. However, another high quality study with 984 high-risk babies showed no association between multiple pregnancy and cerebral palsy.

Moderate quality evidence from 1 study with 2357 preterm babies showed no association between multiple pregnancy and development of cerebral palsy.

4.3.3 Haemorrhagic events

High quality evidence from 1 study with 2382 preterm babies showed no association between the occurrence of maternal haemorrhagic events and the development of cerebral palsy.

4.3.4 Intrauterine growth retardation

Moderate quality evidence from 1 study with 324 very low birth weight babies showed that being small for gestational age was associated with a reduced risk of developing bilateral spastic cerebral palsy. However, the same study did not find the same association when looking at subsamples of babies born at 24-31 weeks, 28-31, and when using an age-matched sample.

4.4 Description of clinical evidence: perinatal risk factors

Fifteen studies have been identified for this review (Bear 2016; Himpens 2010; Han 2012; Sukhov 2012; Ahlin 2013; Natarajan 2013; Alshaikh 2013; Laptook 2005; Wang 2014; Alshaikh 2014; Mitha 2013; Shatrov 2010; Nasef 2013; Pappas 2014; Soraisham 2013).). One study was a meta-analysis of 17 observational studies including very low birth weight infants (Alshaikh 2013). One study was a meta-analysis of 15 observational studies (Shatrov

2010). Six studies were prospective cohorts including children referred from the neonatal intensive care unit (NICU) from 1 centre for developmental disorders in Belgium (Himpens 2010), preterm survivors from 1 centre in Korea (Han 2012), very low birth weight babies from 14 centres (Laptook 2005), very low birth weight and pretermbabies from 18 tertiary referral centres in Taiwan (Wang 2014), children of 22-32 weeks of gestational age from the EPIPAGE study (Mitha 2013), and 1 study (Pappas 2014) included preterm babies from 16 centres. Five studies were retrospective cohorts that used 3 different state databases (Sukhov 2012): a neonatal database of a single centre (Alshaikh 2014), hospital charts (Bear 2016; Nasef 2013), and children from 1 regional NICU (Soraisham 2013). One study was a secondary analysis of RCT data (Natarajan 2013) including children who had hypoxic ischaemic events. One study (Ahlin 2013) used a case-control design using data from a national registry in Sweden.

Sample sizes ranged from n= 174 to 6.1 million children.

Three studies reported on hypoxic ischaemic events or birth asphyxia as a risk factor for developing cerebral palsy (Himpens 2010; Han 2012; Sukhov 2012).

One study reported on neonatal encephalopathy as a risk factor indicating cerebral palsy (Ahlin 2013).

One study reported on Apgar score at 10 minutes as a risk factor for cerebral palsy (Natarajan 2013).

Six studies reported on neonatal sepsis as risk factor for developing cerebral palsy (Han 2012; Alshaikh 2013; Laptook 2005; Wang 2014; Alshaikh 2014; Mitha 2013).

Five studies reported specifically on chorioamnionitis as a risk factor for developing cerebral palsy (Bear 2016; Shatrov 2010; Nasef 2013; Pappas 2014; Soraisham 2013). This risk factor has not been specified in the protocol, but it has been recognised as in important perinatal feature to be reviewed.

The quality of each study was assessed using the NICE manual methodology checklists. Please see section 4.9.6 on quality of the evidence for more details.

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, forest plots in Appendix I, study evidence tables in Appendix J and exclusion list in Appendix K.

4.4.1 Summary of included studies

A summary of the studies that were included in this review and their results for perinatal factors are presented in Table 12.

1 **Table 12: summary of included studies**

Study	Data source	Sample and population studied	Risk factor(s) studied	Adjustment for:	results	Quality of the study
Ahlin 2013	Swedish Medical Birth Registry (national registry)	N=309 cases and 618 controls	• Neonatal encephalopathy	All risk factors from univariate analyses attaining P<0.1 for CP were included in a stepwise multiple logistic regression analysis.	Neonatal encephalopathy • aOR for all spastic and dyskinetic CP = 69.22 (9.24-511.9) • aOR for spastic CP = 22.21 (2.8-174.1)	Low
Alshaikh 2013	Meta-analysis	17 studies involving N=15.331 VLBW infants	• Neonatal sepsis	n/a	pooled OR for CP from 11 studies = 2.09 (1.78-2.45) I-squared = 36.9%, p=0.064	High
Alshaikh 2014	neonatal database of single centre	N=332 preterm babies	• Neonatal sepsis	GA, severe IVH, chorioamnionitis and postnatal steroids	CoNS sepsis: aOR = 0.63 (0.24-1.64)	Moderate
Laptook 2005	14 centres of the National Institute of Child Health and Human Development Neonatal Research network	N=1473 VLBW babies	• Neonatal sepsis	prenatal variables, birth weight, gender, multiple births, pneumothorax, late-onset sepsis, ventilation	• Late-onset sepsis aOR = 1.2 (0.8-1.7)	High
Mitha 2013	EPIPAGE	N=2665 born 22-32 weeks of gestational age	• Neonatal sepsis	For EOS: PROM, spontaneous preterm labour, gender, GA, and SGA, antenatal corticosteroid therapy. For LOS: PROM, spontaneous preterm labour, type of pregnancy, gender, GA, and SGA,	• Early onset sepsis n=20/131; aOR = 1.55 (0.90-2.67) • Late onset sepsis n=73/557; aOR = 1.45 (0.95-2.20)	Moderate

Study	Data source	Sample and population studied	Risk factor(s) studied	Adjustment for:	results	Quality of the study
				antenatal corticosteroid therapy, and duration of central venous catheter use.		
Wang 2014	children admitted to NICU of 18 tertiary referral centres in Taiwan	N=5,807 VLBW and preterm	• Neonatal sepsis	GA, birth weight, sex, and retinopathy of prematurity >stage III	• Neonatal sepsis aOR = 1.22 (0.59-2.62) p=0.71	Moderate
Han 2002	Children born in 1 centre in Korea	N=437 preterm survivors	• Hypoxic ischaemic events or birth asphyxia • Neonatal sepsis	GA, BW, PROM or preterm labour, frequent miscarriage, birth asphyxia, neonatal sepsis, respiratory distress syndrome, neonatal seizures, ventriculomegaly, brain atrophy, periventricular echodensity, IVH, grade3 IVH, PVL.	• HIE aOR = 1.003 (0.98-1.02) • Neonatal sepsis aOR = 1.012 (0.97-1.04)	High
Nasef 2013	hospital charts	N=274 preterm babies <30 weeks admitted to NICU	• Chorioamnionitis	mode of delivery and presence of PROM	• Clinical chorioamnionitis and CP n=2/33 aOR = 1.3 (0.2-7.9); P=0.72 • Histological chorioamnionitis and CP n=2/95 aOR = 0.4 (0.08-2.1); P=0.3	Low
Pappas 2014	16 centres	N=2390 preterm babies <27 weeks	• Chorioamnionitis	maternal age, multiple birth, parity, antenatal steroids, maternal hypertension, antepartum haemorrhage, sex, GA,	• Histological chorioamnionitis alone vs none aOR = 0.80 (0.42-1.53) • Histological plus clinical	Moderate

Study	Data source	Sample and population studied	Risk factor(s) studied	Adjustment for:	results	Quality of the study
				small for GA, insurance, race and centre.	chorioamnionitis vs none aOR = 1.39 (0.67-2.87) • Histological alone vs histological plus clinical chorioamnionitis aOR = 0.58 (0.29-1.16)	
Shatrov 2010	Meta-analysis	15 studies included	• Chorioamnionitis	n/a	• Clinical chorioamnionitis and CP n studies= 12 OR = 2.41 (1.52-3.84); I-squared = 70.5%; P<0.001 • Histological chorioamnionitis and CP n studies=8 OR = 1.83 (1.17-2.89); I-squared = 28.8%; P<0.198	High
Soraisham AS 2013	1 regional NICU	N=384 preterm <29 weeks	• Chorioamnionitis	gestational age, maternal hypertension, PROM >24 hours, multiple pregnancy	Histological chorioamnionitis vs no HCA • aOR = 2.45 (1.11-5.40) p=0.02	Moderate
Bear 2016	California Office of State-wide Health Planning an d Development,	N = 6,018,504 Californian births over an 11-year period	• Chorioamnionitis	Maternal age, race, education, and socioeconomic status; maternal hospital diagnosis of obesity, and infant sex.	OR = 3.1 (2.9-3.4)	High
Himpens 2010	children assessed at the 'centre for developmental	N=984 high-risk children (referred from NICU)	• Hypoxic ischaemic events or birth asphyxia	GA, gender, MG, PA, MV, WM disease and DGM lesion	Perinatal asphyxia n=32/113; • aOR = 2.4 (1.3-4.6)	High

Study	Data source	Sample and population studied	Risk factor(s) studied	Adjustment for:	results	Quality of the study
	disorders Ghent'				• aOR for non-spastic CP (reference category = spastic CP) aOR = 3.6(1.2-10.9)	
Suchov 2012	3 databases (state databases)	N=6.1M (all children born in California 1991-2001)	• Hypoxic ischaemic events or birth asphyxia	maternal age, parity, maternal education, payer-source, race/ethnicity, timing of initiation of prenatal care, number of prenatal visits, GA, BW, and obstetric and neonatal comorbidities	Mild to severe birth asphyxia aOR = 5.98 (5.28-6.58)	Low
Natarajan 2013	secondary analysis of RCT data	N=174 children with HIE	• Apgar score at 10 min	birth weight, GA, gender, outborn status, hypothermia treatment and centre	Association between each point increase in Apgar at 10min and CP aOR = 0.69 (0.63-0.89) p<0.001	Moderate

CP cerebral palsy, sCP spastic cerebral palsy, aOR adjusted odds ratio, aHR adjusted hazard ratio, GA gestational age, BW birth weight, VLBW very low birth weight, SES socioeconomic status, CoNS coagulase-negative staphylococcus, RDS respiratory distress syndrome, BPD bronchopulmonary dysplasia, PDA patent ductus arteriosus, IVH intra-ventricular haemorrhage, PVL peri-ventricular haemorrhage, PROM premature rupture of membranes, NICU neonatal intensive care unit, HIE hypoxic ischaemic event, SGA small for gestational age, EOS early onset sepsis, LOS late onset sepsis, MG multiple gestation, PA perinatal asphyxia, MV mechanical ventilation, WM disease white matter disease, DGM lesion deep grey matter lesion, RCT randomised controlled trial.

4.5 Evidence statements

4.5.1 Hypoxic ischaemic events or birth asphyxia

High quality evidence from 1 study with 984 high-risk babies showed an increased risk of cerebral palsy in children who experienced perinatal asphyxia (collected and defined using medical records); the same study showed an increased risk of developing non-spastic cerebral palsy compared to spastic cerebral palsy in these children.

High quality evidence from 1 study with 437 preterm babies showed no association between hypoxic ischaemic event (defined as a 10-min Apgar score <6 and combined hypoxia identified by means of a blood test) and development of cerebral palsy.

Low quality evidence from 1 study with 6.1M children showed an increased risk of developing cerebral palsy in children who experienced mild to severe birth asphyxia (collected and defined using ICD classification).

4.5.2 Neonatal encephalopathy

Low quality evidence from 1 study with 927 children showed an increased risk of both spastic and dyskinetic cerebral palsy in children with neonatal encephalopathy.

4.5.3 Apgar score at 10 min

Moderate evidence from 1 study with 174 children who had hypoxic ischaemic event showed a decreased risk of developing cerebral palsy for each point increase in Apgar score at 10 min.

4.5.4 Neonatal sepsis

High quality evidence from 1 meta-analysis of 11 studies showed an increased risk of developing cerebral palsy in children with neonatal sepsis.

High to moderate quality evidence from 5 studies with 10704 high-risk children showed no association between neonatal sepsis and cerebral palsy.

4.5.5 Chorioamnionitis

High quality evidence from 1 meta-analysis with 15 observational studies showed an increased risk of cerebral palsy in children born after pregnancy with clinical evidence of chorioamnionitis; the same study also found increased risk of cerebral palsy in children who showed histological chorioamnionitis.

High quality evidence from 1 study with 6,018,504 participants (mother-infant dyads) reported an increased risk of cerebral palsy in children whose mothers had a hospital discharge diagnosis of chorioamnionitis (odds ratio = 3.1). Moderate evidence from 1 study with 384 preterm babies showed an increased risk of cerebral palsy in children born after pregnancy with histological evidence of chorioamnionitis; however, moderate quality from another study with 2390 preterm babies showed no association between histological chorioamnionitis and cerebral palsy.

Low quality evidence from 1 study with 2390 preterm babies showed no association for both histological and clinical chorioamnionitis and development of cerebral palsy.

4.6 Description of clinical evidence: postnatal risk factors

Six studies have been identified for this review (Beaino 2010; Himpens 2010; Sukhov 2012; Petrini 2009; Bonellie; Stoll 2004). Two studies were prospective cohorts, of which 1 was based on the EPIPAGE cohort (Beaino 2010) and included babies born between 22 and 32 weeks of gestational age; 1 study (Himpens 2010) included children assessed at 1 centre for developmental disorders and referred from NICU. Four studies used a retrospective design: 1 used 3 different state databases (Sukhov 2012), 1 used hospitalization and outpatient databases from the Northern California Kaiser Permanente Medical care program (Petrini 2009), 1 used a registry of very low birth weight infants maintained by the National Institute of Child health and Human Development Neonatal Research Network (Stoll 2004), and 1 study used a national database (Bonellie 2005).

Sample sizes ranged from n= 646 to 6.1 million children.

Five studies reported on gestational age as a risk factor for cerebral palsy (Beaino 2010; Himpens 2010; Sukhov 2012; Petrini 2009; Bonellie).

One study reported on neonatal infections as a possible risk factor for cerebral palsy (Stoll 2004).

No evidence was retrieved for trauma or non-accidental injuries, or clotting disorders.

The quality of each study was assessed using the NICE manual methodology checklists. Please section 4.9.6 on quality of the evidence for more details.

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, forest plots in Appendix I, study evidence tables in Appendix J and exclusion list in Appendix K.

4.6.1 Summary of included studies

A summary of the studies that were included in this review and their results for postnatal factors are presented in Table 13.

1 **Table 13: summary of included studies**

Study	Data source	Sample and population studied	Risk factor(s) studied	Adjustment for:	results	Quality of the study
Beaino 2010	EPIPAGE	N=2357 born 22-32 weeks of gestational age	• Gestational age	Gestational age, sex, small for GA, multiple pregnancy and PROM, neonatal factors (RDS).	Gestational age aOR = 1.00 (0.89-1.12) • sub-group analysis for 30-34 weeks only (from Marret et al. 2007) • gestational age at birth (wk.) = 30 reference aOR=1.00 • gestational age at birth (wk.) = 31 aOR = 1.3 (0.7-2.4) • gestational age at birth (wk.) = 32 aOR=0.6 (0.3-1.1) • gestational age at birth (wk.) = 33 aOR=0.5 (0.2-1.3) • gestational age at birth (wk.) = 34 aOR=0.08 (0.01-0.6) P for trend <0.001	Moderate
Bonellie 2005	Scottish registry	N=646	• Gestational age	Not specified	Singletons (reference = 37+ wk.): • 24-27 wk.: aOR = 93.56 (64.26-136.2) • 28-31: aOR = 64.45 (51.65-80.41) • 32-36 wk.: aOR = 7.69 (6.21-9.51) • Twins (reference = 37+ wk.): • 24-27 wk.: aOR = 49.25 (20.37-119.1) • 28-31: aOR = 13.62 (6.21-30.06)	Low

Study	Data source	Sample and population studied	Risk factor(s) studied	Adjustment for:	results	Quality of the study
					• 32-36 wk.: aOR = 2.72 (1.29-5.73)	
Himpens 2010	children assessed at the 'centre for developmental disorders Ghent'	N=984 high-risk children (referred from NICU)	• Gestational age	GA, gender, MG, PA, MV, WM disease and DGM lesion	Gestational age n=25/165; aOR = 1.1 (0.9-1.1) p=0.05 • adjusted OR for non-spastic CP (reference category = spastic CP) aOR = 1.1 (1-1.2) • adjusted OR for unilateral CP (reference category = bilateral CP) aOR = 1.2 (1-1.4)	High
Petrini 2009	hospitalization and outpatient databases from the Northern California Kaiser Permanente Medical care program	N=141321 children ≥30 weeks born 2000-2004 with follow up June 2005	• Gestational age	Maternal race/ethnicity, sex, plurality, and size for gestational age status.	• gestational age at birth 30-33 wk. aHR = 7.87 (5.38-11.51) • gestational age at birth 34-36 wk. aHR=3.39 (2.54-4.52) • gestational age at birth ≥42 wk. aHR = 0.90 (0.34-2.43) • gestational age at birth 37-41 wk. reference aOR=1.00	Low
Suchov 2012	3 databases (state databases)	N=6.1M (all children born in California 1991-2001)	• Gestational age	maternal age, parity, maternal education, payer-source, race/ethnicity, timing of initiation of prenatal care, number of prenatal visits, GA, BW, and obstetric and neonatal comorbidities	• gestational age at birth <28wks aOR = 18.21 (16.70-19.86) • gestational age at birth 28-31 wk. aOR = 8.83 (8.04-9.70) • gestational age at birth 32-36 wk. aOR = 2.20 (0.2-1.3) gestational age at birth 37+ wk. reference aOR= 1.00	Low

Study	Data source	Sample and population studied	Risk factor(s) studied	Adjustment for:	results	Quality of the study
Stoll B. 2004	registry of VLBW infants maintained by the National Institute of Child health and Human Development Neonatal Research Network	N=7892 eligible, 6314 available at follow-up	• Neonatal infections	infection group, study centre, GA, BW, sex, race/ethnicity, PROM more than 24 hours before delivery, mode of delivery, MB, antenatal antibiotic and steroids use, postnatal surfactant and steroids use, RDS, BPD, PDA, IVH, PVL, and maternal age at time of delivery	Meningitis with or without sepsis n=184/5740 aOR = 1.6 (1.0-2.5)	Moderate

CP cerebral palsy, sCP spastic cerebral palsy, aOR adjusted odds ratio, aHR adjusted hazard ratio, GA gestational age, BW birth weight, VLBW very low birth weight, SES socioeconomic status, RDS respiratory distress syndrome, BPD bronchopulmonary dysplasia, PDA patent ductus arteriosus, IVH intra-ventricular haemorrhage, PVL peri-ventricular haemorrhage, PROM premature rupture of membranes, NICU neonatal intensive care unit, HIE hypoxic ischaemic event, SGA small for gestational age, EOS early onset sepsis, LOS late onset sepsis, MG multiple gestation, PA perinatal asphyxia, MV mechanical ventilation, WM disease white matter disease, DGM lesion deep grey matter lesion, RCT randomised controlled trial.

4.7 Evidence statements

4.7.1 Gestational age

High quality evidence from 1 study with 984 high-risk babies showed an association between longer gestational age and type of cerebral palsy; children with higher gestational age were at increased risk of developing non-spastic cerebral palsy versus spastic cerebral palsy, as well as of developing unilateral cerebral palsy versus bilateral.

Moderate quality evidence from 1 study with 2357 preterm babies showed no association between gestational age and cerebral palsy.

Low quality evidence from 1 study with 646 children showed an increased risk of cerebral palsy for extreme preterm (24-27 weeks), preterm (28-31 weeks), and late preterm babies (32-36 weeks) compared to babies born 37+ weeks in both singletons and twins. Another low quality study with 6.1 million children showed an increased risk of cerebral palsy for extreme preterm (<28 weeks), and preterm (28-31 weeks) babies compared to babies born 37+ weeks; however, no association was found for late preterm babies (32-36 weeks) compared to babies born 37+ weeks.

Low quality evidence from 1 study with 141321 children showed an increased risk of developing cerebral palsy in children with gestational age at birth of 30-33 weeks and 34-36 weeks compared to children born 37-41 weeks; no association was found between children born at 42+ weeks and those born at 37-41 weeks.

4.7.2 Neonatal infections (meningitis and encephalitis)

Moderate quality evidence from 1 study with 7892 babies found no association between meningitis with or without sepsis and development of cerebral palsy.

4.7.3 Trauma/non-accidental injuries

No evidence was retrieved for this risk factor.

4.7.4 Clotting disorders

No evidence was retrieved for this risk factor.

4.8 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations on identifying the most important risk factors for cerebral palsy were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

4.9 Evidence to recommendations

4.9.1 Relative value placed on the outcomes considered

The aim of this review was to identify the most important risk factors for developing cerebral palsy with the view to providing information for parents/carers and to inform the need for more frequent assessment and early intervention. The Committee prioritised the following risk factors, based on those commonly perceived to be implicated and expert opinion:

Antenatal factors

- Infections (for example rubella, toxoplasmosis, CMV, herpes simples)
- Multiple pregnancy
- Intrauterine growth retardation
- Haemorrhagic events

Perinatal

- Hypoxic ischaemic events at term/post term
- neonatal encephalopathy
- Apgar score at 10 min (Low/very low below 4/3)
- Neonatal sepsis

Post-natal

- Extreme prematurity 24 - 27 (+6 days) weeks gestational age)
- Premature 28 - 31 (+6 days) weeks gestational age
- Late premature babies (32-37 weeks gestational age)
- Infections: meningitis and encephalitis
- Clotting disorders /hyper coagulation in mother
- Trauma/non-accidental injury

4.9.2 Consideration of clinical benefits and harms

The Committee recognised that cerebral palsy is aetiologically a multifactorial condition and in any affected person, a number of other clinical and socioeconomic risk factors may have contributed to the outcome. Thus, children born preterm may be at risk due to prematurity but may also have a risk arising from infection. Most of the studies analysed the magnitude of independent risk factors by using adjusted analyses. As part of the protocol for this evidence review, the Committee agreed that they wanted to understand the evidence for independent risk factors for cerebral palsy.

The Committee considered that studies in this area published before 2000 should not be included in the review because of changes in antenatal and neonatal clinical practice since then may have had a significant impact on relative risk factors for cerebral palsy.

The Committee agreed that low birth weight was frequently a proxy for preterm birth in the literature. The Committee noted that very low birth weight infants were the population considered for some of risk factors such as multiple pregnancies and neonatal sepsis. Therefore, the Committee decided to add low birth weight to the recommendation as a risk factor itself given that it was frequently reported in the populations included in the studies.

4.9.2.1 Antenatal risk factors

Maternal infections

The evidence showed that effect sizes reached significance when vaginal or genitourinary infections were analysed separately from all the other infections during pregnancy. Evidence was also provided of increased risk for developing cerebral palsy associated with genitourinary and respiratory tract infections in the mother that was recognised in a hospital setting. Specific evidence was retrieved in other studies, indicating a direct association with chorioamnionitis, and the Committee agreed that it should be listed as an independent risk factor for cerebral palsy.

Multiple pregnancy

The evidence showed conflicting results with regards to multiple pregnancy acting as a risk factor for cerebral palsy, with 1 study showing an increased risk, a second study showing reduced risk, and a third showing no significant risk. The Committee noted that 1 study looked at a population of low birth weight infants and another at population of preterm infants and these found different results in relation to multiple pregnancy. This would not have been expected as low birth weight is a proxy for prematurity.

The Committee agreed that infants born in multiple pregnancies are more likely to be preterm and have low birth weight. The studies included in the review adjusted for that.

The Committee agreed that the evidence did not support including multiple pregnancies as an independent risk factor for the development of cerebral palsy.

Intra uterine growth restriction

Only 1 study met the inclusion criteria for this review. This study suggested that being small for gestational age was associated with a reduced risk of developing bilateral spastic cerebral palsy. The value of this study was limited by the fact that it was carried out in a population of very low birthweight babies. The Committee discussed how not all small for gestational age infants will be growth restricted. The category of very low birthweight babies includes infants of varying gestational ages, some of whom will be appropriate weight for gestation, some of whom will be more developed but small for gestation. The Committee agreed that this made the study findings more difficult to interpret and therefore agreed not to develop a specific recommendation that IUGR be considered an independent risk factors in cerebral palsy.

The Committee were aware of 3 other studies on intra uterine growth restriction which were not included in the evidence review as they did not meet the inclusion criteria specified in the protocol. Main reasons for exclusion included date of publication (before 2000) and lack of comparative data (all children had cerebral palsy). A study by Jarvis et al. concluded that preterm babies either below the 10th percentile or above the 97th percentile were more likely to have cerebral palsy than those in a reference band between 25th and 75th percentile; however, they did not adjust for IUGR as an independent risk factor. Two other studies (Uvebrant and Blair) showed that the risk of cerebral palsy was associated with poor intrauterine growth and dependent on gestation at delivery; however, these studies were performed prior the 2000 cut off specified in the review protocol, and the Committee considered that changes in neonatal care rendered the findings less appropriate in modern practice.

Maternal Haemorrhagic events

One study showed increased and reduced risk of cerebral palsy in twins and singletons respectively; however, both estimates were not statistically significant. Based on the

reviewed evidence, the Committee agreed that haemorrhagic events should not be considered as an independent risk factor for the development of cerebral palsy.

4.9.2.2 Perinatal risk factors

Hypoxic ischaemic events (HIE)

Two of the 3 included studies included for HIE showed an increased risk of developing cerebral palsy for babies who had a hypoxic ischaemic event. However it was not clear from the studies what was to be considered as a hypoxic ischaemic event, making the evidence difficult to interpret. In addition, the studies differed in how they measured and reported HIE; for example, Han 2002 measured HIE based on low Apgar score at 10 minutes and combining this with means of blood tests, while Himpens 2010 used medical records to collect data on this risk factor.

Neonatal encephalopathy

Only 1 study was included that assessed neonatal encephalopathy as a risk factor. Although this evidence was of low quality, the Committee was persuaded of its importance, as it showed a very large effect. They therefore recommended that neonatal encephalopathy be recognised as an independent risk factor for developing cerebral palsy.

Apgar score

One study showed that increasing Apgar score at 10 min was associated with a reduced risk of developing cerebral palsy. However, it did not identify the risks associated with particular Apgar scores at 10 min (as it was indicated in the review protocol), and so the Committee was not able to recommend a specific Apgar score as at risk factor.

Neonatal sepsis

Five studies showed an association (albeit non-significant) in terms of an increased risk between history of neonatal sepsis and cerebral palsy, all carried out in populations of preterm infants. In addition, a meta-analysis did show a significant association between a history of neonatal sepsis and an increased risk of cerebral palsy, again in populations of preterm infants.

The Committee noted that neonatal sepsis occurred more frequently in preterm infants as reflected in these studies, and there was a lack of evidence in relation to term infants. Despite this lack of published evidence the Committee believed that neonatal sepsis was an independent risk factor for cerebral palsy in neonates generally, and so they recommended that it be recognised as such.

Chorioamnionitis

One high quality meta-analysis one high quality cohort with large sample size showed an increased risk of cerebral palsy in babies born with a history of chorioamnionitis. The Committee were in agreement that chorioamnionitis should be recognised as an independent risk factor for the development for cerebral palsy.

4.9.2.3 Post-natal risk factors

Gestational age

Five studies were presented that examined the association between gestational age and risk of developing cerebral palsy. The Committee agreed that the evidence suggested an increased risk of cerebral palsy with reducing length of gestation. This was particularly high

when considering a gestational age at birth of less than 28 weeks and was also increased in those born between 28-32 weeks gestation

The Committee pointed out that although not demonstrated in the retrieved evidence, it was their view that preterm delivery increased the risk of different forms of cerebral palsy differently. The Committee agreed that in high risk infants delivered closer to full term the resultant motor subtype of cerebral palsy was more likely to be dystonic rather than spastic in nature, and unilateral rather than bilateral in distribution. Conversely, in early preterm cohorts the motor pattern was more likely to be spastic and bilateral.

Neonatal infection

One study showed a small increased risk for the development of cerebral palsy in very low birthweight babies who had suffered from meningitis. The Committee recognised the lack of evidence in relation to higher birthweight infants, but believed that clinical experience showed meningitis to be a serious risk factor. Again, the lack of evidence for the latter group reflected the fact that infection is more common in very preterm infants. Given the lack of evidence, the Committee decided not to make a specific recommendation for neonatal infection as a risk factor.

Trauma/non-accidental injuries

The Committee was made aware that a few papers evaluated the association between neonatal seizures and adverse neurological outcomes, including the development of cerebral palsy. However, the Committee were in agreement that this information was more relevant as part of the 'causes of cerebral palsy' review. Given the lack of evidence on other trauma or non-accidental injuries, the Committee decided not to make a specific recommendation for these as a risk factors.

Clotting disorders

No evidence was found for this risk factors.

The Committee discussed how limited the evidence base was looking at whether chorioamnionitis, other genitourinary infections and respiratory tract infections requiring admission to hospital are significant risk factors for the child of a pregnancy being given a diagnosis of cerebral palsy. They agreed that high priority research to look at the effects of different antibiotic regimes for treating genito-urinary infections in pregnant women on subsequent rates of cerebral palsy was needed.

4.9.3 Consideration of economic benefits and harms

Knowing the most important risk factors for developing cerebral palsy may lead to better prediction and identification (and thus more timely management) and has therefore, indirectly, potentially important resource implications. However, this was an epidemiological review question and economic analysis was not applicable as it does not involve a comparison of competing alternatives.

4.9.4 Quality of evidence

The quality of each study was assessed using the NICE methodology checklist (2012) for prognostic studies, the NICE methodology checklist (2012) for systematic reviews and the NICE methodology checklist (2012) for cohort studies. Meta-analyses of observational studies and cohort studies were the most appropriate study designs for addressing this question, so were initially assigned high quality and downgraded based on potential sources of bias. Prospective and retrospective cohorts were both initially assigned high quality, as the majority of retrospective studies used very large national databases. Only studies presenting

adjusted analyses were included in the review, and the following covariates were indicated as the most relevant: gestational age, multiple birth, socioeconomic status, hypoxic events, and neonatal sepsis. Studies have been downgraded when their multivariate analysis included less than 3 of these covariates.

4.9.4.1.1 Quality of studies on antenatal risk factors

- Fetal growth retardation: 1 study, moderate quality
- Haemorrhagic events: 1 study, high quality
- Maternal infections: 3 studies, moderate to very low quality
- Multiple pregnancy: 3 studies, high to moderate quality

4.9.4.1.2 Quality of studies on perinatal risk factors

- Hypoxic ischaemic events: 3 studies, high to low quality
- Neonatal encephalopathy: 1 study, low quality
- Neonatal sepsis: 6 studies, high to moderate quality
- Choriomanionitis: 4 studies, high to low quality
- Apgar score at 10 min: 1 study, moderate quality

4.9.4.1.3 Quality of studies on postnatal risk factors

- Gestational age: 5 studies, high to low quality
- Neonatal infections: 1 study, moderate quality

4.9.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

4.9.6 Key conclusions

The Committee concluded that multiple factors play a key role in the aetiology of cerebral palsy, but that most of the studies analysed the magnitude of independent risk factors by using adjusted analyses. Clear evidence was shown for the following factors that have an independent role in contributing to the aetiology of cerebral palsy: gestational age, birth weight, serious maternal infections, neonatal encephalopathy, and neonatal sepsis.

4.10 Recommendations

1. Recognise the following as independent risk factors for cerebral palsy:

- antenatal factors:
  - preterm birth (with risk increasing with decreasing gestational age)[h]
  - chorioamnionitis
  - maternal respiratory tract or genito-urinary infection treated in hospital
- perinatal factors:
  - low birth weight
  - chorioamnionitis
  - neonatal encephalopathy
  - neonatal sepsis (particularly with a birth weight below 1.5 kg)

[h] The NICE guideline on developmental follow-up of preterm babies (publication expected August 2017) will contain more information about risk factors specific to preterm birth.

- maternal respiratory tract or genito-urinary infection treated in hospital
- postnatal factors:
  - meningitis.

2. Provide an enhanced clinical and developmental follow-up programme (see recommendation 12) for infants who have any of the risk factors listed in recommendation 1.

4.11 Research recommendations

1. What is the association between different antibiotic regimes to treat genito-urinary and respiratory tract infections in pregnant women and subsequent rates of cerebral palsy in children?

Table 14: Research recommendation rationale

Research question	What is the association between different antibiotic regimes to treat genito-urinary and respiratory tract infections in pregnant women and subsequent rates of cerebral palsy in children?
Why this is needed	
Importance to 'patients' or the population	Treatment of infection in pregnancy is of prime importance for the health of the mother. There is potential for beneficial and adverse effects on the foetus. In large population studies of pregnant women, choriamnionitis, other genitourinary infections and respiratory tract infections requiring admission to hospital are significant risk factors for the child of that pregnancy being given a diagnosis of cerebral palsy. The mechanisms are uncertain but include cytokine-induced damage to developing white matter leading to periventricular leukomalacia and sensitisation of the fetal brain to damage from hypoxia. Chorioamnionitis may precipitate preterm labour. Other infections are a risk to the mother's general health. Pyrexia during labour is a risk factor for neonatal encephalopathy and cerebral palsy.
Relevance to NICE guidance	High priority: Minimising known risk factors for development of cerebral palsy
Relevance to the NHS	Very large, if cases of cerebral palsy were reduced this would reduce the requirement in health, social and educational settings
National priorities	
Current evidence base	Conflicting
Equality	Risks of maternal infections are recognised at different prevalence in diff social-economic groups
Feasibility	
Other comments	

Table 15: Research recommendation statements

Criterion	Explanation
Population	Large multi-centre cohort of children and their mothers delivered in a number of the regions of the UK
Intervention	Data collection: Maternal infection and specific anti-biotic use from: Primary care and hospital data

Criterion	Explanation
	Neonatal and maternal discharge information Looking at outcomes: Developmental outcome via national screening programme at age 2 and 5
Comparator	No cerebral palsy
Outcome	Rates/risk of cerebral palsy
Study design	A prospective multi-centre study collecting prospective primary care and hospital data then linked to neonatal discharge diagnosis and outcome
Timeframe	Within 5 years

1

5 Causes of cerebral palsy

Review question: What are the most common causes of cerebral palsy in resource-rich countries with a view to informing relevant investigation and change in management?

5.1 Introduction

When parents are given a diagnosis of cerebral palsy for their child, it is natural that they wish to know the cause. Many children as they grow older wish to know what caused their problems with walking or talking or eating and drinking; hence, this is an important part of the initial discussions with parents and carers.

Overall, the number of children diagnosed with cerebral palsy in resource-rich countries has not significantly decreased in the last 30 years despite the introduction of investigations and interventions that have changed obstetric and neonatal practice. To be able to prevent cerebral palsy, it is essential to first understand the causes.

Understanding the difference between 'cause' and 'risk' is key. When looking for causation the clinician is working with the child who has cerebral palsy and is looking back. When looking at risk, the clinician is dealing with a child without diagnosis and is recognising potential factors that looking forward may lead to cerebral palsy in that child.

When reflecting on the history there are many factors found in the antenatal, perinatal and post-natal stages of children who are diagnosed with cerebral palsy. As such the individual child may have more than 1 factor which ultimately causes the non-progressive impairment of the brain. This lends strength to the concept of there being "Causal Pathways to Cerebral Palsy". Various risk factors acting at different times in the development of the fetal and neonatal brain may lead to similar pathologies resulting in brain damage and thereby a diagnosis of cerebral palsy.

There have been causes of cerebral palsy, in resource-rich countries, which have almost been eradicated over the last 20 years. With increasing mobility and population migration, these causes may re-appear within society as well as emergent new disease processes that can lead to cerebral palsy.

The aim of this evidence review was to identify the most common causes for cerebral palsy with the view to providing information for parents/carers and when appropriate to inform the need for further investigation and any change in management. The Committee prioritised the following as possible causes of cerebral palsy to be searched for in this review:

- Congenital brain malformations
- Congenital and acquired infection
- Intraventricular haemorrhage
- Periventricular leukomalacia (PVL)/ damage of the white matter/ white matter injury
- Hypoxic ischaemic injury (including perinatal and antenatal injury, stroke or focal infarcts)
- Neonatal Hypoglycaemia
- Neonatal encephalopathy
- Kernicterus
- Post-natal acquired traumatic brain injury

5.2 Description of clinical evidence

Seven studies have been included in this review that reported on the prevalence of causes of cerebral palsy in resource-rich countries (Ipek 2007; McIntyre 2013; O'Callaghan 2011; Cans 2004; Garne 2007; Bax 2006; Reid 2014).

The sample size ranged from 347 to 4584 cases of cerebral palsy.

One study included children with cerebral palsy from 8 European study centres (Bax 2006); 1 study looked at cerebral palsy of post-natal origin from the surveillance of cerebral palsy in Europe (SCPE) cohort (Cans 2004); 1 study used 11 cerebral palsy registries contributing to the SCPE cohort (Garne 2007); 1 study was a retrospective investigation of hospital cases of cerebral palsy (Ipek 2007); 1 study collected data by linkage to state-based perinatal repositories and cerebral palsy registries, and using a maternal questionnaire (O'Callaghan 2011); 1 study used the western Australian births register (McIntyre 2013); and finally 1 study included publications from 1995 to 2012 reporting imaging findings in cerebral palsy population cohorts (Reid 2014).

The following causes of cerebral palsy were covered by the included studies: white matter damage, basal ganglia lesions, focal infarcts, congenital malformations, infections, head injury, encephalopathy, and kernicterus.

In the selection process of papers, priority was given to studies that used registry data from a developed country.

Quality of the evidence was appraised by using the methodological tool validated by Munn 2014 which assesses critical issues of internal and external validity that must be considered when addressing validity of prevalence data. The criteria address the following issues:

- Ensuring a representative sample
- Ensuring appropriate recruitment
- Ensuring an adequate sample size
- Ensuring appropriate description and reporting of study subjects and setting
- Ensuring data coverage of the identified sample is adequate
- Ensuring the condition was measured reliably and objectively
- Ensuring appropriate statistical analysis
- Ensuring confounding factors/subgroups/differences are identified and counted for.

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

5.2.1 Summary of included studies

A summary of the studies that were included in this review are presented in Table 16.

Table 16: Summary of included studies

Study reference	Data source	Cause (s)	Quality of the study
Bax 2006	• 8 European study centres, 1996-1999 • 585 cases of cerebral palsy • 10.9% were preterm , with a very low gestational age (< 28 weeks)	Maternal infections, white-matter damage including PVL, basal ganglia lesions, malformations, focal infarcts, miscellaneous lesions.	HIGH

Study reference	Data source	Cause (s)	Quality of the study
Cans 2004	• SCPE (7 registers included) 1976-1990 • 347 cases of post-natal cerebral palsy	Infection, head injuries.	MODERATE • Data not reported by GA • Post-neonatal origin cerebral palsy only
Garne 2007	• 11 CP registries contributing to the SCPE, 1996-1976 • 4584 children with cerebral palsy, of whom 547 with a congenital malformation. • 5% were preterm , born at <28 weeks GA.	cerebral malformations non-cerebral malformations	HIGH
Ipek 2007	• Retrospective investigation of hospital cases (Turkey) • 371 cases of cerebral palsy • 22.6% were preterm .	Kernicterus	LOW • Hospital based population • Unclear how cerebral palsy diagnosis was made • Lack of details in reporting how causes of cerebral palsy were ascertained. • Data not reported by either gestational age, or cerebral palsy severity/motor distribution
O'Callaghan 2011	• Data were collected by linkage to state-based perinatal repositories and cerebral palsy registries, and using a maternal questionnaire. • 587 children with cerebral palsy. • 29.3% of children with cerebral palsy were preterm , with a GA<32 weeks (mean gestational age = 35.3)	Maternal infection during pregnancy: any, upper respiratory infections, gastrointestinal, herpes, fever, other infections (including cytomegalovirus, Ross River virus, chicken pox, staphylococcus, streptococcus, cystitis, wound infections, and UTI), labour and delivery complicated by infection, urinary tract infection (data reported by timing of infection).	MODERATE • Use of maternal questionnaire to identify infections (and other variables related to the CP population). • Data not reported by either gestational age, or CP severity/motor distribution.
McIntyre 2013	• Western Australian births register from 1980 to 1995. • 494 cases of cerebral palsy (singletons born after 35 weeks of gestation).	Encephalopathy, no encephalopathy, hypoxic-ischaemic encephalopathy. Data by distribution and type of CP.	MODERATE • Population limited to after 35 weeks GA

Study reference	Data source	Cause (s)	Quality of the study
Reid 2014	• Publications from 1995 to 2012 reporting imaging findings in population cohorts. Tot = studies from 5 different sites. • Sweden N = 289 • Quebec N = 213 • Victoria N = 563 • California N = 78 • Germany N = 56 • All children had cerebral palsy. • Data reported by gestational age, cerebral palsy subtype, and GMFCS level.	Distribution of MRI patterns: white matter injury, grey matter injury, malformations, focal vascular insults, miscellaneous.	HIGH

CP cerebral palsy, GA gestational age, GMFCS gross motor function classification system, MRI magnetic resonance imaging, UTI urinary tract infection, CMV cytomegalovirus, CNS central nervous system, SCPE surveillance of cerebral palsy in Europe.

5.2.24 Summary of results

5.2.2.15 White matter damage

Table 17: Prevalence of white matter damage (including PVL)

	Total						
Reid 2014, % range	**19.2 - 45.3**						
Bax 2006	**42.5 (25% were born >34 weeks of gestation)**						
Gestational age	**< 37 w**	**37 + w**					
Reid 2014, % range	31.3 – 70.9	11.9 – 31.8					
CP subtype	Spastic hemiplegia (unilateral spastic)	Spastic diplegia (bilateral spastic LL > UL)	Spastic quadriplegia (bilateral spastic LL + UL)	Bilateral spasticity	All spasticity	Ataxia	Dyskinesia
Reid 2014, % range	18.3 - 47.4	30.6 - 50.9	20.3 - 27.6	23.5 – 66.1	21.5 - 46.6	24%	6.7 – 39.4
Bax 2006	34.1%	71.3% (mixed)	35.1%	-	-	-	-
GMFCS level	**I/II**	**III**	IV	**V**			
Reid 2014, % range	22.2 – 49.7	16.7 – 43.7	12.8 – 45.9	7.7 – 29.3			

CP cerebral palsy, GMFCS gross motor function classification system, UL upper limbs, LL lower limbs, PVL periventricular leukomalacia

5.2.2.2 Basal ganglia lesions

Table 18: Prevalence of basal ganglia lesions

	Total	Dystonic CP
Bax 2006	12.8%	75.6%

CP cerebral palsy.

5.2.2.3 Focal infarcts

Table 19: Prevalence of focal infarcts

	Total
Bax 2006	7.4% (among children with unilateral cerebral palsy 27.5% were found to have a focal infarct).

5.2.2.4 Congenital malformations

Table 20: Prevalence of cerebral malformations

	Total						
Reid 2014, weighted mean % (95%CI)	**10.9 (9.0 – 12.7)**						
Bax 2006	**9.1%, of which 37.5% had unilateral cerebral palsy.**						
Garne 2007	**12%**						
Gestational age	**< 28 w**	**28 - 31 w**	**32 – 36 w**	**> 37 w**			
Reid 2014, weighted mean % (95%CI)	6.9 (4.1 – 9.6)			13.2 (10.4 – 16.0)			
Garne 2007	3%	2%	14%	71%			
CP subtype	**Spastic hemiplegia (unilateral spastic)**	**Spastic diplegia (bilateral spastic LL>UL)**	**Spastic quadriplegia (bilateral spastic LL+UL)**	**Bilateral spasticity**	**All spasticity**	**Ataxia**	**Dyskinesia**
Reid 2014, weighted mean % (95%CI)	13.2 (9.9 – 16.5)	5.2 (2.1 – 8.2)	15.7 (10.7 – 20.7)	10.4 (7.8 – 13.0)	11.4 (9.1 – 13.6)	18.0 (4.8 – 31.2)	3.9 (0.0 – 10.6)
Garne 2007	Spastic unilateral = 9%		-	8%	-	14%	6%
GMFCS level	**I/II**	**III**	**IV**	**V**			
Reid 2014, weighted mean % (95%CI)	8.2 (5.9 – 10.6)	6.6 (1.7 – 11.4)	12.2 (6.7 – 17.7)	18.2 (12.2 – 24.2)			

CP cerebral palsy; GMFCS gross motor function classification system; CI confidence intervals; w weeks, UL upper limbs, LL lower limbs.

5.2.2.5 Infections

Table 21: Prevalence of infections

Maternal infections	Any	UTI	Upper respiratory	Gastrointestinal	Herpes	Fever	Other
Bax 2006	39.5%	19.2%	-	-	-	-	-
O'Callaghan 2011	39.9%	• 4.4 %	• 0-20 wk GA= 10.1% • 21-40 wk GA= 9.4% • Within 1 wk after birth= 1.2%	• 0-20 wk GA= 2.4% • 21-40 wk GA= 3.7% • Within 1 wk after birth= 0.3%	• 0-20 wk GA= 2.9% • 21-40 wk GA= 2.0% • Within 1 wk after birth= 1.2%	• 0-20 wk GA= 2.2% • 21-40 wk GA= 3.4% • Within 1 wk after birth= 1.0%	• 0-20 wk GA= 2.7% • 21-40 wk GA= 5.6% • Within 1 wk after birth= 3.4%
Baby's infections	Total	Spastic unilateral	Spastic bilateral	Dyskinetic	Ataxia		
*Cans 2004**	50%	42.7%	45.3%	4.2%	7.6%		

Wk week; GA gestational age; UTI urinary tract infection
**post-neonatal cerebral palsy cases only*

5.2.2.6 Head injury

Table 22: Prevalence of head injury

	Total	Spastic unilateral	Spastic bilateral	Dyskinetic	Ataxia
*Cans 2004**	12.0%	60%	40%	0	0

**post-neonatal cerebral palsy cases only*

5.2.2.7 Encephalopathy

Table 23: Prevalence of encephalopathy

Neonatal encephalopathy						
	Total	Hemiplegia (unilateral spastic)	Diplegia (bilateral spastic LL>UL)	Quadriplegia (bilateral spastic LL+UL)	Dyskinesia	Ataxia or hypotonia
McIntyre 2013	12.4%	25%	8.3%	41.6%	13.3%	11.6%
Hypoxic-ischaemic encephalopathy						
	Total	Hemiplegia (unilateral spastic)	Diplegia (bilateral spastic LL>UL)	Quadriplegia (bilateral spastic LL+UL)	Dyskinesia	Ataxia or hypotonia
McIntyre 2013	21.2%	10.7%	18.4%	37.8%	27.2%	5.8%

Population limited to after 35 weeks GA, UL upper limbs, LL lower limbs.

5.2.2.8 Kernicterus

Table 24: prevalence of kernicterus

	Kernicterus, %
Ipek 2007	4.6

5.3 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations on the most common causes of cerebral palsy in resource-rich countries with a view to informing relevant investigation and change in management were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

5.4 Evidence statements

5.4.1 White matter damage

High quality evidence from two studies with 1784 infants and children with cerebral palsy found that the prevalence of white matter damage (including PVL) ranged between 19.2% and 45.3%. Evidence showed that the prevalence was higher in children born preterm, and varied depending on GMFCS level. Prevalence of white matter damage also varied depending on cerebral palsy subtypes, being higher in children with spastic cerebral palsy.

5.4.2 Basal ganglia lesions

High quality evidence from 1 study with 585 infants and children with cerebral palsy found that the prevalence of basal ganglia lesions was 12.8%. These damages were mainly associated with dystonic cerebral palsy, which accounted for 75.6% of the basal ganglia group.

5.4.3 Focal infarcts

High quality evidence from 1 study with 585 infants and children with cerebral palsy found that prevalence of focal infarcts was 7.4%. These infarcts were mainly associated with hemiplegia (unilateral spastic).

5.4.4 Congenital malformations

High quality evidence from 3 studies with 6368 infants and children with cerebral palsy found that the prevalence of congenital malformations ranged between 9.1% and 12%. Evidence showed that the prevalence was higher in children born at term compared to those born preterm, and varied depending on GMFCS level (higher prevalence with worse severity). Prevalence of malformations also varied depending on cerebral palsy subtypes, being 15.7% and 14-18% in children with spastic quadriplegia (bilateral spastic LL+UL) and ataxia, respectively.

5.4.5 Infections

High to moderate quality evidence from 2 studies with 932 infants and children with post-neonatal cerebral palsy (cases with an age of onset above 24 months) found that the

prevalence of maternal infections ranged between 39.5% and 39.9%, with UTI and upper respiratory tract infections being the most frequent.

Moderate quality evidence from 1 study with 587 infants and children with post-neonatal cerebral palsy found that the prevalence of infections in children was 50%, and it varied with the type of cerebral palsy (higher prevalence in spastic cerebral palsy).

5.4.6 Head injuries

Moderate quality evidence from 1 study with 587 infants and children with post-neonatal cerebral palsy (cases with an age of onset above 24 months) found that the prevalence of head injuries was 12%, and it varied with the type of cerebral palsy (higher prevalence in spastic cerebral palsy).

5.4.7 Encephalopathy

Moderate evidence from 1 study with 494 infants and children with cerebral palsy found that the prevalence of neonatal encephalopathy and hypoxic-ischaemic encephalopathy was 12.4% and 21.2%, respectively. The evidence also showed that both neonatal encephalopathy and hypoxic-ischaemic encephalopathy were more frequent in children with quadriplegia (bilateral spastic LL+UL).

5.4.8 Kernicterus

Low quality evidence from 1 study with 371 infants and children with cerebral palsy found that the prevalence of kernicterus was 4.6%.

5.5 Evidence to recommendations

5.5.1 Relative value placed on the outcomes considered

The aim of this review was to identify the most common causes for cerebral palsy with the view to providing information for parents/carers and to inform the need for further investigation and changes in management.

5.5.2 Consideration of clinical benefits and harms

The Committee agreed that when parents are given a diagnosis of cerebral palsy for their child, it is natural that they wish to know the cause. Causation of the brain impairment is therefore an important part of the initial clinical discussions with parents and carers. A full reflection on causation can also help young people as they become increasingly independent through adolescence, transition and young adulthood.

The Committee in particular recognised the importance of informing parents about antenatal, perinatal, postnatal factors associated with cerebral palsy, and agreed that it is often about a combination of ‘causes’ that leads to the overall diagnosis.

There was a long discussion about the clinical importance of differentiating cause as a reflective practice and consideration of potential risk as a forward thought process.

A recommendation for each possible cause was drafted based on the prevalence evidence presented. The Committee considered important to highlight the prevalence for white matter damage, deep grey matter/ basal ganglia damage, congenital malformation and focal infarcts.

The Committee was aware that the prevalence given by the papers was approximate, and therefore decided to supplement the evidence with their clinical knowledge and judgement.

Most of the evidence base was from very large registries with loose definitions of potential causation.

For white matter damage, the Committee formulated a recommendation about its distribution in preterm versus term babies, as well as in different motor presentation, i.e. spastic and dyskinetic cerebral palsy types. The Committee agreed that the information had been provided without confidence intervals and therefore should be used as a guide to the frequency rather than as accurate rates. The Committee recognised that in particular the ataxic form of cerebral palsy was the most difficult to identify for clinicians, and it was considerably rarer, hence it was a problem to be represented by the data.

When reviewing the evidence on cerebral malformations as possible causes of cerebral palsy, the Committee agreed the evidence showed a link with gestational age and motor distribution types.

The Committee referred to qualitative evidence in the literature, not reviewed within this protocol, which addressed the cumulative impact of pathological factors that in turn leads to causation of cerebral palsy. Based on their experience and knowledge of such additional evidence, they unanimously agreed it was important to develop a consensus recommendation to that effect. Neonatal encephalopathy was specifically noted as a clinical syndrome or endpoint resulting from a number of different pathological pathways. This highlights that it is not in its own right the cause, it is often the manifestation. It may be a symptom of brain damage that has already occurred as well as a symptom of ongoing brain damage from causes such as neonatal infection, or hypoglycaemia. The initial encephalopathic event can impact on the grade of severity of any hypoxic ischaemic event to the brain. It is usually more associated with a dyskinetic type of cerebral palsy.

The Committee considered the role of infection in causation of cerebral palsy. They agreed that there are specific viral infections of the fetal brain and infections of the neonate such as meningitis which can be direct causes of cerebral palsy. The Committee agreed that the role of maternal infections as risk factors and as a possible cause should also be explored in more detail. The prevalence of mothers of children with cerebral palsy reporting having background infection was not different from general population, the place of recurrent urinary tract infection and link to chorioamnioniitis and local inflammatory factors on the fetal environment in particular needs to be looked at carefully. The Committee considered that without a clarity of evidence base it was important to stress that maternal infections are commonly observed in every pregnancy and that specific linkage to an outcome of cerebral palsy in the child is limited. There are however a number of congenital viral infections that can lead to non-progressive impairment of the developing brain. Based on their clinical knowledge and although not presented by the evidence in the parameters of the review process, the Committee recommended that certain congenital infections have been associated with neurodevelopmental disorders.

The Committee decided not to comment specifically on Kernicterus as a possible cause of cerebral palsy. The evidence base presented was limited as it used a hospital-based population, without clear details on both how cerebral palsy was diagnosed and causes of cerebral palsy were ascertained. Historically very high levels of neonatal bilirubin are linked in particular to the development of a bilateral dystonic cerebral palsy. However routine screening for bilirubin levels in neonates and clear agreed pathways of management limits the impact in the wider population. It is however important to think about this as a potential cause particularly in migrant populations, where delivery has happened outside the UK. Further guidance on this is seen in other NICE guidelines on intrapartum care and Postnatal care up to 8 weeks after birth.

Finally, based on the evidence provided, the Committee drafted a specific evidence based recommendation on prevalence of postnatal causes of cerebral palsy, and mentioned specifically meningitis as the most reported among infective cause of non-progressive brain impairment.

In terms of minimising the impact of impairment to the development brain, thereby reducing risk, there are a number of interventions that the Committee is aware of, but they have not been reviewed specifically in this guideline. These include:

- antenatal steroids in threatened preterm delivery
- minimising fluctuation to cerebral blood flow and oxygenation in preterm infants
- minimising use of postnatal steroids
- neuroprotective approaches post neonatal encephalopathy, such as therapeutic hypothermia, xenon inhalation and the use of medicines that prevent secondary neuronal degeneration such as allopurinol.
- magnesium sulphate given to mother in preterm labour.

5.5.3 Consideration of economic benefits and harms

Knowing the most common causes of cerebral palsy may lead to better identification (and thus more timely management) and has therefore, indirectly, potentially important resource implications. However, this is an epidemiological review question and economic analysis is not applicable.

5.5.4 Quality of evidence

The quality of the evidence has been assessed by using the tool developed and published by Munn 2014.

Prevalence data can be sourced from various study designs. Therefore, studies have been assigned high quality and downgraded based on the limitations identified. Quality of the included evidence ranged between high and low; main reasons for downgrading were incomplete data reporting and unclear definitions used to identify either cerebral palsy or the cause.

5.5.5 Other considerations

The Committee considered the evidence for common causes of cerebral palsy as individual causes as well as sequences of interlinked factors termed “Causal Pathways to Cerebral Palsy”. This is important as there is a need for preventing the triggering factor, such as premature labour, as well as preventing and managing the downstream risk factor such as intraventricular haemorrhage. In addition, and for the same reason, the Committee examined the evidence presented together with the recommendations drafted and evidence presented for the magnetic resource imaging (MRI) causation review.

The recommendations related to this evidence review were based on the evidence and the Committee’s clinical experience.

5.5.6 Key conclusions

The Committee concluded that a number of brain abnormalities are reported in the evidence as possible causes of cerebral palsy, including white matter damage, basal ganglia damage, congenital malformations, and focal infarcts. The prevalence of such causes varies with the type and severity of cerebral palsy as well as level of prematurity of the child.

5.6 Recommendations

3. When assessing the likely cause of cerebral palsy in a child, recognise that a number of MRI-identified brain abnormalities have been reported at the following approximate prevalences in children with cerebral palsy:

- white matter damage: 45%
- basal ganglia or deep grey matter damage: 13%
- congenital malformation: 10%
- focal infarcts: 7%.

4. **When assessing the likely cause of cerebral palsy, recognise that white matter damage, including periventricular leukomalacia shown on neuroimaging:**
   - is more common in children born preterm than in those born at term
   - may occur in children with any functional level or motor subtype, but is more common in spastic than in dyskinetic cerebral palsy

5. **When assessing the likely cause of cerebral palsy recognise that basal ganglia or deep grey matter damage is mostly associated with dyskinetic cerebral palsy.**

6. **When assessing the likely cause of cerebral palsy, recognise that congenital malformations as a cause of cerebral palsy:**
   - are more common in children born at term than in those born preterm
   - may occur in children with any functional level or motor subtype
   - are associated with higher levels of functional impairment than other causes.

7. **Recognise that the clinical syndrome of neonatal encephalopathy can result from various pathological events, such as a hypoxic–ischaemic brain injury or sepsis, and if there has been more than one such event they may interact to damage the developing brain.**

8. **When assessing the likely cause of cerebral palsy, recognise that neonatal encephalopathy has been reported at the following approximate prevalences in children with cerebral palsy born after 35 weeks:**
   - attributed to a perinatal hypoxic–ischaemic injury: 20%
   - not attributed to a perinatal hypoxic–ischaemic injury: 12%.

9. **Recognise that for cerebral palsy associated with a perinatal hypoxic–ischaemic injury:**
   - the extent of long-term functional impairment is often related to the severity of the initial encephalopathy
   - the dyskinetic motor subtype is more common than other subtypes.

10. **Recognise that for cerebral palsy acquired after the neonatal period, the following causes and approximate prevalences have been reported:**
    - meningitis: 20%
    - other infections: 30%
    - head injury: 12%.

11. **When assessing the likely cause of cerebral palsy, recognise that independent risk factors:**
    - can have a cumulative impact, adversely affecting the developing brain and resulting in cerebral palsy

- may have an impact at any stage of development, including the antenatal, perinatal and postnatal periods.

5.7 Research recommendations

None prioritised for this topic.

6 Clinical and developmental manifestations of cerebral palsy

Review question 1: What are the key clinical and developmental manifestations of cerebral palsy at first presentation?

Review question 2: What are the best tools to identify clinical and developmental manifestations of cerebral palsy at first presentation?

6.1 Introduction

The diagnosis of cerebral palsy is often made over a period of time, based on sequential clinical observations and assessments of movement and posture, associated with activity limitation. In clinical practice, the diagnosis of cerebral palsy is typically based on observations and parent report on attainment and quality of motor milestones, such as sitting, pulling to stand, and walking, feeding and evaluation of posture, deep tendon reflexes, and muscle tone.

Infants with risk factors are monitored and watched for developing possible signs of cerebral palsy. Infants without risk factors may present with signs and symptoms noticed by parents or during routine baby surveillance. Some signs are visible in the neonatal period, whilst others evolve as the infant develops. The time taken between original suspicion of developmental problems and actual diagnosis can be frustrating for families. Early intervention should be based on the child's need and not dependant on diagnosis but it is vitally important to give the family an accurate diagnosis and this can take time.

Early signs and symptoms, particularly among preterm children can be transient and may not result in long term impairment. Not all signs are visible at birth and may evolve and become more obvious as babies develop. Some of these symptoms are not specific for cerebral palsy.

The Committee hence looked for reliable objective and valid tools that could be used when an infant first presents to predict those who are at likely to develop cerebral palsy and those where the likelihood of developing cerebral palsy is low.

The objectives of this review were to determine the key clinical and developmental manifestations of cerebral palsy and to assess the tools that can assist health professionals (community, primary or secondary) to recognise children with cerebral palsy.

6.2 Description of clinical evidence

A list of clinical and developmental manifestations, including features which are commonly observed in clinical practice, was compiled by the Committee. Two relevant age subgroups were identified: infants below 8 months and infants and children above 8 months. The Committee recognised that routine developmental screening in the UK utilises the lack of independent sitting at 8 months as a sign of abnormal motor development. Therefore, before 8 months, it is more difficult to use delay in motor development as a clue for evolving cerebral palsy and so you need to look for more subtle signs.

In these review questions, the study design prioritised was a prospective cohort. The quality of cohort designs were classed as high quality and downgraded according to the adapted GRADE method.

A total of 18 studies with a total of n = 8239 participants were included in this review. Studies were carried out in Norway (Adde 2007), USA (Allen 1992/Allen1994, Morgan 1996), South

Africa (Burger 2011)India (Chaudhari 2010), Italy (Brogna 2013, Ferrari 2002), UK (Johnson 1990), Slovenia (SemiCiglenecki 2003), Australia (Spittle 2013; Morgan 2016), Zimbabwe (Wolf 1997) and 4 studies were from the Netherlands (Bouwstra 2010, Bruggink 2008/2009, Groen 2005, Heineman 2011). 17 studies included had a prospective cohort study design, in which an index test to measure clinical and/or developmental manifestations was carried out at baseline and a reference test to diagnose cerebral palsy was carried out at follow-up. One study (Allen 1992/1994) was a case control design which used population norms as a control group.

Sixteen studies (Adde 2007, Allen 1992/1994, Boustra 2010, Brogna 2013, Bruggink 2008/2009, Burger 2011, Ferrari 2002, Heineman 2011, Johnson 1990, Morgan 1996, Morgan 2016; SemeCiglenecki 2003, Spittle 2013 and Wolf 1997) provided diagnostic accuracy measures including: sensitivity, specificity, positive predictive value, negative predictive value and area under the receiver operating characteristic (ROC) curve, referred to as area under the curve (AUC) throughout this review. The remaining studies provided associations between the manifestation at presentation and diagnosis at follow-up.

There were two studies that looked at using tools to identify clinical and developmental manifestations of cerebral palsy (Morgan 1996, Spittle 2013). The tools investigated were the Early Motor Pattern Profile and the Bayley Scales of Infant and Toddler Development.

For full details see review protocol in Appendix D. Evidence are summarised in the clinical GRADE evidence profile in Appendix H. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

6.2.12 Summary of included studies

A summary of the studies that were included in this review are presented in Table 25.

Table 25: summary of included studies

Study	Index and reference tests	Population	Outcomes	Comments
Adde 2007	Index: GMA using Prechtl classification of fidgety movements by video recordings at 10 to 18 weeks post-term Reference: diagnosis at 2 years by MDT	Preterm infants were enrolled through NICU and healthy term infants through maternity ward. High risk: n = 25 (both preterm and term) Low risk: n = 49 (both term and healthy preterm)	Outcome of GMA: abnormal or normal fidgety movements. Sensitivity, specificity, positive predictive value and negative predictive value available.	
Allen 1993	Index: Developmental assessments including history of delayed motor milestones Reference: Diagnosis of CP based on a significantly abnormal neurological examination at	N= 173 High risk preterm infants discharged through NICU N=381 population controls (term infants followed until 2 years old)	Motor milestone attainment determined by population norms: • Roll over from supine to prone • Sit with arm-support • Sit without arm support • Creep • Crawl • Come to a sitting	Controls are from the wider population. No 95% CI given in the paper.

Study	Index and reference tests	Population	Outcomes	Comments
	18-24 months		position from prone to supine independently • Pull to a stand from crawl or sit • Cruise • Walk independently Sensitivity, specificity and positive predictive value available.	
Bouwstra 2010	Index: quality of GMs using Hadders-Algra 2004 classification by video recording at 3 months Reference: diagnosis of CP using criteria of the international collaboration Surveillance of Cerebral Palsy in Europe at 3 years and 9 months.	N = 455 infants in the primary care setting, attending 6 'well-baby' clinics which provide scheduled assessments.	Outcome of quality of general movements: definite abnormal or non-definite abnormal general movements. Sensitivity, specificity, positive predictive value and negative predictive value available.	
Brogna 2013	Index: GMA (writhing stage at 1 month and fidgety stage at 3 months) Reference: Neurodevelopmental outcome at 2 years (Touwen's criteria and Bayley scale)	N=640 eligible infants N=574 included due to missing data	Sensitivity and specificity	Unable to calculate other measures and the 95% CI
Bruggink 2008/2009	Index: quantitative aspects of the motor repertoire between 6 and 24 weeks, specifically ATN Reference: Towen's neurological examination at 7-11 years of age	N=82 (out of a larger group of 99 recruited for other prospective studies). Preterm, NICU infants.	Under 8 months: Abnormal muscle tone (assessed by ATN) at 11-16 weeks Data was given for quality of fidgety movements but sensitivity/ specificity data could not be calculated without adding bias (combining groups).	Sensitivity, specificity, positive predictive value and negative predictive value were calculated from the data provided in the study.
Burger 2011	Index: GMA at 12 weeks corrected	N= 115 preterm infants admitted to	Outcome of GMA: abnormal or normal	95% CI for data was not

Study	Index and reference tests	Population	Outcomes	Comments
	age Reference: Neurological examination at 12 months (in line with those of Amiel-Tison, Gosselin, the Peabody Developmental Motor Scale and Alberta Infant Motor Scale)	level 2 neonatal ward or NICU	fidgety movements. Sensitivity, specificity, positive predictive value and negative predictive value available.	provided in the study and has been calculated. Sensitivity analysis was carried out for the 'suspect' infants Note: study was carried out in South Africa
Chaudhari 2010	Index: assessment of tone abnormality according to Amiel-Tison (1986) method at 3, 6, 9 and 12 months. Infants then were followed up to at least 5 years and classified to: normal, transient tone abnormalities and CP. Reference: preschool inventory described by Ayres, Bobath consisting of 7 areas of development.	N = 190 high risk N = 49 controls, all from neonatal unit.	Proportion diagnosed with CP.	This study was conducted in India- to discuss generalizability to a UK population with committee.
Ferrari 2002	Index: GMA; cramped synchronized character Neurological examination (Dubowitz and Dubowitz (preterm), Prechtl (term), Touwen (post term) Reference: Neurological outcome (Griffiths scale at 2-3 years)	N= 93 infants enrolled preterm, ultrasound scan showed abnormalities highly suggestive of a brain parenchymal insult N=84 included in final sample (9 missing data)	Outcome of GMs, cramped synchronized GMs, and neurological examination results Sensitivity, specificity, positive predictive value and negative predictive value and area under the curve available.	No 95% CI provided
Groen 2005	Index: GMA using Prechtl 1977 classification with age-specific	N = 24 high risk N = 28 low risk	Proportion diagnosed with CP at 4 to 9 years. Association	

Study	Index and reference tests	Population	Outcomes	Comments
	adaptions according to Touwen 1976) during preterm GMs age (before 38 weeks postmenstrual age, during writhing GMs age (38 to 47 weeks) and during fidgety GM age (8 to 17 weeks) Reference: standardised and age-specific neurological examination according to Touwen 1979 at follow up.		between GMs classification and diagnosis. Association between discrepancy in movement quality and diagnosis at writhing GM age and fidgety GMs age. Association between type of non-fluent general movement (e.g. jerky and stiff) at writhing and fidgety GMs age.	
Heineman 2011	Index: IMP at 4, 6, 10 and 12 months. Reference: Hempel assessment at corrected age of 18 months	N = 59 preterm (high risk) N = 30 term (low risk)	AUC for 4, 6, 10 and 12 months.	It is important to note that the lowest AUC values (poorest discriminative ability) were obtained for the 'symmetry' domain of the IMP score, while the highest (excellent discriminative ability) were for 'variation' and 'motor performance' domains of IMP.
Johnson 1990	N/A	N=4527 eligible infants (<2kg birthweight or admitted to a special care nursery for >24hrs in the neonatal period N=61 died before 18 months N=4275 assessed at 18 months	Walking at 18 months Proportion diagnosed, sensitivity, specificity and PPV.	No 95% CI reported Note: not corrected for gestational age
Morgan 1996	EMPP Reference: Motor outcome	N=1336 eligible high risk infants N=1247 (36	Proportion diagnosed, sensitivity, specificity, PPV and	No 95% CI reported. This has been calculated.

Study	Index and reference tests	Population	Outcomes	Comments
		months of follow up data)	NPV available at 6 and 12 months.	
Morgan 2016	GMA	N = 259 high risk infants, 1-year follow up data available for N = 187	Sensitivity and specificity of GMA in detecting cerebral palsy	
SemeCiglenecki 2003	Index: GMA Neurological examination (Amiel-Tison and Grenier) at 3 months Reference: Neurological examination (Illingworth) at 2 years	N=232 High risk group n=120 (had GMA and neurological examinations) Low risk group n=112 (neurological examinations only) Age corrected by calculated delivery date	Proportion diagnosed, sensitivity, specificity, positive predictive value and negative predictive value.	No 95% CI reported.
Spittle 2013	Index tool: Bayley-III Motor Scale Index: MABC-2	N= 115 completed the Bayley III at 2 years N=96 completed the MABC-2 at 4 years	Proportion diagnosed, sensitivity, specificity, positive predictive value and negative predictive value.	
Wolf 1997	Index: NNE at term or by latest 5 days after birth adapted from Prechtl (1977) and several items included (see GRADE table in appendix H). Reference: At 1 year, examination including medical history, physical examination BSID.	All infants with Apgar score of below 5. N = 142 term, of which 16 were SGA N = 26 preterm, of which 4 were SGA	Proportion diagnosed, sensitivity, specificity, positive predictive value and negative predictive value available.	It is important to note that all these infants had a low Apgar score.

GMA General Movement Assessment, SGA small for gestational age, MDT multidisciplinary Team, NICU neonatal intensive care unit, CI confidence interval, CP cerebral palsy, ATN asymmetric tonic neck posture, UK United Kingdom, GMs general movements, KG kilogram, AUC area under the curve, IMP Infant Motor Profile, EMPP Early Motor Pattern Profile, MABC-2 Movement Assessment Battery for children – second edition, NNE Neonatologist Neurological Assessment, BSID Bayley Scale of Infant Development, PPV positive predictive value, NVP negative predictive value, N/A not applicable.

6.3 Clinical evidence profile

The following is an overview of the diagnostic accuracy outcomes presented in the modified GRADE tables:

True positive:

The patient has the disease and the test is positive.

Sensitivity:

Probability of being test positive when disease present. Calculated:

= true positive / (true positive + false negative)

Specificity:

Probability of being test negative when disease absent. Calculated:

= true negative / (true negative + false positive)

PPV:

Probability of patient having disease when test is positive. Calculated:

= true positive / (true positive + false positive)

NPV:

Probability of patient not having disease when test is negative. Calculated:

= true negative / (false negative + true negative)

AUC:

A graphical plot of true positive rate (sensitivity) against false positive rate (1 − specificity)

The following criteria was used to define the diagnostic accuracy outcomes:

Sensitivity and Specificity:

- High – 90% and above
- Moderate – 75% to 89.9%
- Low – 74.9% or below
- PPV:
- High – 75% and above
- Low – below 75%
- NPV:
- High – 70% and above
- Low – below 70%
- AUC:
- The classifications of area under the ROC curve (AUC) are as follows (Cook 2008):
- ≥ 0.900 = excellent discriminative ability
- 0.800–0.899 = good discriminative ability
- 0.700–0.799 = fair discriminative ability
- 0.501–0.699 = poor discriminative ability
- 0.000–0.500 = no discriminative ability.

These values have been used in previous NICE guidelines. The Committee was presented with these thresholds and they were comfortable with using them. The specific uses of a diagnostic test and which measures were to be of most interest (e.g. for rule in / rule out) were discussed with the Committee and recommendations were made accordingly.

Please see all GRADE tables in Appendix H.

6.4 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations of the key clinical and developmental manifestations that are predictive of cerebral palsy were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

6.5 Evidence statements

6.5.1 Clinical manifestations

6.5.1.1 Abnormality of movement

High quality evidence was obtained for 1 study with n = 187 participants which used the General Movement Assessment (GMA) to assess the quality of fidgety movements at 12 to 20 weeks post-term in high risk infants. Forty-eight high risk infants had absent fidgety (high risk for cerebral palsy), resulting in high diagnostic accuracy of this method in predicting cerebral palsy (above 90%) for sensitivity and specificity.

Moderate quality evidence was obtained for 1 study with n = 74 participants which used the GMA (Prechtl 1977) to assess the quality of fidgety movements at 10 to 18 weeks post-term in high and low risk infants. Ten high risk infants were diagnosed with cerebral palsy cerebral palsy (quadriplegia, right hemiplegia, left hemiplegia and 1 unspecified cerebral palsy cerebral palsy). The diagnostic accuracy of this method in predicting cerebral palsy was high (above 90%) for sensitivity, specificity, PPV and NPV.

Moderate quality evidence from 1 study with n = 142 participants used the neonatal neurological examination (NNE) adapted from Prechtl 1977 with several added predictors including variation of movement in term and preterm infants at birth or by 5 days after birth. This method had low sensitivity, but high specificity, PPV and NPV.

Moderate quality evidence from 1 study with n = 52 participants used GMA used the Prechtl 1977 method with age adaptions of the norm according to Touwen 1976. Of the 8 diagnosed with cerebral palsy, 3 were classified by GMA as having definitely abnormal (DA) movements, 4 were DA and 1 was mildly abnormal at fidgety age (8 to 17 weeks post-term). Seven diagnosed with cerebral palsy had cramped synchronised general movements, which was significantly associated with cerebral palsy development. Four had predominantly jerky movement at fidgety General Movements (GMs) age and 4 had jerky and stiff movements at writhing age (38 – 47 weeks post-term).

High quality evidence was obtained for 1 study with n = 455 participants which assessed quality of movements, grouped into ‘definite abnormal general movements’ according to method described by Hadders-Algra 2004 in the primary care setting (‘well-baby’ clinics providing routine assessments). Definite abnormal GMs had high specificity and NPV when predicting cerebral palsy, but low sensitivity and PPV.

Very low quality evidence was obtained from 1 study with n = 89 participants which used infant motor profile (IMP) to assess motor behaviour in preterm and term infants at 4, 6, 10 and 12 months. IMP had excellent discriminative ability at predicting cerebral palsy, as calculated by AUC, at 6, 10 and 12 months and good discriminative ability at 4 months.

Low quality evidence from 1 study with n=574 high risk infants used the GMA at 1 and 3 months. The reference test was carried out at 2 years and consisted of a neurodevelopmental assessment (Touwen's and Bayley scale). 22 infants were diagnosed with cerebral palsy (4%). The sensitivity and specificity were 100% and 86% during the writhing period (1 month) and 100% and 97% respectively during the fidgety period. No 95% confidence intervals (CI) were provided.

Low quality evidence from 1 study with n=115 preterm infants used the GMA (Prechtl 1977) to determine the quality of fidgety movements at 12 weeks. 9 infants were diagnosed with cerebral palsy (quadriplegia (n=1), diplegia (n=5), hemiplegia (n=2 left, n=1 right). Sensitivity analysis was carried out incorporating the 'suspect' infants into the normal group, abnormal group and excluded from analysis. Excluded from analysis (n=110) there was high specificity, NPV and PPV with moderate sensitivity (89% [95% CI 51.75%-99.72, calculated from the paper]. Suspect infants included in the normal group resulted in a moderate sensitivity, specificity and NPV, and high PPV (no CI reported). Including the 'suspect' infants in the abnormal group resulted in a moderate sensitivity and high specificity, PPV and NPV,

Moderate quality evidence from 1 study with 84 preterm high risk infants used the quality of GMs, cramped synchronized movements and neurological examination at preterm (<37 weeks), term (38-42 weeks) and post term to predict cerebral palsy in patients aged 2-3 years. 44 infants were diagnosed with cerebral palsy (n=22 diplegia, n=14 tetraplegia, n=8 hemiplegia). The area under the ROC for GMs was 97.4 (no 95% CI given). GM assessment had 100% sensitivity and NPV for all ages, the specificity and PPV only becomes moderate at 47-60 weeks postmenstrual age. Cramped synchronized character has high specificity and PPV for all age groups. Sensitivity and NPV is low until > 43 weeks where it is moderate. Neurological performance is low across all measures up to 43 weeks. Sensitivity and NPV are high only at 47-60 weeks.

Moderate quality evidence from 1 study with 232 infants (randomly selected from 930 eligible infants) of which 120 were classed as high risk and 112 (control group) low risk. The GMA was carried out at 3 months in the high risk group and a classical neurological examination in both groups. At 2 years all infants had a further neurological examination according to Illingworth. The high risk group had 32 (27%) infants with abnormal neurological development (13 cerebral palsy without mental retardation, 18 cerebral palsy with mental retardation, 1 mental retardation). The low risk group had 35 (31%) infants with abnormal neurological development (11 cerebral palsy without mental retardation, 22 cerebral palsy with mental retardation, 3 mental retardation). The GMA had high sensitivity, specificity and NPV with moderate PPV. The classic neurological examination had high sensitivity and NPV with low specificity and PPV (No 95% CI provided).

Under 8 months old

6.5.1.2 Excessive crying/irritability

Moderate quality evidence from 1 study with n = 142 participants used the NNE adapted from Prechtl 1977 with several added predictors including irritability and consolability in term and preterm infants at birth or by 5 days after birth. This method had low sensitivity, but high specificity, PPV and NPV.

6.5.1.3 Feeding difficulties

Moderate quality evidence from 1 study with n = 142 participants used the NNE adapted from Prechtl 1977 with several added predictors including nasogastric tube feeding in term and preterm infants at birth or by 5 days after birth. This method had low sensitivity, but high specificity, PPV and NPV.

6.5.1.41 Asymmetry of movement

Very low quality evidence from 1 study with n = 89 participants which used IMP to assess motor behaviour in preterm and term infants at 4 and 6 months. Total IMP score had excellent discriminative ability at predicting cerebral palsy at 6 months and good discriminative ability at 4 months. However, the subscale of 'movement symmetry' had poor discriminative ability at predicting cerebral palsy at both 4 and 6 months (only total IMP score presented in GRADE).

6.5.1.58 Abnormal muscle tone

Low quality evidence from 1 study with n = 239 participants assessed tone abnormalities using the method described by Amiel-Tison 1986 at 3 and 6 months until 12 months in high and low risk infants. Ten high risk infants were diagnosed with cerebral palsy (4 hypertonia, 5 hypotonia) when followed up for 5 years and all of these infants had tone abnormalities.

Moderate quality evidence from 1 study with n=82 infants reviewed the quantitative aspects of the motor repertoire between 6 and 24 weeks (post term) and the results of a neurological examination (Touwen's) at 7-11 years of age. Results were given for the presence and absence of an obligatory asymmetric tonic neck posture (ATN) at 11-16 weeks and neurological findings at school age, taking in to account the quality of the fidgety movements (FMs) and concurrent motor repertoire (smooth and variable, abnormal: monotonous, jerky and/or stiff). No children were diagnosed with cerebral palsy who had abnormal FMs or normal FMs with a smooth and variable motor repertoire at 11-16 weeks. One infant was diagnosed with cerebral palsy who had normal FMs but abnormal motor repertoire (100% sensitivity, 74% specificity, 12.5% PPV, 100% NPV [large 95% CI for all figures]. The remaining diagnoses of cerebral palsy were children who had absent FMs and abnormal motor repertoire with an equal presence of an obligatory ATN posture (6 and 6 respectively) which had 100% specificity, 50% sensitivity (very large CI).

Over 8 months old

6.5.1.67 Asymmetry of movement

Very low quality evidence from 1 study with n = 89 participants which used the IMP to assess motor behaviour in preterm and term infants at 10 and 12 months. Total IMP score had excellent discriminative ability at predicting cerebral palsy at 10 and 12 months. However, the subscale of 'movement symmetry' had poor discriminative ability at predicting cerebral palsy at both 10 and 12 months (only total IMP score presented in GRADE).

6.5.1.73 Feeding difficulty

No evidence was retrieved for this clinical manifestation.

6.5.1.85 Persistent toe walking

No evidence was retrieved for this clinical manifestation.

However, it is important to note that very low quality evidence from 1 study with n = 89 participants using IMP has a 'variability' subscale (reported as 'variation' in the study) which includes 'variability of toe movements'. This subscale has excellent discriminative ability at predicting cerebral palsy at 10 and 12 months (only total IMP score reported in GRADE).

6.5.21 Developmental manifestations

6.5.2.12 Delayed sitting in under 8 months old

3 Very low quality evidence from 1 case control study (Allen 1992, Allen 1994) looked at the
4 delay in attaining motor milestones in very preterm infants (n=173). The controls used were
5 term infants (n=381) that were followed to 2 years of age. Analyses were carried out against
6 population and race specific norms. Sitting without support and come to sit for both white and
7 non-white very preterm infants had poor PPV (range 31-56%). White very preterm infants
8 had similar sensitivity (range 87- 94%) and moderate to low specificity compared to the non-
9 white very preterm infants for both milestone measures.

10 The delay criteria of 12.5%, 25%, 37.5% and 50% were also analysed. It was found that as
11 the delay criteria increased the sensitivity decreased and specificity and PPV increased.

12 Very low quality evidence from 1 study with n = 89 participants using IMP has a
13 'performance' subscale which includes 'ability to sit'. This subscale has excellent
14 discriminative ability at predicting cerebral palsy at 4 months and good discriminative ability
15 at 6 months (only total IMP score reported in GRADE).

6.5.2.216 Delayed walking in over 8 months old

17 Very low quality evidence from 1 case control study (Allen 1992, Allen 1994) looked at the
18 delay in attaining motor milestones in very preterm infants (n=173). The controls used were
19 term infants (n=381) that were followed to 2 years of age. Walking independently had high
20 sensitivity in white and non-white preterm infants against population and race specific norms
21 (range 94-100%). Specificity was moderate (73-75%), and PPV low (37-44 in non-white, 58%
22 white infants).

23 Moderate quality evidence from a prospective cohort study (n=4275 analysed) assessed the
24 proportion of infants (low birthweight (<2kg) or >24 hours in special care nursery) who were
25 walking at 18 months and its relationship with the diagnosis of cerebral palsy. There were
26 410 infants walking of which 66 were diagnosed with definite cerebral palsy and 11
27 suspected. Including the suspected cases, there was moderate sensitivity and high
28 specificity with low PPV (no 95% CI provided).

29 Very low quality evidence from 1 study with n = 89 participants using IMP has a
30 'performance' subscale which includes 'walking. This subscale has excellent discriminative
31 ability at predicting cerebral palsy at 10 and 12 months (only total IMP score reported in
32 GRADE).

6.5.2.33 Use of tools to identify clinical and developmental manifestations of cerebral palsy

6.5.2.434 The Early Motor Pattern Profile (EMPP)

35 Moderate quality evidence from a prospective cohort study looked at the use of the EMPP to
36 predict cerebral palsy at 6 and 12 months (corrected age). 1247 high risk infants were
37 included in the study. Both time points yielded moderate or high sensitivity, specificity, PPV
38 and NPV.

39 • The Bayley Scales of Infant and Toddler Development – Third edition (Bayley-III)

40 High quality evidence from a prospective cohort study which used the Bayley-III to assess
41 motor impairment at 2 years of age to predict motor outcome at 4 years. 115 infants
42 completed the Bayley-III assessment and 96 the Movement Assessment Battery for Children
43 – Second Edition (MABC-2) at 4 years. When a cut off of -1SD was used, there was
44 moderate sensitivity (wide 95% CI), high specificity and NPV with a low PPV (wide 95% CI).

A cut off of -2SD had low sensitivity (wide 95% CI) and high specificity, NPV and PPV (wide 95% CI).

6.63 Evidence to recommendations

6.6.14 Relative value placed on the outcomes considered

Critical outcomes, as stated by the Committee, were sensitivity and specificity. Important outcomes included: PPV, NPV, AUC, likelihood ratios and proportion diagnosed.

6.6.27 Consideration of clinical benefits and harms

The Committee discussed that the prediction and diagnosis of cerebral palsy are distinct areas. Prediction is as much about recognising risk factors in the history as well as subtle abnormalities on examination. Diagnosing is about hard neurological findings on examination with a history of delay in achieving a developmental milestone or skill. The prediction of cerebral palsy involves the recognition of clinical and developmental manifestations, such as atypical movements, which can allow further assessment and later diagnosis of cerebral palsy. The Committee agreed that these clinical and developmental manifestations allow the early detection of cerebral palsy and are important as they are not widely assessed or recognised at first presentation, which means that children with cerebral palsy can remain undetected until clinical diagnosis at a later age, and therefore not receive beneficial early care.

The Committee agreed that those at high risk should have neonatal follow up for the first few months of infancy and those at low risk should receive the standard follow-up assessments that are undertaken as part of the healthy child programme. The Committee were aware of the NICE guideline currently in development (due for publication in August 2017) on developmental follow-up of preterm babies which would provide guidance in terms of the babies born preterm. Additionally, the Committee noted that there was a need for the continuous record of what children do from presentation so there is a record of change and that signs may not be obvious at first presentation. For example, dyskinetic cerebral palsy may often present as stiffness, irritability and/or low muscle tone in the first year of life. The Committee also pointed out that children with milder forms of cerebral palsy may present to health services for the first time with difficulties of motor function even after age 5 years.

For high risk infants, the GMA was recommended in the first 6 months to identify features suggestive of cerebral palsy to supplement routine clinical examination. This was supported both by the evidence as most studies used the GMA as part of their assessments and was in line with the Committee's experience. The GMA allows health care professionals to identify high risk infants which require further assessment and follow up. Therefore, it has not been recommended as a method of diagnosis, rather as a method of identifying children requiring further assessment. If false positives or false negatives arise using this method, children will still receive further assessment and follow-up until the diagnosis of cerebral palsy is ruled in or out. Additionally, the Committee agreed that high risk infants should continue to receive multidisciplinary assessment undertaken by professionals with specialist training for the first 2 years of life.

In the low risk infants and children, the Committee agreed that it was reasonable to expect that routine screening assessments would identify infants with delayed and abnormal motor milestones and to facilitate onward referral to the child development centre for further assessment.

The Committee agreed that based on the evidence reviewed and their clinical experience that health care professionals who are working with young infants either as part of a follow-up of high risk infants or a developmental surveillance programme should be able to recognise the following clinical features as suggestive of cerebral palsy: unusual fidgety and

abnormal movements, asymmetric movements, abnormal tone, and abnormal motor development.

In terms of developmental milestones, the Committee considered that the evidence reviewed and their clinical experience supported a recommendation to refer children who demonstrated late sitting and late walking for further assessment. Based on their clinical experience, the Committee agreed that hand preference before the age of 1 should also be a developmental concern to trigger further assessment as they recognised that hand preference is often not seen until children are 2-3 years of age.

Although no significant evidence was found on toe walking, the Committee considered that based on their clinical experience, children who display obvious and persistent toe-walking on its own should be referred for onward assessment.

Finally, the Committee pointed out that in children in which there is a motor delay concern and if a cerebral palsy diagnosis cannot be made then health care professionals should explain to parents the reasons of the increased surveillance. Motor delay may be a sign of muscle disease, peripheral nerve disorders, or learning difficulties. It may also be due to the child being at the slower end of the normal developmental spectrum. As it may take some time for the abnormal neurological signs to appear that would help confirm a diagnosis of cerebral palsy, it may not be possible to give the child a definite diagnosis at first presentation. Therapy can be started based on the child's developmental problems whilst waiting for a diagnosis to be made with time.

The Committee noted the importance of communication between all tiers of service involvement to ensure the best quality care is provided to all children and young people with cerebral palsy. They also agreed that involvement of primary care services in all discussions about ongoing management of the child and young person with cerebral palsy is crucial.

6.6.3 Consideration of economic benefits and harms

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action. Even so, there are considerations for the resources and costs enhanced surveillance and referrals to child development centres may entail.

Specifically, the Committee highlighted that identifying the clinical and developmental manifestations requires enhanced surveillance for infants and children who have spent time in specialist neonatal care who are at increased risk of developing cerebral palsy. To prevent geographical variation the Committee wanted to make recommendations that identified the levels of surveillance infants and children with cerebral palsy should receive.

The Committee agreed that referrals to child development centres, or enhanced clinical and developmental follow-up programmes would not be considered cost-effective if they do not add any additional information to routine monitoring and do not lead to an improvement in the infant or child's management strategy. The Committee noted that recommendations on the population identified to require enhanced surveillance, and the frequency of that surveillance could have significant resource implications. However, as the Committee advised that enhanced follow-up programmes should only be provided for infants and children who are at increased risk of developing cerebral palsy there should not be a large increase in the demand for enhanced surveillance as those risk factors outlined for cerebral palsy in recommendation 1 already trigger closer surveillance and is already accepted current clinical practice.

The Committee advised that infants with delayed and abnormal motor milestones would be identified during routine screening assessments, at no additional cost as this is part of the national 'red book' screening programme. The Committee also noted that delayed and abnormal motor milestones already facilitate onward referral to the child development centre

for further assessment in current clinical practice. The Committee concluded that the findings from the clinical evidence review, combined with their clinical experience, supported a recommendation to justify current NHS expenditure to refer all infants and children who demonstrated late sitting and late walking for further assessment.

The Committee also added that although no significant evidence was found on toe-walking, children who display obvious and persistent toe-walking are often referred for onward assessment in clinical practice, and many are subsequently identified with cerebral palsy. Therefore, referrals initiated from toe-walking or delayed and abnormal motor milestones may lead to a timely change in the child's management, potentially increasing their quality of life and evading downstream costs from complications that could arise from unidentified cases of cerebral palsy.

Overall, knowing the key clinical manifestations of cerebral palsy may lead to better identification (and thus more timely management) and has therefore, indirectly, potentially important resource implications. However, while the costs of referrals or enhanced surveillance could be significant, without knowing the outcomes of those services, we cannot know if they will be cost-effective.

6.6.4 Quality of evidence

The QUADAS-2 checklist was used when appraising diagnostic evidence for the best tools to identify clinical and developmental manifestations of cerebral palsy at first presentation. The methodology checklist for prognostic studies (2012) was used instead when appraising evidence for the key clinical and developmental manifestations of cerebral palsy at first presentation. The quality of evidence ranged from very low to high. The main sources of bias in the studies were selection bias and the reference test undertaken with knowledge of index text.

6.6.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

6.6.6 Key conclusions

The Committee concluded that certain manifestations such as abnormality of movement and tone may be suggestive of cerebral palsy and that infants and children with delayed milestones such as late sitting and late walking should be referred for onward assessment.

6.7 Recommendations

12. Provide an enhanced clinical and developmental follow-up programme for infants and children who are at increased risk of developing cerebral palsy (see recommendation 1):

- From 0–6 months: consider using the General Movement Assessment (GMA) during routine neonatal follow-up assessments.
- From 6–24 months: use a multidisciplinary neurological assessment if continued follow-up assessments are needed.

13. Recognise the following as possible early motor features in the presentation of cerebral palsy:

- unusual fidgety movements or other abnormalities of movement, including asymmetry or paucity of movement

- abnormalities of tone, including hypotonia (floppiness), spasticity (stiffness) or dystonia (fluctuating tone)
- abnormal motor development, including late sitting, crawling or walking, or problems with feeding.

14. **Recognise that the most common delayed motor milestones in infants and children with cerebral palsy are:**
    - late sitting (after 8 months)
    - late walking (after 18 months)
    - early asymmetry of hand function (hand preference before 1 year).

15. **Refer all infants and children with delayed motor milestones to a child development service for further assessment.**

16. **Refer children who have obvious and persistent toe walking to a child development service for further assessment.**

17. **If there are concerns that an infant or child may have cerebral palsy but a definitive diagnosis cannot be made, discuss this with their parents or carers and explain that an enhanced clinical and developmental follow-up programme will be necessary to try to reach a definite conclusion.**

18. **Refer all infants and children with suspected cerebral palsy immediately to a child development service for a multidisciplinary assessment, in order to facilitate early diagnosis and intervention.**

19. **Recognise that ongoing communication between all levels of service provision in the care of children and young people with cerebral palsy is crucial, particularly involvement of primary care from diagnosis onwards.**

6.8 Research recommendations

None identified for this topic.

7 Red flags for other neurological disorders

Review question: What clinical manifestations should be recognised as 'red flags' that suggest a progressive neurological or neuromuscular disorder rather than cerebral palsy?

7.1 Introduction

Cerebral palsy is the commonest cause of movement disorders in childhood but not every child with a movement disorder has cerebral palsy. It is very important to establish the correct diagnosis as this has implications for treatment, prognosis and family planning. The clinical team should always try to identify risk factors and a cause of cerebral palsy for each child or young person in their care.

As cerebral palsy is due to a non-progressive injury or dysfunction in the developing brain, even though the clinical signs may not be obvious in the early months of life there is a typical pattern of progression in motor activities and cognitive development. When there is any deviation from this typical pattern such as loss of previous physical and cognitive skills or deterioration in vision and speech then an alternative diagnosis should be sought. The deviation may occur at any age.

Even before 'red flag' signs and symptoms are considered, there are features of the medical history, which may alert the family or professional to an alternative diagnosis to cerebral palsy. These include features such as normal magnetic resource imaging (MRI) brain scans, disproportionate bowel and bladder disturbance, a strong family history or variations in movement difficulty during the day. These features should guide the medical team to investigate for genetic, metabolic or even spinal problems.

Red flags were identified by the Committee and were based on existing guidelines, published reviews and personal experience. Those felt to be the most important were prioritised for detailed systematic review.

To identify the most important clinical manifestations that suggest a progressive neurological or neuromuscular disorder.

7.2 Description of clinical evidence

No relevant clinical studies were identified for this review.

7.3 Clinical evidence profile

No relevant clinical studies were identified for this review.

7.4 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations relevant to recognising 'red flags' were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

7.5 Evidence statements

7.5.1 Prevalence of the progressive disease in patients with clinical markers that indicate a diagnosis other than cerebral palsy

No relevant clinical studies were identified for this outcome.

7.6 Evidence to recommendations

7.6.1 Relative value placed on the outcomes considered

The aim of this review was to identify the most important clinical manifestations that suggest a progressive neurological or neuromuscular disease such as neurometabolic disorders (leukodystrophy, mitochondrial disorder), neuromuscular disorders (SMA, spinal muscular atrophy; muscular dystrophy), tumours (benign and malignant), genetic disorders (for example hereditary spastic paraparesis, primary dystonia, dopa-responsive dystonia, Pelizaeus Merzbacher syndrome and Rett syndrome), and spinal cord disorders, rather than cerebral palsy. The Committee indicated the prevalence of the progressive disease in patients other than cerebral palsy to be the critical outcome for this evidence review.

7.6.2 Consideration of clinical benefits and harms

No evidence was retrieved for this evidence review and given that the Committee was not aware of any studies that could have been missed they agreed to develop consensus recommendations based on their clinical judgement and expertise as they recognised the importance of identifying red flags for neurological disorders other than cerebral palsy.

The Committee agreed that the following were the most important forms of progressive neurological disorders:

- Neurometabolic (leukodystrophy; iron deposition disorders, mitochondrial disorders)
- Neuromuscular disorders including muscular dystrophy and spinal muscular atrophy
- Tumours of the central nervous system (benign and malignant)
- Genetic disorders (hereditary spastic paraparesis, primary dystonia, dopa-responsive dystonia [Segawa syndrome], Pelizaeus Merzbacher syndrome and Rett syndrome)
- Other spinal cord disorders such as intradural lipoma, diastatomyelia

The Committee discussed the importance of recognising that while cerebral palsy is caused by a non-progressive impairment of the brain, the manifestations, do change over time.

However, those changes tend to follow patterns that are readily recognised by trained health care professionals. If the changes do not follow such typical pattern, the Committee agreed it was important to consider the possibility of some form of progressive neurological disorder. A consensus recommendation was made on some of the important features that may suggest the presence of a progressive disorder rather than cerebral palsy.

Based on their clinical experience and knowledge and by consensus, the Committee agreed that the following should be considered red flags for alternative neurological disorders for further specialist assessment: absence of known risk factors; family history of a progressive neurological disorder; loss of already attained cognitive or developmental abilities; development of unexpected abnormal or focal neurological signs; and MRI findings that are inconsistent with the clinical signs of cerebral palsy and/or are more suggestive of a progressive disorder.

The Committee noted that in the UK there is currently no universal register of children with cerebral palsy which captures the number of people with cerebral palsy, the subtype or the

complexity of their cerebral palsy. As such there is no real national estimate of the level of medical and social care needed for this population. The Committee agreed to develop a research recommendations to set up a national cerebral palsy register aiding epidemiological collection of data on the total number of children with cerebral palsy. The Committee also considered that this should include information about comorbidities, function and the natural history of their condition including on-going medical and social care needs.

7.6.3 Consideration of economic benefits and harms

This is an epidemiological review question and economic analysis to assess cost-effectiveness is not applicable as it does not involve a comparison of competing alternatives. However, referring the child or young person to a specialist in paediatric neurology when red flags are observed will have cost implications. According to NHS Reference Costs 2014/15, the cost of an attendance with a paediatric neuro-disability specialist is £281 (WF01A, Non-Admitted Face to Face Attendance, Follow-up, 291, Consultant led, Paediatric Neuro-Disability).

The Committee agreed that this cost would be negligible compared to the downstream costs an incorrect diagnosis of cerebral palsy would incur, from unnecessary treatment costs, treatment related adverse events and the negative psychological impact on the child and young person and their family. Overall, knowing what clinical manifestations should be recognised as ‘red flags’ that suggest a progressive neurological or neuromuscular disorder rather than cerebral palsy may lead to better identification and thus more timely management and has therefore, potential cost savings.

7.6.4 Quality of evidence

No relevant clinical studies were identified for this review.

7.6.5 Other considerations

No relevant clinical studies were identified for this review. The recommendations related to this evidence review were based on the Committee’s clinical experience.

7.6.6 Key conclusions

The Committee concluded that there is a lack of evidence with regards to what are the most important clinical manifestations that suggest a progressive neurological or neuromuscular disorder other than cerebral palsy.

7.7 Recommendations

20. Review a diagnosis of cerebral palsy if clinical signs or the child's development over time do not follow the patterns expected for cerebral palsy, taking into account that the functional and neurological manifestations of cerebral palsy change over time.

21. Recognise the following as red flags for neurological disorders other than cerebral palsy, and refer the child or young person to a specialist in paediatric neurology if any of these are observed:

- absence of known risk factors (see recommendation 1)
- family history of a progressive neurological disorder
- loss of already attained cognitive or developmental abilities
- development of unexpected focal neurological signs

- MRI findings suggestive of a progressive neurological disorder
- MRI findings not in keeping with clinical signs of cerebral palsy.

7.8 Research recommendations

2. Can epidemiological recording in the UK of the burden of care of cerebral palsy improve equity of access to care?

Table 26: Research recommendation rationale

Research question	Can epidemiological recording in the UK of the burden of care of cerebral palsy improve equity of access to care?
Why this is needed	
Importance to 'patients' or the population	Cerebral palsy is an extremely heterogeneous condition with disability ranging from minor gait difficulties to severe disability with immobility, profound learning disability and total dependence on carers for feeding and activities of daily living. In the UK there is currently no universal register of children with cerebral palsy which captures the numbers of people with cerebral palsy, the subtype or the complexity of their cerebral palsy. As such there is no real national estimate of the level of medical and social care needed for this population. Currently some parts of the UK have excellent provision of services whereas in others there are limited facilities for diagnostic investigation let alone provision of social care needs and specialised equipment. A national cerebral palsy register and epidemiological collection of data will not only allow the total numbers of children with cerebral palsy to be collected but also their comorbidities and the natural history of their condition including on-going medical and social care needs. With this information accurate allocation of NHS resources can be determined to different areas of the country. This includes the resources needed in terms of medical and allied health personnel, diagnostic equipment, and social and educational need. This will make services equitable across the country for families and also allow identification of patterns of disease progression and intervention which will in turn help dictate new interventions or help decide which intervention works best for different cohorts of cerebral palsy - an example would be hip migration surveillance in cerebral palsy and standardising the most effective timing of orthopaedic surgery
Relevance to NICE guidance	There is an urgent need to understand the burden of health and care needs of all children with cerebral palsy. Without accurate population data on this it is very difficult to monitor natural progression in this very heterogeneous group and allocate resources accordingly.
Relevance to the NHS	The initial high cost of setting up an appropriate database and secure electronic recording infrastructure will be offset by better evidence on appropriate care need and the timing of appropriate care for children and young people with cerebral palsy. In areas where there is inadequate funding for the numbers of children with cerebral palsy this will of course lead to an increased need for funding in these areas. The benefits will be widespread across health, social care and education domains.
National priorities	Yes – will assist in the allocation of NHS resources across England.
Current evidence base	Much of the current evidence on the complexity and burden of health care in cerebral palsy is either done in small cohorts or is from outside of the UK.
Equality	Not identified

Research question	Can epidemiological recording in the UK of the burden of care of cerebral palsy improve equity of access to care?
Feasibility	The research project is not difficulty in its content but does face challenge in terms of setting up secure databases and the IT infrastructure to allow professionals to collect the data. The database will need to secure and confidential. Data on current service provision in each health district will also need to be collated.
Other comments	The initial expense needed to set up the system is justified as the project will allow longitudinal data collection which will not only allow research on burden of health needs but also allow appropriate commissioning of services geographically in terms of medical, social and educational need.

1

2 **Table 27: Research recommendation statements**

Criterion	Explanation
Population	UK population of children with cerebral palsy.
Intervention	Development of a national cerebral palsy register focusing on: Diagnosis and use of MRI Developmental surveillance (in line with the development of the national CPIPS register [monitoring of hip dysplasia]) Functional ability Motor pattern and severity Communication Cognition Burden of disability Comorbidity Pain Sleep disturbance Equipment
Comparator	n/a
Outcome	Prevalence/proportion
Study design	Registry
Timeframe	Within 5 years

3

4

8 MRI and identification of causes of cerebral palsy

Review question: Does MRI in addition to routine clinical assessment (including neonatal ultrasound) help determine the aetiology in children and young people with suspected or confirmed cerebral palsy and if so in which subgroups is it most important?

8.1 Introduction

Cerebral palsy is a descriptive term incorporating many different non-progressive aetiologies. The pathogenesis is dependent upon structural or functional abnormalities of the developing brain occurring in the ante-, peri- or post-natal phases. The particular underlying structural pathology observed is dependent on the stage of fetal or neonatal brain development at the time of abnormal formation or insult.

Some genetic and progressive disorders may mimic cerebral palsy in their early stages and might be identified by magnetic resonance imaging (MRI). The addition of MRI to aetiological assessment might potentially identify such individuals.

As stated elsewhere, children with cerebral palsy generally present from either a 'high risk' population or if there is developmental diversion from population norm. As such a child who is suspected of having or confirmed to have cerebral palsy will be usually a few months old. When there is a clear antenatal, perinatal or postnatal history of possible risk clinical and developmental examination is important in revealing the type and extent of the motor disorder. However, the committee were aware that type of motor disorder and geographical pattern of motor disorder – i.e. which limbs are affected – did not always correlate with presumed aetiology.

Imaging of the brain may show an explanation for impairment. Neonatal ultrasound of the brain is readily available in most neonatal units and with appropriate training is easy to perform and painless for the baby. However neonatal ultrasound does not provide as much detail of brain structure and requires the operator to be skilled in interpretation. Babies who do not have any difficulties in the neonatal period, or were not born preterm, are unlikely to have had neonatal ultrasound scans.

The Committee considered that help in determining aetiology was important for parents particularly to identify whether there were any avoidable risk factors for future pregnancies and if genetic factors may be present. As diagnostic techniques evolve children with cerebral palsy, particularly those who have normal MRI scan, may benefit from other investigations including newer genetic techniques.

However in practice, children older than 3 months of age usually need sedation or general anaesthetic for an MRI and the committee were aware of the small risk associated with this. In determining the value of MRI scanning of all children it was also important to consider the cost implications including anaesthetic and day admission balanced against any extra information on possible aetiology that an MRI would bring.

A comparison of accuracy in determining aetiology of cerebral palsy using a variety of clinical, developmental and imaging assessments was felt to be necessary by the Committee.

8.2 Description of clinical evidence

No relevant clinical studies that provided diagnostic accuracy for MRI as an index test for the identification of aetiological findings in cerebral palsy were found, in comparison to a reference test of:

- clinical assessment alone
- clinical assessment with cranial ultrasound
- clinical assessment with cranial ultrasound and other blood urine or cerebro-spinal fluid (CSF) investigations
- When comparing neuroimaging techniques, 1 study (De Vries 1993) was included which conducted cranial ultrasounds on infants with periventricular leukomalacia (PVL) who were later confirmed as cerebral palsy using MRI. It is important to note the following limitations with this study:
  - Participants included were neonates in neonatal intensive care unit (NICU) identified with PVL on cranial ultrasound who later developed cerebral palsy.
  - No statistical analysis including diagnostic accuracy, p-values or correlation co-efficients were reported.

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

8.2.1 Summary of included studies

The summary of the included study is presented in Table 28.

Table 28: Summary of included study

Study	Aim	Intervention/Comparison	Population	Outcomes
De Vries 1993	To assess whether the degree of periventricular leukomalacia (PVL) diagnosed using cranial ultrasound in the neonatal period, correlates well with the degree of adverse neurological sequelae and with the findings on MRI, performed later during infancy in a group of preterm infants who developed cerebral palsy.	Ultrasound scans were performed daily during the first week and twice a week thereafter until discharge and then again in the clinic as long as the fontanelle remained open. Following discharge, all infants were seen back at 40 weeks postmenstrual age (PMA). MRI scans performed between 11 and 30 months chronological age.	N = 20 infants who had PVL and developed cerebral palsy.	Ultrasound: PVL grade I, II and III. MRI: PVL ventricular size, periventricular and deep white matter, degree of myelination, the presence and distribution of areas of periventricular hyperintensity (PVHI) and thinning of corpus callosum.

8.3 Clinical evidence profile

The results from the 1 study included (De Vries 1993) is presented in Table 29.

Table 29: Results of included study

	Test	
Leukomalacia	**Ultrasound**	**MRI**

	Test	
grade		
Grade I leukomalacia (n = 8)	Present beyond 10 days of age in 4/8, remaining 4/8 were discharged between day 7 - 10 and were scanned again at 40 weeks postmenstrual age (PMA), not showing any evolution of cysts.	Parental consent was given for 5/8 cases. Ventricular enlargement was present in 1/5 case and 3/5 had an irregular ventricular shape. 3/5 showed diminished peritrigonal white matter. Delay in myelination was present in the occipital area in 1/5. Periventricular hypersensitivity was seen in all infants, restricted to trigone along the body of the lateral ventricle in 4 and also tending into the frontal periventricular white matter in 1 infant. Thinning of corpus callosum was seen in 2/5.
Grade II leukomalacia (n = 4)	2/4 developed localised cysts and 2/4 were asked back for a repeat ultrasound within 4 weeks following discharge. They showed an evolution to local cystic lesions, which were still present when reviewed at 40 weeks post menstrual age. These infants were between 16 - 28 months when last examined. 1 learned to walk independently though with an abnormal 'clumsy' gait pattern at 18 months	Permission received for all cases. Ventricular enlargement present in all cases and 2/4 infants had an irregular ventricular shape. 3/4 showed diminished peritrigonal white matter. Delay in myelination was present in 1/4 infant. Periventricular hyperintensity was present on the T2-weighted image was present in all, restricted to trigone area and along the body of lateral ventricle in 2/4 cases and extending into frontal periventricular white matter in 2/4 cases. Thinning of corpus callosum was seen in 3/4 cases.
Grade III leukomalacia (n = 8)	7/8 developed extensive cysts before discharge and in 1 case, extensive cysts were first seen at 40 weeks PMA. Infants were between 12 - 36 months when last examined and none were able to walk independently.	MRI carried out in 6/8 infants. All showed ventricular enlargement associated with an irregular ventricular shape. All showed diminished peritrigonal white matter and a delay in myelination was noted in 5 infants, restricted to occipital area in 2 infants. Periventricular hypersensitivity on T2-weighted images extended from the occipital into the frontal periventricular white matter in all cases. All cases showed thinning of corpus callosum.

8.41 Economic evidence

No economic evaluations of MRI scans in children and young people with cerebral palsy were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

Table 30 below presents the cost of MRI scans, taken from NHS Reference Costs 2015. It is important to note that the national average unit costs presented in Table 30 are likely to be underestimated for scans performed in children and young people with cerebral palsy. This is because many patients would require a general anaesthetic, and the procedure may take longer than average to perform.

Table 30: Cost of MRI scans

MRI scan	National average unit cost	Currency code
One area, no contrast, 19 years and over	£137	Diagnostic imaging, RD01A
One area, no contrast, 6 to 18 years	£132	Diagnostic imaging, RD01B

MRI scan	National average unit cost	Currency code
One area, no contrast, 5 years and under	£134	Diagnostic imaging, RD01C

The clinical evidence base to identify if MRI scans can provide additional information to a clinical assessment in children and young people with cerebral palsy was limited. If a model was built on the study by De Vries 1993 included in the clinical evidence review, MRI would never be considered cost-effective compared to ultrasound. Ultrasound was treated as the reference standard in the study; hence, MRI would be dominated by ultrasound as it is more expensive. According to NHS Reference Costs 2015 the cost for an ultrasound scan is £55 (RD40Z, diagnostic imaging, ultrasound scan less than 20 minutes). Due to the lack of evidence on the effectiveness of MRI scans, economic considerations were restricted to a description of the costs

MRI scans in additional to a clinical assessment would not be considered cost-effective if there is not an effective treatment for the condition being diagnosed, or if the patient's management is not changed by the results of the scan. In other words, if MRI scans do not add any additional information to a clinical assessment and do not change the patient's management strategy, MRI scans should not be recommended.

Overall, cost data for MRI scans have little use without associated benefits; hence, while the costs of MRI scans could be significant, without knowing the benefits of MRI scans we cannot know if they will be cost-effective. Recommendations on the population identified to need MRI scans, and the frequency of scans will have significant resource implications. Therefore a research recommendation to consider the effect of MRI scans, in addition to a clinical assessment, preferably at different frequencies, would benefit from health economic input to assess the cost-effectiveness of providing an additional intervention to the clinical assessment.

8.5 Evidence statements

One study with low quality was included which showed that PVL grade I, II and III was identified using cranial ultrasound up until 40 weeks post-menstrual age. Further detail was identified using MRI between 11 and 30 months, including ventricular enlargement, periventricular hypersensitivity, delay in myelination and thinning of corpus callosum.

8.6 Evidence to recommendations

8.6.1 Relative value placed on the outcomes considered

Outcomes considered in this evidence review relate to the identification of the proportion of participants with each neuroimaging pattern against aetiologies including periventricular leukomalacia (PVL) and diffuse encephalopathy. No studies reporting this outcome were identified for this evidence review. However, 1 study was included which provided a description of findings from cranial ultrasound and MRI in children with PVL who were later diagnosed with cerebral palsy.

8.6.2 Consideration of clinical benefits and harms

The Committee noted that evidence presented was limited and did not provide a thorough answer to the review question.

Therefore, all recommendations developed as part of this planned evidence review were based on the Committee's clinical experience and guidance from co-opted expert opinion and were agreed by consensus. The Committee discussed at length the difficulties and limitations of assessing aetiology of cerebral palsy using only radiological imaging.

Based on expert opinion and their clinical expertise it was agreed that MRI alone does not accurately determine the aetiology of cerebral palsy and that health care professionals need to take account of family, antenatal, perinatal and postnatal histories; the child or young person's ongoing medical history; the results of clinical examination and early cranial ultrasound examination if that has occurred.. They agreed that children who are suspected or known to have cerebral palsy where there is no clear aetiology of cerebral palsy based on antenatal, perinatal or postnatal history, neurological examination or other investigations, they are recommended to be offered an MRI scan. It was the Committee's view that despite the limited evidence to support a strong recommendation, if clear aetiology could not be established from the above criteria, then performing the MRI would be the next option for these children, in line with international consensus. Equally in the presence of family history, they considered that an MRI can help with decision-making regarding the possibility of an inherited genetic cause.

The Committee discussed that limited evidence showed ultrasound (US) scans performed during the neonatal period found the same areas of damage in the brain as an MRI scan perform at follow-up (around 2 years of age). As such it was noted that US are routinely used in high risk infants on the NICU, especially in preterm babies.

In determining aetiology, the Committee discussed if findings from an MRI scan could inform or alter the management of a person with cerebral palsy. It was noted that it could alter management in some cases. For example, the MRI findings in a child and young person with hemiplegic cerebral palsy may alter clinical management for example the need to monitor size of enlarging porencephalic cyst as it may indicate evolving hydrocephalus or the need for further investigations such as visual assessment for hemianopia

It was noted that having a radiological diagnosis of explanation of impairment only acts as a guide and does not always provide clarity of the full extent of a child's functional difficulties.

Following presentation of the evidence and after expert opinion, the Committee concluded that MRI is useful in clarifying aetiology of cerebral palsy in the absence of a clear clinical history but not necessarily the timing of the cerebral injury.

The Committee agreed various aspects should be taken into account in terms of the timing of an MRI scan. Brain structure continues to change rapidly during early childhood. It is important to note that any abnormality may not be apparent until 2 years of age as maturation of the myelination process and development of the deep grey structures may be less obvious until around this time. However, there may be clinical circumstances that require urgent clinical decision making in which an MRI must be conducted.

In the presence of an abnormal clinical or developmental trajectory an urgent MRI might find aetiology suggestive of red flags for conditions other than cerebral palsy such as progressive disorders. As such the Committee noted that there were certain cases which would require a repeat MRI scan and recommended that this should only be performed when there is a change in expected clinical and developmental profile or there any red flags for a progressive disorder.

The Committee considered that the reasons to perform MRI should be discussed with the child or young person with cerebral palsy if age appropriate and their parents and carers in each individual circumstance.

The Committee were aware that there are older children and young people with cerebral palsy who did not have access to MRI as young children. If aetiology is uncertain, it may be appropriate to offer an MRI scan as part of information giving to the person or relatives on the possibility of the aetiology being a genetic disorder – for example cortical migration disorder.

8.6.3 Consideration of economic benefits and harms

Currently, MRI scans are widely performed although their additional value above a detailed clinical assessment in clear cases was considered to be overestimated by the Committee. The expert opinion and Committee advised that a Paediatric Neuroradiologist would be well equipped to assess the aetiology of cerebral palsy from an MRI when provided with a clear clinical history and examination.

If a clinical and developmental history and examination in the presence of clear risk factors can sufficiently determine the patient's aetiology of cerebral palsy the Committee agreed an MRI should not routinely be used to confirm diagnosis. Consequently this will reduce the number of cost-ineffective MRIs that are performed, freeing up resources to generate benefits elsewhere in the NHS.

Ideally, MRI would be used at the time of presentation in a child with suspected cerebral palsy where there is no clear aetiology based on obstetric perinatal or postnatal history, neurological examination or other investigations, or if there is any unexpected change in clinical or developmental profile. It is important to rule out disorders other than cerebral palsy as patients incorrectly diagnosed with cerebral palsy, but with a progressive motor disorder, may not get access to available therapies which may adversely impact on their health related quality of life

The Committee agreed that because of the developmental and maturational processes of the brain, the aetiology of cerebral palsy may not be fully apparent until 2 years of age; for this reason an MRI should not be performed in neonates or infants if the purpose of the MRI is to determine the aetiology of cerebral palsy, unless there were other clinical reasons to do so. As a result there are potential cost savings to the NHS if only 1 MRI is performed to determine the aetiology of cerebral palsy.

The use of ultrasound scans to determine the aetiology of cerebral palsy was also raised by the Committee. The Committee advised that an ultrasound scan can illustrate abnormalities earlier than MRI and every high-risk neonate should undergo an ultrasound scan on the neonatal unit. As a result the findings from an ultrasound could be discussed with the family at an early stage, helping discussion about diagnosis and evading the need for an MRI at presentation, or delaying the MRI until the brain has structurally developed.

8.6.4 Quality of evidence

One cohort study was included in this evidence review. The quality the evidence for this review was rated as low based on the cohort study methodology checklist (NICE Manual 2012). The reasons for this was because the study included participants from an indirect population initially (neonates from NICU as opposed to infants diagnosed with cerebral palsy) and lack of outcome reporting of any statistical analysis including diagnostic accuracy outcomes or correlation coefficients.

8.6.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

8.6.6 Key conclusions

The Committee concluded that MRI should be used to confirm aetiology when this is not clear from antenatal, perinatal or postnatal history, neurological examination or other investigations.

8.7 Recommendations

22. Offer MRI for a child or young person with suspected or known cerebral palsy if the aetiology is not clear after consideration of:

- antenatal, perinatal and postnatal history
- their ongoing developmental and medical history
- the findings on clinical examination
- early cranial ultrasound examination.

23. Recognise that MRI will not accurately establish the timing of a hypoxic-ischaemic brain injury in a child with cerebral palsy.

24. When deciding the best age to perform an MRI scan for a child with cerebral palsy, take account of the following:

- Subtle neuro-anatomical changes that could explain the aetiology of cerebral palsy may not be apparent until 2 years of age.
- The presence of any red flags for a progressive neurological disorder (see section 7.7).
- That a general anaesthetic is usually needed for young children having MRI.
- The views of the child or young person and their parents or carers.

25. Consider repeating the MRI scan if:

- there is a change in the expected clinical and developmental profile **or**
- any red flags for a progressive neurological disorder appear (see section 7.7).

26. Discuss with the child or young person and their parents or carers the reasons for performing MRI in each individual circumstance.

8.8 Research recommendations

None identified for this topic.

9 MRI and prognosis of cerebral palsy

Review question:

Does MRI undertaken at the following ages:

- before 1 month (corrected for gestation)
- 1 month to 2 years
- 2-4 years

help to predict the prognosis of children and young people with cerebral palsy?

9.1 Introduction

Current clinical practice varies with MRI being performed in some neonatal units as part of the monitoring of treatment and recovery from neonatal encephalopathy or intracranial haemorrhage. However, only a few units have the capability to do this and transferring a sick ventilated baby to another unit for an MRI scan is not without risk.

Interpretation of MRI in a sick neonate is difficult as at that age the brain contains a lot of water and the images do not show the same clear distinction between different parts of the brain as seen in older brains.

MRI may also be done between 1 month and two years either because the child has been diagnosed as having cerebral palsy or after follow-up of neonatal difficulties. The distinction between the different parts of the brain is becoming clearer by this age.

The argument for delaying MRI until after the age of two years is based on brain development. An important part of development of the white matter of the brain – myelination - continues throughout childhood with the majority occurring by two years. White matter growth and development is important in cerebral palsy and associated comorbidities such as vision, language and learning. Development of the deep grey matter structures / basal ganglia occurs at a similar stage, which is particularly important in considering the prognosis in dystonic forms of cerebral palsy.

The Committee acknowledged the desire of parents to know prognosis for their child early to allow for planning of potential intervention and multidisciplinary management but also recognise the early scan may not be sufficiently specific to give prognosis. A scan at a later date may not give more information on prognosis than is apparent for the progress that the child has made developmentally in the intervening period. The later scan will involve sedation or general anaesthetic for the child and the small risk and costs of this need to be balanced against additional information on prognosis obtained from the MRI

The aim of this review is to analyse what is the best age to predict the severity of functional impairment in motor and other developmental skills in children and young people with cerebral palsy using MRI findings classified according to the type of brain injury. An early and accurate prognosis allows for planning and initiation of therapies that improve prognostic outcomes.

9.2 Description of clinical evidence

One cohort study was included in this review (Van Kooij 2010).

The study cohort consisted of 80 full-term children who had development of

- Mild neonatal encephalopathy (n=34, including 2 children with cerebral palsy), or

- Moderate neonatal encephalopathy (n=46, including 9 with cerebral palsy), on the basis of the highest Sarnat score as assessed during the first week after birth.

Neonatal and childhood MRI were analysed for the 80 participating children with neonatal encephalopathy, and for 51 control subjects during childhood. Neonatal and childhood MRI were compared with regard to site and pattern of injury. To assess the relationship between neurodevelopment and MRI findings, the MRI findings were categorised in 3 grades: no injury, mild injury, moderate to severe injury.

- The following neurodevelopmental outcomes were considered:
  - Motor function, assessed with the Movement Assessment battery for Children band 3. A total impairment score (TIS) ≤15th percentile was classified as abnormal.
  - Intelligence quotient (IQ) ≤85 was classified as abnormal
  - Other disabilities, classified as no disabilities, cerebral palsy (level I-V according to GMFCS) diagnosed between 3 and 5 years of age, post-neonatal epilepsy, and need for special education.
- For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

9.2.17 Summary of included studies

A summary of the studies that were included in this review are presented in Table 31.

Table 31: Summary of included studies

Study	Aim	Intervention/Comparison	Population	Outcomes
B. J. M. van Kooij et al. 2010	To assess the relation between patterns of brain injury on neonatal and childhood MRI and long-term neurodevelopmental outcome.	Neonatal MRI and childhood MRI - both graded as normal, mildly abnormal, or moderately/severely abnormal. Comparison: Normal/mild lesions versus moderate/severe lesions in neonatal and childhood MRI.	80 children with neonatal encephalopathy and 51 control subjects.	Total impairment score, IQ, CP, epilepsy, special education (see results below).

MRI magnetic resonance imaging, IQ intelligence quotient, CP cerebral palsy, TIS total impairment score.

Table 32: Results

Adverse outcome	Normal/mild lesion: n/total in MRI class (%)	Moderate/severe lesions: n/total in MRI class (%)	p value
Neonatal MRI (n=34)			
TIS ≤15 percentile	8/13 (61.5)	11/11 (100)	0.021
IQ ≤85	3/13 (23.1)	14/21 (66/7)	0.013
CP	0/13 (0)	10/21 (47/6)	0.003
Epilepsy	0/13 (0)	7/21 (33.3)	0.019

Adverse outcome	Normal/mild lesion: n/total in MRI class (%)	Moderate/severe lesions: n/total in MRI class (%)	p value
Special education	2/13 (15.4)	9/21 (42.9)	0.096
Childhood MRI (n=77)			
TIS ≤15 percentile	24/51 (47.1)	14/14 (100)	<0.001
IQ ≤85	12/55 (21.8)	15/21 (71.4)	<0.001
CP	3/55 (5.5)	8/22 (36.4)	<0.001
Epilepsy	0/55 (0)	8/22 (36.4)	<0.001
Special education	5/55 (9.1)	11/22 (50)	<0.001

(a) MRI magnetic resonance imaging, IQ intelligence quotient, CP cerebral palsy, TIS total impairment score.

9.32 Economic evidence

No economic evaluations of MRI scans in children and young people with cerebral palsy were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

The clinical evidence base to identify the best age to predict the progression of cerebral palsy was limited. Due to the lack of evidence on the effectiveness of MRI scans, economic considerations were restricted to a description of the costs.

Table 33 below presents the cost of MRI scans, taken from NHS Reference Costs 2015. It is important to note that the national average unit cost presented in Table 33 is likely to be underestimated for scans performed in children and young people with cerebral palsy. This is because many patients would require a general anaesthetic, and the procedure would take longer than average to perform.

Table 33: Cost of MRI scans

MRI scan	National average unit cost	Source
One area, no contrast, 19 years and over	£137	Diagnostic imaging, RD01A
One area, no contrast, 6 to 18 years	£132	Diagnostic imaging, RD01B
One area, no contrast, 5 years and under	£134	Diagnostic imaging, RD01C

MRI scans in additional to a clinical assessment would not be considered cost-effective if there is not an effective treatment for the condition being diagnosed, or if the patient's management is not changed by the results of the scan. In other words, if MRI scans do not add any additional information to a clinical assessment and do not change the patient's management strategy, MRI scans should not be recommended.

In the US it is recommended that all children and young people with cerebral palsy should receive an MRI scan; generating similar expectations in many UK patients. Knowing the likely aetiology of their child's cerebral palsy may reduce a parent's anxiety and distress, but if the findings from the scan would not change the patient's prognosis or management strategy, an MRI in the presence of a clear history and clinical assessment would not necessarily be considered cost-effective.

Cost data for MRI scans have little use without associated benefits. Therefore, while the costs of MRI scans could be significant, without knowing the benefits of MRI scans we cannot know if they will be cost-effective. Recommendations on the population identified to

need MRI scans, and the frequency of scans will have significant resource implications. Therefore a research recommendation to consider the effect of MRI scans, in addition to a clinical assessment, preferably at different frequencies, would benefit from health economic input to assess the cost-effectiveness of providing an additional intervention to the clinical assessment.

9.4 Evidence statements

9.4.1 Motor function

One study with 80 children showed that all children with moderate/severe lesions on neonatal MRI and 61.5% children with normal/mild lesions on neonatal MRI had a TIS ≤15th percentile (p value = 0.021). When looking at childhood MRI results, the study showed that all children with moderate/severe lesions and 47.1% children with normal/mild lesions on neonatal MRI had a TIS ≤15th percentile (p value <0.001).

9.4.2 Intelligence quotient

One study with 80 children showed that 66.7% children with moderate/severe lesions on neonatal MRI and 23.1% children with normal/mild lesions on neonatal MRI had a IQ ≤85 (p value = 0.013). When looking at childhood MRI results, the study showed that 71.4% children with moderate/severe lesions and 21.8% children with normal/mild lesions on neonatal MRI had an IQ ≤85 (p value <0.001).

9.4.3 Cerebral palsy

One study with 80 children showed that 47.6% children with moderate/severe lesions on neonatal MRI and none of the children with normal/mild lesions on neonatal MRI had cerebral palsy (p value = 0.003). When looking at childhood MRI results, the study showed that 36.4% children with moderate/severe lesions and 5.5% children with normal/mild lesions on neonatal MRI had cerebral palsy (p value <0.001).

9.4.4 Epilepsy

One study with 80 children showed that 33.3% children with moderate/severe lesions on neonatal MRI and none of the children with normal/mild lesions on neonatal MRI had epilepsy (p value = 0.019). When looking at childhood MRI results, the study showed that 36.4% children with moderate/severe lesions and none of the children with normal/mild lesions on neonatal MRI had epilepsy (p value <0.001).

9.4.5 Special education

One study with 80 children showed that 42.9% children with moderate/severe lesions on neonatal MRI and 15.4% children with normal/mild lesions on neonatal MRI needed special education (p value = 0.096). When looking at childhood MRI results, the study showed that 50% children with moderate/severe lesions and 9.1% children with normal/mild lesions on neonatal MRI needed special education (p value <0.001).

9.5 Evidence to recommendations

9.5.1 Relative value placed on the outcomes considered

The aim of this review was to analyse what is the best age to predict the progression of cerebral palsy using MRI findings classified according to the type of brain injury. The Committee's view was that an early and accurate prognosis allows for planning and initiation

of therapies that improve prognostic outcomes. The Committee prioritised the following outcomes for this evidence review:

- Proportion of children and young people with epilepsy
- Proportion of children and young people with feeding problems
- Severity of functional disability using - Gross Motor System Classification
- The Manual Ability Classification System
- Communication problems
- Cognitive problems
- Changes in health-related quality of life (for example Lifestyle Assessment Questionnaire – Cerebral Palsy [LAQ-CP])
- Mortality

9.5.2 Consideration of clinical benefits and harms

The Committee noted the lack of evidence for this review and was not aware of any other relevant studies that should have been included. However, they acknowledged that there were many studies looking at other aspects of the use of MRI in cerebral palsy, such as comparisons between MRI changes in different types of cerebral palsy, abnormalities that predict cerebral palsy, MRI changes in infants exposed to different risk factors, and follow-up of infants exposed to treatment for brain injury for example therapeutic hypothermia-cooling. In the absence of a clear evidence base on prognosis derived from neuroimaging, the recommendations developed from this evidence review were mainly based on expert opinion and the clinical experience of the Committee and were agreed by consensus.

They considered as part of their clinical experience that some of the features on MRI (causation/aetiology) correlate with functional outcome, particularly regarding motor patterns and presence of developmental comorbidity such as sensory, hearing or visual impairment. However the Committee did not feel confident to recommend the use of MRI solely to guide prognosis in cerebral palsy.

The Committee agreed that prognosis should not be discussed if the aetiology of cerebral palsy in the first instance is not clear. However, they discussed how a good understanding of MRI findings can help to explain to parents the likelihood of severity and of future outcomes. The Committee recognised the importance of involving families and carers in the discussion about prognosis, as it can help them to understand and look out for possible signs of associated disorders.

With regard to the best timing for MRI, the Committee agreed that the developmental and maturational processes of the brain means that the radiological signs observed in some individual's scans can change over time. Therefore the Committee agreed there is less value in conducting them too early for example as the myelination process in the brain is usually mostly complete at 2 years of age. .

Based on all the above points, the Committee decided therefore to recommend that health care professionals should take into account findings from MRI scans alongside the likely cause of cerebral palsy when discussing prognosis with the child or young person and their parents and carers, and to not rely on MRI scans alone but rather to use it as part of a decision pathway also based on history, clinical and developmental assessment They also agreed that many other variables, such as the intervention received and family environment, can impact on the prognosis of the condition.

9.5.3 Consideration of economic benefits and harms

The Committee highlighted that although the causative brain injury is static in cerebral palsy, the findings from MRI scans would not be wholly informative until the brain has developed.

For this reason, the Committee agreed performing MRI scans in neonates and infants would not be as cost-effective a use of NHS resources as those performed after 2 years of age.

The Committee considered they did not have a strong evidence base to recommend MRI in informing prognosis in cerebral palsy as it was unclear if an MRI alone would lead to a change in the person's management without clear clinical, functional and developmental parameters.

9.5.4 Quality of evidence

One cohort study was included in the review. The quality of the evidence was rated as very low based on the prognostic study methodology checklist (NICE Manual 2012). Main reasons of bias were: the study sample did not fully represent the population of interest with regard to key characteristics, sufficient to limit potential bias to the results; important potential confounders are not appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.

9.5.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

9.5.6 Key conclusions

The Committee concluded that MRI alone should not be used for predicting prognosis in infants and children with cerebral palsy.

9.6 Recommendations

27. **Take account of the likely cause of cerebral palsy and the findings from MRI (if performed) when discussing prognosis with the child or young person and their parents or carers.**

28. **Do not rely on MRI alone for predicting prognosis in infants and children with cerebral palsy.**

9.7 Research recommendations

None identified for this topic.

10 Prognosis for walking, talking and life expectancy

Review question: In infants, children and young people with cerebral palsy, what are the clinical and developmental prognostic indicators in relation to:

- **the ability to walk**
- **the ability to talk**
- **life expectancy?**

10.1 Introduction

Although the central nervous system lesion of cerebral palsy is not progressive, it affects the development of children and young people with cerebral palsy in different ways according to their age, severity of activity limitation, type of motor disorder and cognitive ability. Skills attained in early development can be 'lost' due to growth-associated factors such as muscle tightness, contracture formation and weakness. The parents of children usually want to know what the future holds for their child, and yet the development of key activities is usually unknown at diagnosis.

There are many areas of development that are crucial for independence in everyday life such as independence in transfers, being able to communicate meaningfully, and to have effective upper limb activity for carrying out all activities of daily living and for using mobility aids such as walkers and wheelchairs. However, parents particularly wanted to know if their child will 'walk and talk'. Life expectancy is another area regularly discussed at an early point after diagnosis, particularly in children with a severe impairment.

Most children and young people with cerebral palsy live at home with their parents, and there are understandable concerns from families as to what arrangements can be made for when their children are older and they are no longer able to care for them. The clinical team need to be able to provide prognostic information for families about these areas where possible.

The Committee agreed with the 3 main areas for review based on parental views, clinical experience and published literature to determine clinical and developmental prognostic indicators.

The aim of this review was to determine which clinical and developmental indicators are able to predict the future ability of a child with cerebral palsy to talk, walk, and his or her life expectancy, with the view to providing information for parents/carers. Other reviews within this guideline and NICE clinical guideline on Spasticity in under 19s provided more information in the area of independent mobility and communication, which were felt by the Committee to be as important in informing future management.

The quality of each study was assessed using the NICE methodology checklist (2012) for prognostic studies.

10.2 Description of clinical evidence

10.2.1 Prognosis for walking

Three studies were included for the prognosis of walking: two applied a prospective cohort design (Beckung 2008 and Wu 2004) and 1 applied a retrospective cohort design (Trahan and Marcoux 1994).

10.2.2 Prognosis for talking

Two studies were included for the prognosis of talking: 1 applied a prospective cohort design (Chen 2013) and 1 analysed a cohort in the Northern Ireland cerebral Palsy Register (Parkes 2010). It is important to note that the prospective cohort study (Chen 2013) had a short follow-up period of 6 months only.

10.2.3 Life expectancy

Four studies were included for the prognosis of life expectancy: two had a prospective cohort design (Blair 2001 and Westbom 2011) and two had a retrospective cohort design (Strauss 2007 and Touyama 2013).

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

10.2.4 Summary of included studies

A summary of the studies that were included in this review are presented in Table 34, Table 35 and Table 36.

Table 34: Summary of included studies for prognosis of walking

Study	Prognostic indicator	Population	Follow-up period	Outcomes	Study quality and comments
Beckung 2008	Unilateral spastic CP, Bilateral spastic CP, Cognition (IQ)	n = 9012, assessment at 5 years of age.	Data from SCPE collected over 21 years.	Unable to walk: aOR	Moderate
Trahan and Marcoux 1994	Distribution of motor problem	n = 187, age at assessment: 2 months to 6 years 10 months	Unclear, assessment at 6 years and retrospectively assessed walking at 12 months.	Inability to walk: aOR	Moderate
Wu 2004	Type of CP, distribution of motor movement, rolls but does not sit without support at 2 years	n = 2295, mean age: 2.7 years at entry	Mean: 5.8 years	Full ambulation (able to walk well alone at least 20 feet without assistive devices) at 6 years among children who were nonambulator	Moderate 'Rolls, does not sit without support' at 2 years used for the indicator listed in the protocol as 'delayed sitting'.

Study	Prognostic indicator	Population	Follow-up period	Outcomes	Study quality and comments
				y at 2 years. aORs	

aOR adjusted odds ratio, CP cerebral palsy, IQ intelligence quotient, SCPE Surveillance of Cerebral Palsy in Europe.

Table 35: Summary of included studies for prognosis of talking

Study	Prognostic indicator	Population	Follow-up period	Outcomes	Study quality and comments
Chen 2013	GMFCS levels	n = 78, mean age; 3 yrs 8 months.	6 months.	"Language" assessed using CDIIT. Language subset includes: expression and comprehension. Unstandardised coefficient (B) and standardised coefficient (β).	Low Short follow-up period. Detail of assessment method (CDIIT) unclear and not provided.
Parkes 2010	CP Subtype (bilateral versus unilateral), GMFCS level, 'intellectual impairment' measured using IQ	n = 1357 born between 1980 and 2001 from NICPR register.	Unclear, approximately median: 1 year and 9 months.	Speech impairment aORs	Moderate Detail of assessment method ("standardised assessment form") unclear and not provided.

aOR adjusted odds ratio, CP cerebral palsy, GMFCS Gross Motor Function Classification System, CDIIT Comprehensive Development Inventory for Infants and Toddlers, NICPR Northern Ireland Cerebral Palsy Register.

Table 36: Summary of included studies for prognosis of life expectancy

Study	Prognostic indicator	Population	Follow-up period	Outcomes	Study quality and comments
Blair 2001	"Intellectual ability", IQ: < 20, 20 – 30, 35 – 49, 50 – 69, 70 – 85, > 85	n = 2014 born in Western Australia between 1956 – 1994. Mean age at entry not reported, death by 5 years of age was recorded.	Birth to 5 years	Mortality aRR,	Very low Severity of CP defined as 'minimal, mild, moderate, severe' – not by GMFCS.
Strauss 2007	Feeding tube 'Severe CP'	N = 28513 Age: 4 – 14.	10 years	Mortality aOR	Moderate Evidence

Study	Prognostic indicator	Population	Follow-up period	Outcomes	Study quality and comments
	classified as: unable to crawl, creep, scoot, stand without support or walks and fed completely by others.	Severe CP: unable to crawl, walk or self-feed, n = 6277 Not-severe CP: n = 22236			for age 15 to over 60 years excluded as passes age limit of guideline (25 years).
Touyama 2013	GMFCS level V	N = 580, mean age at start of follow-up: 24.5 months	Mean = 8 years 8 months	aHR	Low
Westbom 2011	GMFCS level V	N = 708, mean age unclear (children born between 1990 –2005).	16 years	aHR	Moderate

1 *aHR adjusted hazard ratio, aOR odds ratio, GMFCS Gross Motor Function Classification System, IQ intelligence*
2 *quotient*

10.3 Clinical evidence results

4 Table 37, Table 38 and Table 39 below summarise the results from the clinical evidence
5 review on the prognostic indicators for walking, talking and life expectancy, respectively.

6

Table 37: Prognostic indicators for walking

Study	Prognostic indicator	Confounders adjusted for	Effect size	Quality
Beckung 2008	Distribution of motor problem: Unilateral spastic CP, bilateral spastic CP IQ < 50	Distribution of motor problem and type (unilateral spastic, bilateral spastic), cognition (IQ), active epilepsy, gestational age < 34 weeks, birthweight < 2500 g (Walking assessed at 5 years)	Inability to walk Unilateral spastic CP IQ <50 versus IQ >50: OR 55.76 (95%CI 23.57-131.89); p<0.0001 Bilateral spastic CP IQ <50 versus IQ >50: OR 9.35 (95%CI 7.69-11.37); p<0.0001 Dyskinetic CP IQ <50 versus IQ >50: OR 5.43 (95%CI 3.34-8.83); p<0.0001 Ataxic CP IQ <50 versus IQ >50: OR 5.21 (95%CI 1.98-13.73); p=0.0008	Moderate
Trahan and Marcoux 1994	Distribution of motor problem: quadriplegia (bilateral spastic LL + UL), diplegia (bilateral spastic LL > UL).	Age at assessment (12 months) Topography (quadriplegia / diplegia), moro reflex, asymmetric tonic reflex, epilepsy, remains seated	Inability to walk Quadriplegia (bilateral spastic LL + UL) versus diplegia (bilateral spastic LL > UL): OR 2.18 (95%CI 0.73-6.52)	Moderate
Wu 2004	Type of CP (spasticity, ataxia, dyskinesis, hypotonia, other including mixed), distribution of motor movement (Spastic hemiplegia (unilateral spastic), Spastic diplegia (bilateral spastic LL > UL), Spastic quadriplegia (bilateral spastic LL + UL), Bilateral spasticity), rolls but does not sit without support	Type of CP, distribution of motor movement, gross motor function (rolling, sitting, and standing milestones), hand use, expressive language, ability to self-feed, vision, epilepsy Age: assessment of nonambulatory children at 2 years	Ambulation by 6 years among children who were non-ambulatory at 2 years Other CP type versus spastic quadriplegia (bilateral spastic LL + UL): OR 2.2 (95%CI 2.2-9.6), p=0.0001 Rolls and does not sit without support versus does not roll: OR 4.6 (95%CI 2.2-9.6), p = 0.001	Moderate

CP: Cerebral palsy, IQ intelligence quotient, OR odds ratio

Table 38: Prognostic indicators for talking

Study	Prognostic indicator	Confounders adjusted for	Effect size	Quality
Chen 2013	GMFCS levels	Age (All participants aged mean 3.8 years and followed up for 6 months)	Language Standardised coefficient (β) = -0.22 p = < 0.001	Low
Parkes 2010	CP Subtype (bilateral versus unilateral), GMFCS level, 'intellectual impairment': severe = IQ< 50, moderate = IQ 50 – 70, none = IQ > 70	CP subtype, GMFCS level, IQ (All participants assessed at 5 years).	Speech impairment Bilateral spastic CP versus unilateral spastic: OR 1.6 (95% CI: 1.1 – 2.4), p <0.001 Non-spastic CP versus unilateral spastic CP: OR 5.1 (95% CI: 2.8 – 9.1), p <0.001 GMFCS I (reference) GMFCS II: OR 2.1 (95% CI: 1.2 – 3.5) GMFCS III: OR 2.5 (95% CI: 1.3 – 4.9) GMFCS IV: OR 4.0 (95% CI: 1.9 – 8.4) GMFCS V: OR 8.0 (95% CI: 4.1 – 15.6) p< 0.001 IQ > 70 (reference) IQ 50 – 70: OR 2.7 (95% CI: 1.8 – 4.0) IQ < 50: OR 3.6 (95% CI: 1.8 – 4.0) p < 0.001	Moderate

GMFCS Gross Motor Function Classification System, IQ intelligence quotient, OR odds ratio.

Table 39: Prognostic indicators for life expectancy

Study	Prognostic indicator	Confounders adjusted for	Effect size	Quality
Blair 2001	"Intellectual ability", IQ: < 20, 20 – 30, 35 – 49, 50 – 69, 70 – 85, > 85	Age Severity of CP: minimal, mild, moderate, severe (not defined by GMFCS) Adjustment for 'disability score', which includes type of motor disorder and cognition, unclear.	Severity: Mortality RR: 1.39 (95% CI: 1.14 – 1.71) IQ: Mortality RR: 2.14 (95% CI: 1.88 – 2.44)	Very low
Strauss 2007	Life expectancy assessed separately for severe and not severe CP: Feeding tube	Age (5 years) Mobility Mode of feeding (feeding tube/no feeding tube) (Gender not adjusted for as it was found to be not significant in model)	For severe CP Feeding tube: mortality OR 2.34 (95% CI: 2.00 – 2.74) For not severe CP Feeding tube: mortality OR 4.46 (95% CI: 3.74 – 5.33)	Moderate
Touyama 2013	GMFCS level V	Gender Gestational age ≥ 37 weeks Birthweight ≥ 2500 g	HR 16.281 (95% CI: 5.612 – 47.236) p < 0.001	Low
Westbom 2011	GMFCS level V Gastrostomy	Catchment area population GMFCS I – IV Gastrostomy (gender not significant in model)	GMFCS V HR 11.36 (SE: 6.43) p <0.001 Gastrostomy HR 8.79 (SE: 4.29) p< 0.001	Moderate

CP cerebral palsy, GMFCS Gross Motor Function Classification System, HR hazard ratio, OR odds ratio, SE standard error, IQ intelligence quotient, RR risk ratio

10.4 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations on the clinical and developmental prognostic indicators in relation to walking, talking or life expectancy were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

10.5 Evidence statements

10.5.1 Prognostic indicators for walking

High quality evidence from 1 study with 9012 children with cerebral palsy suggests that children with unilateral spastic cerebral palsy with IQ < 50 are more likely to be unable to walk compared with children with unilateral spastic cerebral palsy and IQ > 50.

High quality evidence from 1 study with 9012 children with cerebral palsy suggests children with bilateral spastic cerebral palsy with IQ < 50 are more likely to be unable to walk compared with children with bilateral spastic cerebral palsy and IQ > 50. Moderate quality evidence from 1 study with 187 infants with cerebral palsy suggests that there was no significant difference in risk of not being able to walk in children classified as having diplegic (bilateral LL>UL) or quadriplegic (bilateral LL+UL) cerebral palsy at 12 months of age.

Moderate quality evidence from 1 study with 2295 showed that children without spastic quadriplegia (bilateral spastic LL + UL), are more likely to achieve full ambulation (defined as being able to walk well alone at least 20 feet without assistive devices) compared to those children with spastic quadriplegic distribution of cerebral palsy.

Moderate quality evidence from 1 study with 2295 children with cerebral palsy suggests that children who roll but do not sit without support at 2 years of age are more likely of being capable of full ambulation at 14 years of age (defined as being able to walk well alone at least 20 feet without assistive devices) compared to those children who do not roll only at 2 years.

No evidence was found for the indicator: severity of functional disability (GMFCS levels). However, evidence was found in children who have quadriplegia (bilateral spastic LL + UL), whom are generally of GMFCS level IV – V.

10.5.2 Prognostic indicators for talking

Low quality evidence from 1 study with 78 children with cerebral palsy suggests that an increase in severity of functional disabilities (denoted by GMFCS levels) is associated with a decrease in ‘language’, assessed using the Comprehensive Developmental Inventory for Infants and Toddlers (CDIIT).

Moderate quality evidence from 1 study with 1357 children with cerebral palsy suggests that bilateral spastic cerebral palsy is associated with an increased odds of speech impairment compared to unilateral spastic cerebral palsy and non-spastic cerebral palsy.

Moderate quality evidence from 1 study with 1357 children with cerebral palsy suggests that an increase in severity of functional disabilities (GMFCS levels) is associated with an increase in speech impairment.

Moderate quality evidence from 1 study with 1357 children with cerebral palsy suggests that moderate cognition (IQ 50 – 70) and severe cognition (IQ < 50) are associated with an increase in speech impairment compared to children with 'no intellectual impairment' (IQ > 70).

No evidence was found for the indicators: uncontrolled epilepsy and swallowing difficulties/dysphagia, including need for enteral tube feeding.

10.5.3 Prognostic indicators for life expectancy

Very low quality evidence from 1 study with 2014 children with cerebral palsy suggests an increase in severity (categorised as: minimal, mild, moderate, severe) is associated with an increased risk of mortality.

Very low quality evidence from 1 study with 2014 children with cerebral palsy suggests a decrease in IQ (from IQ > 85 to IQ < 20) is associated with an increased risk of mortality.

Moderate quality evidence from 1 study with 6277 children with severe cerebral palsy (unable to crawl, walk or self-feed) and 22236 children with not severe cerebral palsy suggests that a feeding tube is associated with an increased risk of mortality.

Low quality evidence from 1 study with 580 children with cerebral palsy suggests that severe functional disability (GMFCS level V) is associated with an increased risk of mortality.

Moderate quality evidence from 1 study with 708 children with cerebral palsy suggests that severe functional disability (GMFCS level V) is associated with an increased risk of mortality, taking into account gastrostomy.

Moderate quality evidence from 1 study with 708 children with cerebral palsy suggests that gastrostomy is associated with an increased risk of mortality, taking into account severity of functional disability.

No evidence was found for the indicator: comorbidities (epilepsy, scoliosis and chest infections).

10.6 Evidence to recommendations

10.6.1 Relative value placed on the outcomes considered

All outcomes in this review (ability to walk, talk and life expectancy) in relation to clinical indicators listed in the protocol were considered critical outcomes.

10.6.2 Consideration of clinical benefits and harms

10.6.2.1 Prognosis for walking

The Committee acknowledged the evidence presented and agreed that no additional studies meeting the protocol criteria were missed.

There was some evidence which showed that in children who are non-ambulatory at 2 years, full ambulation at 6 years, defined as being able to walk well alone at least 20 feet without assistive devices, was even less likely if they also did not roll at 2 years of age compared to those who were able to roll but did not sit. The Committee agreed that this evidence supported their observations in clinical practice. Conversely, the Committee recommended that it was important to advise parents that if a child could not sit and could not roll at 2 years of age they would unlikely to be able to walk later in life. This recommendation was based on

the Committee's clinical experience and the information provided by development of the GMFCS levels and was therefore agreed by consensus.

The Committee agreed that the evidence showed that more severe cognitive and physical abnormality in function was associated with increased odds of being unable to walk at 5 years of age. The Committee noted that the disparity between normal and abnormal developmental profiles, as outlined in GMFCS at an early stage led to difficulties in clearly assessing long term functional outcomes on assessment before 12 months of age

The Committee agreed to consider an additional paper (Rosenbaum 2002) that did not meet the review protocol criteria due to non-comparative and unadjusted analysis, but constituted supplementary evidence on the matter of prognosis for walking in children with cerebral palsy. Although no adjusted relative effects were reported, gross motor prognostic curves for children and young people with cerebral palsy were presented. This provided an association between Gross Motor Function Measure (GMFM) assessment, which measures gross motor activity, including a child's ability to walk forward 10 steps unsupported (item 69 of the GMFM) and GMFCS levels enabling a prediction of walking ability and reported that GMFM decreased as GMFCS (level of severity) increased. The GMFM scores gross motor function in lying, crawling, kneeling, sitting, standing and walk-run-jump activities. Divergence between GMFCS levels in terms of gross motor development curves becomes more recognisable between 12 months and 2 years of age. Therefore based on this and their experience, the Committee recommended to advise parents and carers that if a child with cerebral palsy could sit at 2 years of age, it was likely but not certain that the child would be able to walk independently without adult assistance.

10.6.2.23 Prognosis for talking

The evidence showed an association between severity in terms of GMFCS levels and decreased cognition with poor prognosis for language at around 4 years (mean age after follow-up not specified) and speech impairment at 5 years. Additionally, there was evidence which showed that children with bilateral spastic cerebral palsy have increased speech impairment compared with unilateral spastic cerebral palsy, and that non-spastic types of cerebral palsy (dyskinetic and ataxic motor patterns) have increased speech impairment compared with unilateral spastic cerebral palsy. However, the Committee agreed it was important to note that the detail regarding the assessment methods of both language and speech impairment were not reported in the included studies.

The Committee agreed that parents and carers should be advised that with more severe physical, function and/or cognitive impairment then the greater the possibility was of difficulties with talking. Additionally, the Committee agreed parents and carers should be advised that children with bilateral spastic cerebral palsy are more likely to have a speech impairment compared to unilateral spastic cerebral palsy and that dyskinetic or ataxic types of cerebral palsy are likely to have increased speech impairment compared with unilateral spastic cerebral palsy.

Supplementary evidence from Cockerill 2014 that was not included in the review (did not conduct multivariate analysis) was considered by the Committee. This study reported an association ($p<0.001$) between current epilepsy and speech impairment at 16 to 18 years and was considered by the Committee at the meeting as no other evidence for epilepsy and talking was found. The Committee recognised from their clinical experience that the presence of epilepsy in children with cerebral palsy was more likely to be associated with learning and speech difficulties but that this did not necessarily mean a cause and effect. Parents should be advised that the presence of epilepsy may have an additional adverse effect on comorbidities in a child or young person with cerebral palsy.

10.6.2.31 Prognosis of life expectancy

The evidence showed that increased severity in terms of GMFCS levels and decreased cognition was associated with a decreased prognosis for life expectancy. The Committee agreed to advise parents and carers that the more severe the physical, functional and cognitive impairment, the greater the likelihood for reduced life expectancy.

The evidence also showed that tube feeding (reported as feeding tube and gastrostomy) was associated with reduced life expectancy. However, the Committee noted that children and young people who require tube feeding often have swallowing problems associated with increased severity of cerebral palsy. It was therefore a marker of severity and risk of aspiration due to poor swallow safety rather than life expectancy directly.

The Committee noted that, despite retrieving no evidence for life expectancy associated with the presence of comorbidities, two studies included in the evidence review (Blair 2001 and Westbom 2011) reported comorbidities (epilepsy, scoliosis and chest infections, particularly pneumonia) as a cause of death. In 1 study (Blair 2001), out of n = 151 deaths reported, 16.6% was due to aspiration pneumonia and 37.1% due to other pneumonia, with deaths due to aspiration pneumonia increasing from 1967, 1976 and 1986. It was also reported that deaths due to aspiration pneumonia were associated with profound intellectual deficit, particularly for deaths after 5 years of age (Blair 2001). Another study (Westbom 2011) reported that of the 30 who had died, 26 had epilepsy, 12 had scoliosis and pneumonia was reported as the cause of death in 8. As with the presence of a feeding tube, the Committee recognised that aspiration pneumonia as a cause of death was likely to be a reflection of poor swallow safety.

10.6.3 Consideration of economic benefits and harms

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action. As an aside the Committee noted that children and young people with increased severity of cerebral palsy may require interventions to optimise their nutritional status. The resource and cost use regarding such interventions is discussed in Appendix G.

10.6.4 Quality of evidence

Quality of studies ranged from moderate to very low as there was variable adjustment for confounders in the statistical models of the studies. Confounders that were assessed for adjustment in the statistical model for walking and talking were: severity of functional disability, type of motor disorder, cognition and age. Confounders that were assessed for adjustment in the statistical model for life expectancy were: severity of functional disability, type of motor disorder, age, cognition and enteral tube feeding. If the statistical model adjusted for all confounders listed, no downgrading of quality was applied. If some confounders were adjusted for, quality was downgraded by 1, and if only 1 was adjusted for then quality is downgraded by two.

Two studies included in the review (Chen 2013 and Touyama 2013) reported evidence from a cerebral palsy population in Taiwan and Japan, respectively. Possible indirectness of the evidence was noted, yet it was decided that the quality of evidence was not to be downgraded as the aetiology and distribution of cerebral palsy does not largely differ in these countries. Of these studies, 1 was included for the prognosis of life expectancy and it was also noted in discussion that the life expectancy in Japan does not greatly differ from the UK.

10.6.5 Other considerations

The Committee noted that cognitive impairment, reported in terms of IQ in the studies included, was a proxy for the severity of the brain injury in people with cerebral palsy.

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

10.6.6 Key conclusions

Walking

There is indication from the evidence that decreased cognition or not being able to roll at 2 years may indicate poor prognosis for walking.

Talking

There is indication from the evidence that type of cerebral palsy, decreased cognition and increased severity may indicate poor prognosis for speech and language.

The presence of epilepsy not controlled by medication can have a negative impact on speech development.

Life expectancy

There is indication from the evidence that decreased cognition, severe cerebral palsy and need for feeding tube may indicate poor prognosis of life expectancy. However, the Committee agreed that the need for feeding tube tends to be correlated with severity of cerebral palsy and problems with swallowing.

The Committee agreed it was important to consider that individual life expectancy should be adjusted for associated comorbidities.

10.7 Recommendations

29. Provide the following information to parents or carers about the prognosis for walking for a child with cerebral palsy:

- The more severe the child's physical, functional or cognitive impairment, the greater the possibility of difficulties with walking.
- If a child can sit at 2 years of age it is likely, but not certain, that they will be able to walk unaided by age 6.
- If a child cannot sit but can roll at 2 years of age, there is a possibility that they may be able to walk unaided by age 6.
- If a child cannot sit or roll at 2 years of age, they are unlikely to be able to walk unaided.

30. Recognise the following in relation to prognosis for speech development in a child with cerebral palsy, and discuss this with parents or carers as appropriate:

- Around 1 in 2 children with cerebral palsy have some difficulty with elements of communication (see recommendation 125).
- Around 1 in 3 children have specific difficulties with speech and language.
- The more severe the child's physical, functional or cognitive impairment, the greater the likelihood of difficulties with speech and language.
- Uncontrolled epilepsy may be associated with difficulties with all forms of communication, including speech.

- A child with bilateral spastic, dyskinetic or ataxic cerebral palsy is more likely to have difficulties with speech and language than a child with unilateral spastic cerebral palsy.

31. Provide the following information to parents or carers, as appropriate, about prognosis for life expectancy for a child with cerebral palsy:

- The more severe the child's physical, functional or cognitive impairment, the greater the likelihood of reduced life expectancy.
- There is an association between reduced life expectancy and the need for enteral tube feeding, but this reflects the severity of swallowing difficulties and is not because of the intervention.

10.8 Research recommendations

None identified for this topic.

11 Information and support

Review question: What information and information types (written or verbal) are perceived as helpful and supportive by children and young people with cerebral palsy and their family members and carers?

11.1 Introduction

Children and young people with cerebral palsy, their parents and carers often report that the level of information and support available to them from health and social care professionals can be very variable and this inconsistency can impact on their understanding of the condition and services provided.

The effective communication of information, providing effective support to children and young people with cerebral palsy, their family and carers plays a key role in ensuring all feel empowered and supported to maximise their potential.

The variability in how this information is provided across the UK can lead to inconsistent access to and the take up of services and can make informed decision making about treatment and management difficult.

Due to the perceived variation in the level of support and information given to children and young people with cerebral palsy and their parents and carers, the Committee considered it was important to find out what information and support children and young people with cerebral palsy their parents and carers felt was necessary. In addition to this it was deemed important to standardise access to information in a standardised form and support across the country, highlighting what information and support should be available to children and young people with cerebral palsy and their families. Families need to have the right information delivered in the right format at the right time and to the right level for the individuals concerned. Sharing of such information with all relevant providers of health and social care can ensure adequate communication in patient focussed networks and pathways.

Knowledge empowers children and young people with cerebral palsy, their families and carers to take control and make informed decisions about their lives and management of their condition. This in turn impacts on their quality of life and ability to achieve their potential.

This guidance seeks to support health and social care services to standardise access to, and appropriate delivery of, quality information across the country.

11.2 Description of clinical evidence

Qualitative studies were selected for inclusion in this review. We looked for studies that collected data using qualitative methods (such as semi-structured interviews, focus groups, and surveys with open-ended questions) and analysed data qualitatively (including thematic analysis, framework thematic analysis, content analysis, etc.). Survey studies restricted to reporting descriptive data that were analysed quantitatively were excluded.

Findings/themes were summarised from the literature and were not restricted to only those identified as likely themes listed by the Committee in the evidence review protocol. Some of the themes listed in the protocol were identified in the studies (i.e. ‘information regarding cerebral palsy’; ‘information regarding identification’, ‘cause and prognosis of cerebral palsy or information about organisations’). Conversely, themes related with information about ‘intervention type’; ‘feeding and swallowing’; ‘pain recognition and management’; ‘ transition of care’; ‘commonly used medications’; ‘named individual for point of contact’; ‘resources for managing comorbidities’ or information about ‘patient pathway and points of access’ were not

identified in the literature. An additional theme: 'Increased of awareness within society' was identified in the literature and included in this review.

A total of 7 studies were included in this review (Barnfather, 2011; Darrah, 2002; Reid, 2011; Knis-Mattews, 2011; Kruijsen-Terstra, 2016; Miller, 2013 and Wiegerink, 2013).

The following provides a brief description of the studies included:

- Barnfather (2011) was conducted in Canada and used semi-structured interviews in a sample of 22 young adults with a diagnosis of either cerebral palsy or spina bifida. The study reported the satisfaction with an online intervention delivered by young adults with cerebral palsy or spina bifida to the young people who participated in the semi-structured interviews. Results were reported separately for those with cerebral palsy and spina bifida.
- Darrah (2002) was conducted in Canada and used semi-structured interviews in a sample of 88 young adults. The study reported on a number of themes, including the need for information to be shared between the health care professionals and the families; the need to know the available resources in the community and the necessity of having individually and patient-centred information. Ultimately, the study reported on the need for increased awareness of cerebral palsy within society.
- Reid (2011) was conducted in Canada and used semi-structured interviews directed to a sample of 9 parents of children with cerebral palsy. The study reported on several themes, namely the need for personalised and family-centred information and the need of more information regarding access and applicability for cerebral palsy. This study also reported on the need for increased awareness of cerebral palsy within society.
- Knis-Matthews (2011) was conducted in USA and used individual interviews directed to 4 parents of children with spastic hemiplegia. The study reported in particular on the need for timely information sharing between health care professionals and families; especially with regard to early information. This study also reported on the need of support from other parents.
- Kruijsen-Terpstra (2016) was conducted in The Netherlands and used semi-structured interviews directed to 21 parents of young children with cerebral palsy. This study reported mostly on the need for information on cerebral palsy, and in particular on diagnosis, therapy or prognosis and development of the condition.
- Miller (2003) was conducted in the UK and used focus groups of 13 families of children with cerebral palsy. This study explored several themes, including the need for knowing information on the prognosis of cerebral palsy, special equipment or the need for information to be shared between health care professionals and families. This study also reported on the need for an increased awareness of cerebral palsy within society.
- Wiegerink (2013) was conducted in the Netherlands and used focus groups and open interviews in 20 young adults with cerebral palsy to explore the queries these young adults have about sexuality and the way they prefer to receive information.

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

11.2.1 Summary of included studies

A summary of the studies that were included in this review are presented in Table 40.

Table 40: Summary of included studies

Study	Study design/ methods	Population	Aims	Limitations assessed using an adapted Critical Appraisal Skills Programme (CASP,2006)
Barnfather, 2011	Qualitative/ Semi-structured interviews to young people	N=22 young people (on average 15 years old) with a diagnosis of either spina bifida or cerebral palsy.	To determine the extent to which adolescents with disabilities use an online peer support intervention and to evaluate support intervention processes, perceived benefits, and satisfaction with the intervention.	Overall quality based on limitations: moderate
Darrah, 2002	Qualitative/Semi-structured interview in the participant's home	N =49 young people (age range: 13-15 years) and n=39 young adults (age range: 19 to 23 years) and their families.	To examine the satisfaction of families of adolescents and young adults with a diagnosis of cerebral palsy with the service delivery they had experienced in the areas of health, education, recreation, employment, housing and transportation	Overall quality based on limitations: low-moderate
Reid,2011	Qualitative/Semi-structured interviews directed to parents	N=9 parents of children with CP. Children's ages ranged from 17 to 22 years.	To explore the theme "If I knew then what I know now, I would have done things differently" with parents of young adults with CP. In doing so, researchers aimed to identify areas in which health care professionals might be able to improve their practice in order to work more effectively with parents to provide the best care for children with CP.	Overall quality based on limitations: moderate
Knis-Matthews,2011	Qualitative/each researcher met individually with 1 of the 4 participants to interview them.	N = 4 parents of children with unilateral spastic CP. Children's age ranged from 5 to 9 years old.	The original aim of this study was to document the perspectives of 4 parents of children diagnosed with CP who participated in a CIMT program	Overall quality based on limitations: moderate

Study	Study design/ methods	Population	Aims	Limitations assessed using an adapted Critical Appraisal Skills Programme (CASP,2006)
			delivered using a group format. During this process, the parents discussed other issues that are related but separate from the primary aim of the study. To report parents' perspectives, it is important to include these additional issues that address support systems and service delivery.	
Kruijsen-Terpstra, 2016	Qualitative/Semi-structured interviews with parents	N=21 parents of young children with cerebral palsy aged 2-4 years.	To explore the experiences and needs of parents of young children with cerebral palsy regarding their child's physical and occupational therapy process in a rehabilitation setting.	Overall quality based on limitations: low- moderate
Miller,2003	Qualitative/ Focused interviews with parents	N=13 families of children with CP. Children's age ranged between 2 and 16 years old.	To seek families' views about what information they would like about the NECCPS and how they would like this information to be conveyed. While interviewing these families, it became clear that they also wished to discuss their own information needs regarding cerebral palsy as distinct from information about the register so those have also been reported.	Overall quality based on limitations: moderate
Wiegerink, 2013	Qualitative. Topic were explored in open interviews and a focus group.	N=20. Young people ages ranged from 15 to 25 years old	To explore the queries young adults with CP have about sexuality and the way they prefer to be informed.	Overall quality based on limitations: low

1 *CP Cerebral Palsy, CIMT Constraint-induced movement therapy program, NECCPS North of England*
2 *Collaborative Cerebral Palsy Survey.*

11.3 Clinical evidence profile

Individual studies were assessed for methodological limitations using an adapted Critical Appraisal Skills Programme (CASP 2006) checklist for qualitative studies, where items in the original CASP checklist were adapted and fitted into 5 main quality appraisal areas according to the following criteria:

- Aim (description of aims and appropriateness of the study design)
- Sample (clear description, role of the researcher, data saturation, critical review of the researchers' influence on the data collection)
- Rigour of data selection (method of selection, independence of participants from the researchers, appropriateness of participants)
- Data collection analysis (clear description, how are categories or themes derived, sufficiency of presented findings, saturation in terms of analysis, the role of the researcher in the analysis, validation)
- Results / findings (clearly described, applicable and comprehensible, theory production)
- An adapted GRADE approach was then used to then assess the evidence by themes. Similar to GRADE in effectiveness reviews this includes 4 domains of assessment and an overall rating:
- Limitations across studies for a particular finding or theme (using the criteria described above)
- Coherence of findings (equivalent to heterogeneity but related to unexplained differences or incoherence of descriptions)
- Applicability of evidence (equivalent to directness, i.e. how much the finding applies to our review protocol)
- Saturation or sufficiency (this related particularly to interview data and refers to whether all possible themes have been extracted or explored)

The clinical evidence profile for this review question (information and support) is presented diagrammatically in a theme map in Figure 4) and the quality of the evidence as per the adapted GRADE approach for qualitative findings is presented in Table 41, Table 42 and Table 43.

Figure 4: Theme map of the evidence

Table 41: Summary clinical evidence profile (adapted GRADE approach for qualitative findings) – theme: increased of awareness within society

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
Sub-theme 1: carers (teachers, service providers)					
2 studies	2 semi-structured interviews	• 2 studies (Darrah 2002; Reid 2011) reported on the need of increased of awareness within society about cerebral palsy. • Parents felt that many service providers did not understand the needs and abilities of their children. They recommended that teachers and health care providers were provided with more information in their educational training about how to relate to persons with disabilities. • Participants also expressed frustration at having to repeat their child's history with every new teacher, doctor, therapist or new service agency involved with their child. Parents suggested the generation of an educational file or portfolio that described the child's abilities and challenges, methods of learning and communication, etc. This file could travel with the child at school: • *"... at the beginning of the school year, we usually call a meeting, all her teachers get together, so they're all sitting there and they all hear the same thing. I usually make out a form of, like, what she can and can't do, or what she has difficulty with. And I hand it out to all the teachers so they all have a copy, and it's on her file. What we did is: I got pamphlets, and we had them put it in her file this year. But it's like every year starting over, and you do it again the next year ..."* • Parents reported a need for increased education of teachers that fosters awareness, and not fear about cerebral palsy and the corresponding needs for children of all functional levels. Parents recognised the challenges that educators face when teaching a child with CP and found that sensitive	Limitation of evidence	Moderate limitations	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Saturated	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		training, positive personal outlooks, and smaller class sizes were important to optimize their child's education. • Parents of children with relatively mild impairment of motor function (i.e. GMFCS level I) noted that their children experienced unique challenges within the school system related with their more "invisible" impairments. These parents felt that their children's learning and social–emotional impairments were less likely to gather attention and appropriate supports than their physical impairments: • *"Her teacher did not understand because (child) looked very normal. And they just did not understand her condition. And because they didn't understand her condition they didn't make allowances for it".*			
Sub-theme 2: family and peers					
2 studies	1 semi-structured interview and 1 focus group.	2 studies (Darrah 2002; Miller 2003) reported on the need of increased awareness of cerebral palsy among their extended family members and peers. • Participants reported that often the general public and their children's peers were not comfortable with a person with a disability: • *"... a lot of society needs to be more accepting. Educate the general public...when we go to a mall, and there's always someone following, staring, right?"* • *"Just when I seem to think they start to know how I feel, they turn around and do something like collapse my walker... These are some kids who don't even bother to tease me because they don't even know I'm alive, I think, but oh well".* • Parents also reported on the need of the extended family to know more about cerebral palsy: • *'My family know that she's got cerebral palsy but they don't know what it is and I think they're scared to ask us. Often I*	Limitation of evidence	Moderate limitations	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Saturated	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		think they just don't want to know. Sending it to them would educate them and that would help them and us.' 'To doctors and health centres – they have information and newsletters on everything else so why not on cerebral palsy?' 'It's not the carers of people with cerebral palsy that need information or education about the impact of the condition on family life or need to have their awareness raised, it's other people who do – the general public . . . just to be more flaming helpful when you're struggling with a severely disabled child in a wheelchair.'			

1 *CP cerebral palsy, GMFCS gross motor function classification system.*

2 **Table 42: Summary of clinical evidence (adapted GRADE approach for qualitative findings) – theme: condition-specific information**

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
Sub-theme 1: Prognosis, natural history and comorbidities					
2 studies	1 interview, 1 focus group.	2 studies (Kruijsen-Terpstra 2016; Miller 2003) reported on the need of having more information about prognosis as well as information about the specific type of cerebral palsy that their child have: • *'We don't know about prognosis. We're in the dark so any information at all would be appreciated.'* • *'The most I would like to know about cerebral palsy is more about the particular type of cerebral palsy rather than just cerebral palsy because I would like to know about our (daughter's) type of cerebral palsy than just cerebral palsy itself . . . what I find lacking is not enough information about her particular type of hemiplegia.'* • *'Information on behaviour you know we have had some really difficult times in the past . . . not knowing that it is common*	Limitation of evidence	Moderate limitations	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Saturated	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		(with this type of hemiplegia) to get epilepsy and the absences.' • *"If you have to decide for yourself then I wouldn't really know how to do that. What goals you can set, or will she actually be able to do this in three months' time? So I'd think, 'We'll have to wait and see, you know?' And then the others [i.e. therapists] would be fully convinced: 'Yes, I think so'. But they know much more about it than we, of course, so I'd always appreciate it when they did that.* In addition, most parents expressed the desire for their child to live independently in the future. They wanted more information about what to expect for the future although some of them no longer dared to have expectations about their child's development: • *"Yeah, we're always very neutral about it, so that it's all good. So it's not that you expect something and then you're disappointed".*			
Sub-theme 2: Specific resources: social and educational					
2 studies	2 semi-structured interviews.	2 studies (Darrah 2002; Reid 2011) reported that parents recommended that community programs or services should be more widely advertised and used, and requested assistance in negotiating long wait lists to access programs. Across all service areas, parents felt that service providers often did not share information about available services spontaneously, but rather restricted themselves to answering only the specific questions of the parents and caregivers: • *"I said, 'You know, they don't tell you anything, so you don't know what help there is'. She [social worker] said, 'Maybe you don't ask the right questions'. Well, who do we ask those questions? Where do you ask those questions? To whom do you ask? No one tells you".* • *"...the services are there. Sometimes you have to ask*	Limitation of evidence	Moderate limitations	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Saturated	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		specifically. Like they don't just sort of say well these are the services that are out there for you. You have to say, 'I want this'. And then they'll tell…we're finding all these things out ourselves. It would be really kind of nice to have a list of community organizations that help disabled people". • *"...but her transitions and everything have gone relatively smoothly (...) and I think it's just because we have been plugged into the right groups (community programs and services), and we have used them".* 1 study (Reid, 2011) reported on the great importance of the diagnosis to support the child's eligibility and access to needed supports: • *"Put as many labels on her as she needs ... because without the labels, you don't have access to all that. And that opened up everything for her. She got all the equipment she needed, we got her into the social group that she loves..."*			
Sub-theme 3: Access and applicability					
1 study	1 focus group	1 study (Miller 2003) reported on the difficulties that parents experience in accessing appropriate commercial aids, fittings and equipment even when there were no financial barriers to obtaining the items. Difficulty in knowing about and obtaining appropriate aids, fittings, and equipment. This was especially for the older child. It was a practical problem, not a financial barrier: • '*Practical information would be useful – you know, on specialist equipment. We need lots of equipment as our son grows and we didn't know where to get it. It can be very expensive. We only found out by default that some good equipment is available second hand'.* • *'We never get told about equipment we only found out about it by chance. The doctors don't tell us. The NHS doesn't tell us. It would be excellent'.*	Limitation of evidence	Moderate limitations	Moderate
			Coherence of findings	Not applicable	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Saturated	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		• *'Definitely information on equipment. She is getting older now and has started riding a bike with stabilisers and she wants to try without the stabilisers. It is knowing about equipment . . . we don't know much about equipment and types of equipment that we can get and what is available to us and that sort of thing.'*			
Sub-theme 4: Sexuality					
1 study	1 focus group	1 study (Wiegerink 2013) reported on sexuality-related questions about coping with pain, fatigue spasticity or physical limitations. Questions also related to medical devices, pregnancy, fertility, contraception, communication with their partner, parenting. Young adults with cerebral palsy preferred written information as well as the Internet to find answers to their questions and they wished to communicate with other people with cerebral palsy about sexuality.	Limitation of evidence	Very low limitations	Very low
			Coherence of findings	Not applicable	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Not saturated	

Table 43: Summary of clinical evidence (adapted GRADE approach for qualitative findings) – theme: personalised and family-centred information

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
Sub-theme 1: Methods of information delivery					
6 studies	4 semi- structured interviews, 1 interview, 1 focus group	Support from other parents or peers 2 studies (Kruijsen-Terpstra 2016; Knis-Matthews 2011) reported on the importance of receiving support from other parents or peers who are facing similar life experiences. These relationships provided moral support and also served as a resource: • "*I have another mom with a child with a disability and he is in*	Limitation of evidence	Moderate limitations	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Partial	
			Sufficiency or	Saturated	

Study information			Quality assessment		
Number of studies	Design	Description of theme or finding	Criteria	Rating	Overall
		the same grade as Jake. We are on the phone all the time. Jake went to a disabled preschool ...so I met people ...they understand." • *"That was really the light bulb, knowing that there were other people that had walked this path before me. It was a great resource for me".* • *"The first time I was asked that question [defining the child's therapeutic needs], I thought 'What? What should I ask for? How can my child become healthy? So my response was, like, 'What?' So the first few times I asked nothing. But then you get to talk to parents who have been faced with this for some time, and you get some information: 'Oh, yes, that's something you can ask. Right, about toilet training, that's a good question'. So you start to think differently about the way they think"*. 1 study (Barnfather 2011) reported that young people felt a sense of belonging after having participated in an online support intervention. They believed that other young people who have experienced similar situations as them could provide them with support better than parents, friends, or doctors: • "*I always feel that I can never tell anybody because they don't understand; they don't go through what I go through. And here [chat group], it's great, and you can talk about everything and anything, and nobody bashes you for it. Some people disagree with you, but they don't, like, bark at you for it".* • *"It gave me a different window into myself, not just into other people. It made me understand a bit more about myself and my limitations and my goals and the way I can fit them"* • *"The chats made me have a better attitude toward life, going through it and knowing that there were other people like me out there in the world and other who are worse than I am*". Conversely, in this same study (Barnfather 2011) 1 of the	saturation		

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		participants, disagree with the other participant's view: • "I personally don't like being grouped in specifically with people who have disabilities, because it makes me think I'm not normal if I'm being stuck with other people who have disabilities, too. It makes me focus on the fact that I'm different, and I don't really like that". Individually and patient-centred information 3 studies (Darrah 2002; Reid 2011; Miller 2003) reported that parents preferred that the child was addressed directly. Involving the him/her in discussions and paying attention to their needs: • *"But the number one thing I find with my service provider, the first time I meet them if they walk over, if they say hi to me and they walk directly over to her and say hi (name of the child)—right there is the tell-tale for me."* • *"...the secretary talked to me, I was standing back at the door, and she had rolled up to the desk—the secretary looked over her and talked to me and asked me questions ...I think they just ...habit, people just do it"* • *"... the first dentist we would go to, he wouldn't even speak to him. There was no conversation at all. It was just like he was looking at an inanimate object or something, you know. There was nothing, he never acknowledge Fred from the time we went until the time we left".* Families and young people also preferred the health care professional using jargon-free language: • *"I guess, like, the doctors use big terminology and I think that, if I want to be a part of the decision, they kind of should talk so that I can understand it".* • *'Not full of medical or technical jargon. We already get enough of information that we don't understand. The doctor baffles us with jargon and we always have to ask the physio afterwards.'*			

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		• '*We feel intimidated by the doctor and all the medical terms. We always have to ask for explanations and we feel stupid because we don't understand. Something in the information on our terms would be very helpful especially about diagnosis and prognosis.'* 2 of the studies (Barnfather 2011; Miller 2003), reported on the preferred method for information sharing. For the online intervention, participants reported that it created a safe space and fostered social exchange .They mentioned that the support intervention was "enjoyable", "humorous", and "interesting". • *"It's got a sense of community to it, that everybody respects everybody; you have your own opinion, but at the same time, you don't try to shove it down people's throat to get it across..."* In the context of written information, participants stressed that information should be easy to read and non-threatening. Most did not want much detail, rather a general overview: • *"Easily digestible and light-hearted"* • *"Something a bit light-hearted really, not too many facts and figures"*			
Sub-theme 2: Timely share of information between health care professionals and families					
5 studies	1 interview, 3 semi-structured interviews, 1 focus group	Early information 3 studies (Knis-Mattews 2011; Kruijsen-Terpstra 2016; Reid 2011) described parents' experiences upon the child's discharge from the hospital after being born. Most parents reported frustration for the lack of information and recalled a difficult time coping. This was discussed as a communication	Limitation of evidence	Moderate limitations	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		failure on the part of the health professionals. Breaking bad news was an issue and even though children had been diagnosed years ago, many parents remained bitter and angry about the way in which this had been done: • *"We only found out by chance (that daughter had cerebral palsy) when she was a year old. We overheard doctors talking about her".* • *"When I first learned of the diagnosis, I didn't know anything about it, I really had no idea, I tried to look it upon the internet, couldn't find much information".* • *"It's very hard to find somebody who has been through it. People talk to you like you should know what early intervention is. I didn't know what early intervention was."* • *"Yeah, that [i.e. information on the way children with cerebral palsy can function in society] is what I really missed! You enter a world that you know nothing whatsoever about. You leave the hospital with the child and they tell you' Well, keep track of its development".* • *"... when you get the diagnosis you're in shock. They give you all sorts of information and it doesn't sink in ... and nobody really talks to you fully about it after. You know, you get all different services but they're all like separate".* 1 of the studies (Knis-Mattews 2011) reported on the impersonal setting in which some parents received news about their new-born child: • "*The doctors actually came into my room and said that [his] brain bleed was so severe and recommended just stopping all life support and all medical assistance. My husband and I said No! There's no way. We are going to do anything we can to save him."* • *"The hospital was like eight weeks of truly living hell and the whole roller coaster ride of ups and downs .... We had such an emotional time. It was such a roller coaster that we*	Sufficiency or saturation	Saturated	

Study information			Quality assessment		
Number of studies	Design	Description of theme or finding	Criteria	Rating	Overall
		thought our world was ending and the next minute we would get great news." • *"They (hospital staff) were like, why don't you go downstairs and read about [herpes meningitis] and I'm like my child is not even out of intensive care."* Reflective practice 1 study (Miller 2003) reported on parents views about information provision from health care professionals through their child's development. Parents thought that this process was inadequate, and they were equally concerned about the quantity and quality of information: • *"Professionals need to improve information sharing and be more equal"* • *"On the whole I've been treated by most doctors as an equal but the neurologists in particular consistently kept information from us, lulled us into a false sense of security. I don't see why I couldn't have been told and had equal access to information about my child. They said it was due to a fear that I might not bond if I heard anything bad"* • *"My GP allowed me to sit down and read through my daughter's notes and see what the neurologist had written . . . I was very angry and distressed because all the time we were being fed only partial information and being lulled into a false sense of security.'* • *'When we take x (daughter) to see her consultant, there are usually other doctors and health professionals in the room and he (consultant) always talks to them, he never ever talks to us. We always have to ask the physiotherapist to explain to us what was said afterwards."* • *"I feel there is still a notion of power and privilege with regard to information and doctors still keep privileged information. My GP does but he's not the child's parent. It does make me very angry. I'm as qualified in my field as doctors are in theirs*			

Study information			Quality assessment		
Number of studies	Design	Description of theme or finding	Criteria	Rating	Overall
		and they should share information with me as an equal". • *"Being kept abreast of what they (doctors) know and what the current thinking on the condition is would be good, rather than them have their own little secret research societies and groups".* 1 study (Darrah 2003) reported on participant's content after receiving genuine personal comments: • *"I, in particular, with her first operation, before we took her home, I remember. One of the nurses said to me, and they were so busy, just rushes. And she said, you know, 'Are you worrying?' And I said, 'Yes, I'm really worried. I really, I've never nursed, I don't know anything about casts. I don't know anything about operations'. So she said, 'Tell you what, we'll sit down for 15 minutes and we'll go through this'. And she sat down on the bed and she took me through all sorts of stuff that I needed. And she said. 'You will see, you know, blood will start coming through from the operation. It will come through the plaster cast. (...). What she did is she gave me confidence to look after myself. And that was more important than anything else she could do".*			

11.4 Evidence statements

A number of themes emerged from the evidence provided from the interviews, focus groups and discussion groups with parents, children and young people with cerebral palsy. These themes centred around making information specific to cerebral palsy (for example, diagnosis, prognosis, services available) accessible at an early point of the pathway to parents and families as well as the society as a whole. Additionally, evidence related to the methods of information delivery for patients and carers was also found.

Overall, having access to clear, patient-centred information was of crucial importance for the participants of the studies. The themes that emerged after review of the literature were: 'Increased awareness within society', 'condition-specific information' and 'personalised and family-centred information'.

11.4.1 Increased awareness within society

Four studies of moderate to low quality reported on the theme of increased awareness within society.

In 2 of the studies, participants wanted to make cerebral palsy-specific information available for their children's carers (teachers, service providers). Participants felt that most of the times service providers and teachers in particular, were unprepared to manage a child with cerebral palsy. They believed that more education and awareness was essential, as health care professionals and teachers played a pivotal role in the family's life and child development.

In 2 of the studies, parents wanted an increased awareness of cerebral palsy for their extended "family and peers" as often those were not comfortable with a person with a disability. This could help families in an indirect way (for example, by being more tolerant and conscious of their needs when they are struggling with a wheelchair) and make peers more aware of their challenges and ways to support them.

11.4.2 Condition-specific information

Four studies of moderate to low quality reported on the theme of condition-specific information.

In the sub-theme 1, 2 of the studies described the need of information in "prognosis, natural history and comorbidities". Parents were uncertain about the specific development of their child's condition and desired more information on prognosis in general, but also about the specific types of cerebral palsy. Knowing what to expect for their child's future and setting realistic goals were important factors for the participants of these studies.

The second sub-theme: "specific resources: social and educational", reported the difficulties that parents face regarding the access to community centres or recreational services. Most of them were aware that the services were there, but were uncertain about how to access them. They required health care professionals to share this information spontaneously and without being prompted by parents. Parents also highlighted the importance of provision of a specific 'label' or diagnosis to facilitate accessing to services and further support.

One study reported on a third subtheme, "access and applicability": the evidence showed that parents experienced difficulties in accessing individualised specialist equipment to help with posture, mobility, care and communication, even in the absence of financial barriers. They required more information regarding what equipment was appropriate, where to get the equipment and which equipment is available.

One last study reported on the theme of sex and sexuality related information for young adults with cerebral palsy. They preferred written information as well as using e-forums such as the Internet to find answers to their questions. In particular, they wished to communicate with other people with cerebral palsy about their experiences of sex and sexuality.

11.4.3 Personalised and family-centred information

A total of 7 studies of low to moderate quality evidence reported on the theme “personalised and family-centred information”.

Six of the studies reported on the subtheme “methods of information delivery”. Two of those studies described the need of support from other parents or peers. Having contact with other people who have had similar life experiences gave them a feeling of moral support and provided them with meaningful responses for their areas of uncertainties. In addition, 1 of the studies investigated young people’s experiences with an online forum group / intervention provided by peers with their same condition. Overall, young people felt they were very satisfied with this experience as gave them a sense of belonging and helped them to understand more about themselves, their limitations and goals for the future.

Three studies reported on the need of individual, patient-centred information for the patients, their parents and families. The evidence showed that families preferred to have their needs acknowledged by the service providers and to be talked to without medical jargon. Technical language made parents, carers and patients feel intimidated and they felt uncomfortable having to constantly ask for clarification.

Five studies reported on the subtheme “timely sharing of information between health care professionals and families”. This subtheme differentiated between “early information” and “reflective practice”. Three studies were identified reporting on early information. The evidence reflected on the difficulties that parents experienced after their child was born and on discharge from the hospital, in the group considered at high risk of developing cerebral palsy. In this process, parents advocated for a more transparent, universal and fair process. It was highlighted that some of them only found out about developmental concerns or the possibility of their child’s diagnosis by chance or in a very impersonal way. One study described the need for ongoing information throughout the children’s development and supported the necessity of “reflective practice”. The evidence showed that some of the health care professionals kept information out from the parents and gave them a false sense of security. Genuine, clear personal and individual comments were highly appreciated by the participants of the studies.

11.5 Evidence to recommendations

11.5.1 Relative value placed on the outcomes considered

The aim of this review was to identify the information and information types perceived as helpful by children and young people with cerebral palsy and their parents or carers. Evidence on all of the themes relevant to the evidence review question were considered important by the Committee.

11.5.2 Consideration of clinical benefits and harms

The Committee acknowledged the evidence presented and noted the significant differences in the quality of the studies. The Committee noted the theme identified in the evidence that information provided should be person-centred and they agreed that a fundamental aim for the guideline was to recommend that advice should be tailored to the individual needs of each child or young person with cerebral palsy, their families and carers. The Committee drew on other NICE guidelines that contained specific recommendations about information

and support, such as the NICE guidelines on Autism in under 19s and the Spasticity in under 19s. The Committee discussed how a considerable amount of information is already available online for people with cerebral palsy to use, but the clarity, applicability and usefulness of this varied considerably. They agreed that it was important to direct children and young people with cerebral palsy and their families and/or carers to relevant sources according to their needs.

The Committee agreed that consistent information should be provided to children and young people with cerebral palsy and their families and carers on the following areas addressed in the guideline: aetiology, prognosis, identification, natural history, comorbidities, equipment, resources available and access to financial, respite, social care, as well as support for children, young people and their parents, carers and siblings and educational settings.

The Committee highlighted the need for integrated communication to ensure that all agencies involved in the care of the person with cerebral palsy shared information with each other, ensuring that the child, young person, families and carers had access to the same information as those involved in their wider care. This would also help to avoid the use of unclear terms and jargon. The Committee recognised that children and young people with cerebral palsy are looked after by a great variety of professionals, and that as such integrated communication was vital.

It was recognised that a child or young person, or parent-held 'folder', containing the individual's personal information, could be an effective way of sharing up to date information. The individual or their parent could share with this with any new agencies involved in their care. The Committee noted that there are a range of online options which a family could choose to share as they wished in its entirety or allowing access to specific sections of the 'folder' as appropriate. If using an online version, hard copies could be printed off. Based on their experience and by consensus, the Committee agreed that the folder should contain information on a variety of different areas including:

- Birth and early history,
- List of up to date medication,
- The timing and outcome of any medical and surgical interventions,
- Comorbidities
- Functional and developmental abilities, including mobility,
- Preferred way of communication,
- What equipment was provided and was useful,
- On-going care plans
- A list of health, care and emergency contacts.

This folder could be made available for the extended family if parents, carers and patients wished it.

Evidence presented to the Committee showed that 1 of the key concerns raised by families was the need to repeat medical history and other pertinent details regularly to a number of different healthcare professionals, and it was felt that a collection of key information, such as described above, would support this. It was also felt that it would support children and young people with cerebral palsy and their parents and carers during transition.

The lay members on the Committee specifically acknowledged the difficulties that some families and carers faced when trying to access information about specific resources; saying that access was difficult unless there was sufficient knowledge of 'the system and the legislation'. Families need to understand the processes, their rights, the implications of legislation etc., therefore the Committee pointed out that there was also a need for information on what services are available and how to access them in order to help those in need better navigate their way through the current system.

The Committee also mentioned that resources varied locally and over time. Resources that were available one year may not be available the following year. The Committee agreed that it was very important for people with cerebral palsy and their parents and carers to get support from advocacy groups. The Committee mentioned that local authorities also had the responsibility of supporting people with disability and their families; and that they should enable access to support groups to people with cerebral palsy.

One of the themes identified in the evidence showed that young people wanted to have specific information about sex and sexuality. The Committee commented that patients should be supported with information and resources in a timely way. It was acknowledged that schools covered this topic in a general way, but they felt that specific advice for people with cerebral palsy was both wanted and warranted. It was recognised that in order to address this adequately the advice needed to be tailored to the individual and if further support and advice was required, care professionals delivering the advice should be aware of local specialists.

With regard to the way information should be provided, the Committee referred to the recommendations contained in the NICE guideline on Patient experience in adult NHS services. They also agreed on the necessary adjustments required for severely impaired patients. For example, information should be provided in visual format if required, ensuring a range of formats are available.

11.5.3 Consideration of economic benefits and harms

This review question was not relevant for economic analysis because it does not involve a decision between alternative courses of action. Even so, the provision of identified information and support needs may incur opportunity costs. For example, recommendations that promote a transparent dialogue require no resources to achieve, whereas adapting communication and information resources using, for example, augmentative and alternative communication systems. The Committee stated that under current clinical practice, information and support was often provided at the wrong time and/or in the wrong setting leading to a wasteful use of resources if they are not utilised as intended. For example, if key decisions are made without people being fully informed, therapies prescribed without patient and family involvement in the decision may lead to non-adherence. As a result the Committee believed their recommendations would identify information and support needs children and young people with cerebral palsy, parents and carers would find useful, potentially preventing an inefficient use of resources.

The Committee also believed families were unclear as to the resources available to them, potentially limiting the child or young person's health-related quality of life. Therefore, ensuring that families and all relevant agencies have an awareness of services provided for children and young people with cerebral palsy, may lead to more timely management, potentially preventing further downstream costs from delay in service provision.

11.5.4 Quality of evidence

The quality of the evidence ranged from moderate to low. The main reasons for downgrading the evidence were: data collection and/or analysis was not clearly reported and unclear role of the researcher in analysis and validation.

11.5.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

11.5.6 Key conclusions

The Committee concluded that information should be tailored to the individual needs and developmental level of the child or young person. They noted that integrated communication among the agencies involved in the care of the child was essential. They believed that this information should be shared with the child, young person and their parents or carers in a timely manner and without the use of technical language. A 'folder' containing relevant information related with the child's or young person's history was considered to be useful and informative for health, educational and transitional settings.

11.6 Recommendations

32. Ensure that information and support focuses as much on the functional abilities of the child or young person with cerebral palsy as on any functional impairment.

33. Provide clear, timely and up-to-date information to parents or carers on the following topics:

- diagnosis (see section 6.7)
- aetiology (see section 5.6)
- prognosis (see section 10.7)
- natural history
- comorbidities (see section 27.20)
- specialist equipment that is available
- resources available and access to financial, respite, social care and other support for children and young people and their parents, carers and siblings (see also recommendations 139 and 143)
- educational placement
- transition (see section 29.6).

34. Ensure that clear information about the 'patient pathway' is shared with the child or young person and their parents or carers (for example, by providing them with copies of correspondence). Follow the principles in the recommendations about communication, information and shared decision-making in the NICE guideline on patient experience in adult NHS services.

35. Provide information to the child or young person with cerebral palsy, and their parents or carers, on an ongoing basis. Adapt the communication methods and information resources to take account of the needs and understanding of the child or young person and their parents or carers. For example, think about using 1 or more of the following:

- oral explanations
- written information and leaflets
- mobile technology, including apps
- augmentative and alternative communication systems (see section 16.7).

36. Work with the child or young person and their parents or carers to develop and maintain a personal 'folder' in their preferred format containing relevant information that can be shared with their extended family and friends and used in health, social care, educational and transition settings. Information could include:

- early history
- motor subtype and limb involvement
- functional abilities
- interventions
- medication
- comorbidities
- preferred methods of communication
- any specialist equipment that is used or needed
- care plans
- emergency contact details.

37. **Ensure that the child or young person and their parents or carers are given personalised information from a specialist about the following topics as appropriate:**
    - menstruation
    - fertility
    - contraception
    - sex
    - sexuality
    - parenting.

38. **Provide information to the child or young person and their parents or carers, and to all relevant teams around the child and young person, about the local and regional services available for children and young people with cerebral palsy, and how to access them.**

39. **Provide information about local support and advocacy groups to the child or young person and their parents or carers.**

11.7 Research recommendations

None identified for this topic.

12 Assessment of eating, drinking and swallowing difficulties

Review question: In infants, children and young people with cerebral palsy, what is the value of videofluoroscopy or fibreoptic endoscopic evaluation of swallowing in addition to clinical assessment in assessing difficulties with eating, drinking and swallowing?

12.1 Introduction

It is usual practice in the UK for children and young people with eating, drinking and swallowing difficulties to be seen by a 'dysphagia specialist' speech and language therapist for clinical assessment. This typically includes taking a detailed history and a structured mealtime observation. The aim is to identify problems with the oral control of food and drink, and the coordination of swallowing and breathing, in order to advise on strategies to develop skills and reduce risk. Poor coordination of swallowing can result in food/ drink going into the lungs (aspiration), which in turn can cause chest infections or pneumonia.

Children and young people with cerebral palsy are at particular risk of silent aspiration, with no obvious clinical signs such as coughing or wet voice quality. Videofluoroscopic swallow studies (VF) and fibreoptic endoscopic evaluation of swallowing (FEES) are investigations designed to give additional real-time visual information about the effectiveness of airway protection during eating and drinking, and to assess the impact of changes in positioning, food/drink consistency or feeding technique. FEES is rarely used in children in UK practice, although may be available in adult services.

Access to VF is variable as not all x-ray departments have the necessary equipment or staff with competencies in the administration and interpretation of studies in children and young people, particularly those with difficulties in movement, posture and communication. Other limitations include child compliance with the procedure and the short sample of swallowing available for analysis. There are also significant resource implications attached to these investigations. For these reasons the Committee was interested to explore the added value of VF or FEES above clinical assessment alone.

Clinical assessment of infants, children and young people with cerebral palsy with feeding difficulties is part of routine clinical practice. Investigations such as VF or FEES might add additional useful information to the assessment. The objective of this review was to determine the nature of any such added value in clarifying the nature of any difficulties present and potentially informing targeted interventions for management. Description of clinical evidence

12.1.1 Clinical evidence profile

One study (Beer 2014) of 5 children with cerebral palsy was included and reported the accuracy of clinical assessment compared to FEES in detecting aspiration. One study (DeMatteo 2005) with a mixed population of children with various conditions was included as indirect evidence and reported on the accuracy of clinical assessment compared to VF in detecting aspiration. The proportion of children with cerebral palsy was not reported and results for cerebral palsy participants were not stratified.

A modified GRADE approach has been used that allow to include diagnostic outcomes (sensitivity, specificity, predictive values and likelihood ratios) while appraising the evidence for the key GRADE domains (risk of bias, imprecision, indirectness, and inconsistency).

For full details see review protocol in Appendix E. See also the study selection flow chart in Appendix F, modified GRADE profiles in Appendix H, study evidence tables in Appendix J and exclusion list in Appendix K.

For a summary of the study included, see Table 44.

Table 44: Summary of included studies

Study	Index test	Reference test	Population	Outcomes
Beer 2014	Clinical assessment by speech and swallowing therapist	FEES carried out by paediatric neurologists, nurse and 2 speech and swallowing therapists.	N= 5 children with CP aged 41 – 90 months with neurogenic dysphagia.	Diagnostic accuracy of saliva, puree and fluid aspiration.
DeMatteo 2005	Clinical assessment by experienced occupational therapist or speech and language therapist. Used the clinical evaluation form for oral motor and swallowing evaluation.	VS procedure carried out by different occupational therapist or speech and language therapist.	N = 75 infants and children referred to Feeding and Swallowing Service over a 15 month period. Aged 0 – 14 years, 62% < 12 months. Mixed diagnosis including CP, hypoxic ischaemic encephalopathy, failure to thrive and infantile spasms.	Diagnostic accuracy and predictors of fluid and solid aspiration and penetration.

CP cerebral palsy, FEES fiberoptic endoscopic evaluation of swallowing, VFSS Videofluoroscopic swallowing studies (VF).

One study (DeMatteo 2005) identified predictors of fluid and solid aspiration and penetration, which are outlined in Table 45, Table 46, Table 47, and Table 48. Confidence and imprecision in the provided relative risks could not be assessed as confidence intervals were not reported in the study.

Table 45: Predictors of fluid aspiration (DeMatteo 2005)

Model for fluid aspiration[a]	Relative risk
Cough + voice changes + gag	1.7
Cough + voice changes + colour changes	1.6
Cough + delayed swallow + gag	1.6
Cough + voice changes	1.5
Cough + delayed swallow	1.5

(a) Any variable or combination without cough does not predict aspiration (cough was the most significant predictor of fluid aspiration).

Table 46: Predictors of fluid penetration (DeMatteo 2005)

Model for fluid penetration[a]	Relative risk
Cough + gag + reflux behaviours	2.3
Cough + gag	2.1
Cough	1.3
Reflux behaviours + voice changes + colour changes	0.05

(a) Cough alone did not predict penetration but model was stronger when other variables were combined with cough.

Table 47: Predictors of solid aspiration (DeMatteo 2005)

Model for solid aspiration[a]	Relative risk
Colour changes + abnormal respiration	3.0
Cough + abnormal respiration + colour changes	2.9

(a) Cough decreases the strength of the model.

Table 48: Predictors of solid penetration (DeMatteo 2005)

Model for solid penetration[a]	Relative risk
Colour changes + abnormal respiration	2.6
Cough + abnormal respiration + gag	2.7

(a) Cough adds nothing to any model

12.2 Economic evidence

No economic evaluations of interventions relevant to assessing eating, drinking or swallowing difficulties were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

This review question was not prioritised for de novo economic modelling. To aid consideration of cost-effectiveness relevant resource and cost use data are presented in Appendix G.

12.3 Evidence statements

12.3.1 Clinical assessment versus VF for aspiration of fluids

Low quality evidence from 1 cohort study with 59 participants that used clinical assessment was not accurate for ruling in and moderately accurate (uncertainty unclear) for ruling out aspiration of fluids as defined by VF in a mixed population of children with feeding and swallowing difficulties. Sensitivity was 92% (95% CI: 73 – 99) and specificity was 46% (95% CI: 29 – 63).

12.3.2 Clinical assessment versus VF for aspiration of solids

Very low quality evidence from 1 cohort study with 32 participants that used clinical assessment was not accurate for ruling in or ruling out aspiration of solids as defined by VF in a mixed population of children with feeding and swallowing difficulties. Sensitivity was 33% (95% CI: 4.33– 77.7) and specificity was 65% (44.3 – 82.8).

12.3.3 Clinical assessment versus VF for penetration of fluids

Low quality evidence from 1 cohort study with 68 participants that used clinical assessment was not accurate in ruling in or ruling out penetration of fluids as defined by VF in a mixed population of children with feeding and swallowing difficulties.

12.3.4 Clinical assessment versus VF for penetration of solids

Very low quality evidence from 1 cohort study with 68 participants that used clinical assessment was not accurate in ruling in or ruling out penetration of fluids as defined by VF in a mixed population of children with feeding and swallowing difficulties.

12.3.5 Clinical assessment versus FEES for aspiration of saliva

Low quality evidence from 1 cohort study with 5 participants showed that clinical assessment was not accurate in ruling in or ruling out aspiration of saliva as defined by FEES. Sensitivity was 67% (95% CI: 9.4 - 99.2) and sensitivity was 50% (95% CI: 1.7 - 98.7).

12.3.6 Clinical assessment versus FEES for aspiration of puree

Low quality evidence from 1 cohort study with 2 participants could not demonstrate the usefulness of clinical assessment in ruling in or ruling out of aspiration of puree as there were no false negatives. Sensitivity was 100% (95% CI: 15.8 - 100).

12.3.7 Clinical assessment versus FEES for aspiration of liquids

Low quality evidence from 1 cohort study with 2 participants could not demonstrate the usefulness of clinical assessment in ruling in or ruling out of aspiration of liquids as there were no false negatives. Sensitivity was 100% (95% CI: 15.8 - 100).

12.4 Evidence to recommendations

12.4.1 Relative value placed on the outcomes considered

The critical outcomes identified for this evidence review were the diagnostic accuracy in identifying the mechanisms underlying eating, drinking and swallowing difficulties and demonstration of aspiration into the airway. No evidence was retrieved for outcomes other than the diagnostic accuracy of presence/absence of aspiration.

12.4.2 Consideration of clinical benefits and harms

An understanding of the underlying mechanisms responsible for eating, drinking or swallowing difficulties may help in devising effective management strategies. Some children and young people are at risk of aspiration of liquids and / or solids and this may lead to significant complications, including apnoea, breathing difficulties and aspiration pneumonia. If there is a serious risk of aspiration drinking or eating some or all fluids and foods may be unsafe.

The Committee considered and discussed the evidence available and noted that the studies presented did not precisely match the intended evidence review protocol. They had hoped to see evidence on the value of adding either VF or FEES to the normal routine practice of clinical assessment in relation to diagnostic accuracy. The available studies however used either VF or FEES as reference test (the gold standard) and examined the relative risk of penetration (passage of swallowed liquids or solids through the glottis but not beyond the vocal cords) and aspiration (passage beyond the vocal cords) in relation to a range of clinical signs (individually or in combination) used as index tests. The subjects included in both studies were children who had been referred to tertiary centres having been previously identified at high risk for aspiration, through clinical history and assessment.

Broadly, in keeping with the Committee's knowledge and experience, cough, altered respiration and colour change were identified as significant clinical events suggesting an increased likelihood of airway penetration of liquid and/or solid food.

The Committee noted that the current practices in the assessment of eating, drinking and swallowing included a clinical assessment based on the history and sometimes formal observation during mealtimes. They recommended that a clinical assessment should be undertaken in every child or young person when there is concern raised about difficulties with eating and drinking. They advised that the history should particularly note any reported

coughing, gagging, choking behaviour, alteration in breathing pattern or change in colour (particularly of the face). The risk of 'silent aspiration' (where swallow dysfunction is not accompanied by common clinical signs such as coughing) was recognised. Clinical assessment should therefore specifically explore a child or young person's respiratory history. The Committee considered this clinical assessment should be the routine first line investigation to identify problems with eating or drinking and to identify possible reasons for concern regarding its safety, and the ability to feed effectively. The Committee discussed various other aspects of an eating, drinking, and swallowing assessment, but decided not to incorporate more detailed advice in the guideline recommendations.

They did recommend that if concerns arose, based on this routine clinical assessment, then the child or young person should undergo regional tertiary specialist assessment based on direct observation by a person with expertise in the assessment of eating or drinking problems, such as a dysphagia trained Speech and Language Therapist (SLT). They recommended that when concerns existed, this specialist SLT assessment should be undertaken as part of a multi-disciplinary review with all members having the necessary expertise in their roles of managing a clinically safe feeding regime.

The Committee recommended that VF or FEES should not be used as initial assessment. The Committee intended that this recommendation should reduce variation in clinical practice across the UK. Some centres may routinely refer children with suspected difficulties in eating, drinking and swallowing directly for VF and may do so without prior assessment by an expert multidisciplinary feeding team. This approach is supported by the lack of evidence showing that VF provided added value over clinical assessment alone in the wider cerebral palsy population, although evidence did suggest an advantage in a group of children already assessed as high risk.

The Committee and co-opted experts agreed a list of contexts, based on their clinical experience and by consensus, in which the specialist MDT should consider undertaking VF. However, it was noted that sufficient training and expertise in the provision and interpretation of VF swallow studies in children with postural and movement difficulties was essential. This strengthened the argument for the involvement of an expert feeding MDT before deciding to use VF in children and young people with cerebral palsy.

The Committee also discussed the usefulness of undertaking VF prior to consideration of enteral tube feeding. The Committee agreed that VF was not always required in such situations, particularly when there was obvious clinical risk of aspiration, recurring respiratory symptoms, significant nutritional compromise and/or food refusal.

The Committee noted that VF is widely used in UK clinical practice as the investigation of choice for the assessment of eating, drinking and swallowing and based on their clinical knowledge and experience they were confident in the importance of making recommendations regarding its use. The Committee noted that there was less widespread experience in the use of and hence more uncertainty regarding the clinical usefulness of FEES.

12.4.3 Consideration of economic benefits and harms

The Committee believed that the costs for a VF and FEES taken from NHS Reference Costs were underestimated. Firstly, these procedures would tend to take substantially longer in children and young people with cerebral palsy. Secondly, more health care professionals may be present for the procedure.

The Committee noted that FEES is not commonly used in UK clinical practice to assess swallow safety in children and young people with cerebral palsy. Moreover, FEES is an invasive procedure that is not well tolerated in children (with or without cerebral palsy). Combined with the lack of clinical evidence, the Committee felt they were able to justify recommending VF rather than FEES. Consequently the costs of implementing the

Committee's recommendation in favour of VF are reduced because clinical practice would not be significantly changed.

To prevent unnecessary referrals for VF, the Committee agreed the clinical assessment should be undertaken by healthcare professionals with expertise in eating, drinking and swallowing disorder, including a dysphagia-trained speech and language therapist, to decide if any additional value could be achieved from performing VF, as well as the likelihood of a child or young person being able to comply with the procedure. This may incur training costs as the Committee considered that many referrals for VF come from health care professionals who are not trained to assess eating, drinking and swallowing difficulties in children and young people with cerebral palsy. However, they noted that improved training may also reduce costs attached to unnecessary or failed investigations.

12.4.4 Quality of evidence

Two cohort studies were included in the evidence review. The quality of this evidence ranged from low to very low. One study had a very small sample size, which increased the uncertainty around the comparisons. Both studies included only children referred for investigation due to previously identified risk of aspiration i.e. referral filter bias and diagnostic suspicion bias.

12.4.5 Other considerations

In clinical practice VF and FEES provide additional qualitative information to the clinical assessment rather than confirmation or as a pass/fail test for swallow safety. Also parents and carers may reject the results of these investigations as being unrepresentative of the child or young person's usual eating and drinking. To ensure the results from VF are interpreted accurately, the Committee agreed that VF should be performed by a MDT that has expertise in its use in children and young people with cerebral palsy, rather than merely wherever VF may be available. The Committee believed that VF can be useful in demonstrating to parents the risks attached to oral feeding, and the benefits of certain modifications to their feeding strategy, and especially when enteral tube feeding may be required. They did not consider however that VF was routinely necessary prior to commencing tube feeding and made a recommendation to this effect.

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

12.4.6 Key conclusions

The Committee concluded that VF is an important adjunct to multidisciplinary, clinical assessment where there is uncertainty about the safety of swallowing or in situations where a child or young person with cerebral palsy is experiencing recurrent chest infections without overt signs of aspiration on eating and drinking. VF should be undertaken by a team with specific expertise in the assessment and management of children and young people with complex neurodisability to ensure appropriate procedures (that match a child or young person's typical mealtimes, as far as possible), to facilitate management of parent/carer anxiety, and to ensure accurate interpretation of results in the context of a detailed history and ongoing monitoring of health-related outcomes, including growth, weight gain and respiratory health. The potential role of FEES in the assessment of swallowing difficulties remains unclear.

12.5 Recommendations

40. If eating, drinking and swallowing difficulties are suspected in a child or young person with cerebral palsy, carry out a clinical assessment as first-line

investigation to determine the safety, efficiency and enjoyment of eating and drinking. This should include:

- taking a relevant clinical history, including asking about any previous chest infections
- observation of eating and drinking in a normal mealtime environment by a speech and language therapist with training in assessing and treating dysphagia.

41. **Refer the child or young person to a local specialist multidisciplinary team with training in assessing and treating dysphagia if there are clinical concerns about eating, drinking and swallowing, such as:**
    - coughing
    - choking
    - gagging
    - change in colour during eating
    - recurrent chest infection
    - prolonged meal duration.

42. **Do not use videofluoroscopy or fibroscopic endoscopy for the initial assessment of eating, drinking and swallowing difficulties in children and young people with cerebral palsy.**

43. **The specialist multidisciplinary team should consider videofluoroscopy if any of the following apply:**
    - There is uncertainty about the safety of eating, drinking and swallowing after specialist clinical assessment.
    - The child or young person has recurrent chest infection without overt clinical signs of aspiration.
    - There is deterioration in eating, drinking and swallowing ability with increasing age (particularly after adolescence).
    - There is uncertainty about the impact of modifying food textures (for example, use of thickeners or pureeing).
    - Parents or carers need support to understand eating, drinking and swallowing difficulties, to help with decision- making.

44. **Videofluoroscopy should only be performed in a centre with a specialist multidisciplinary team who have experience and competence in using it with children and young people with cerebral palsy.**

45. **Do not routinely perform videofluoroscopy when considering starting enteral tube feeding in children and young people with cerebral palsy.**

46. **Ensure that children and young people with ongoing eating, drinking and swallowing difficulties have access to regional tertiary specialist assessment.**

12.6 Research recommendations

None identified for this topic.

13 Management eating, drinking and swallowing difficulties

Review question: In children and young people with cerebral palsy, what interventions are effective in managing difficulties with eating, drinking and swallowing?

13.1 Introduction

For most children and young people eating and drinking is an enjoyable experience, undertaken several times a day, usually in the company of family or friends. Meals and snacks serve the purpose of obtaining nutrition and hydration, but also provide a context for social interaction. Children typically progress from a liquid diet, via breast or bottle, through a soft diet to foods that require chewing. They also achieve increasing levels of independence.

Cerebral palsy can disrupt the motor control and coordination of sucking, drinking, biting, chewing and swallowing, particularly in children and young people with severe functional disabilities. This can lead to problems with inadequate intake, the risk of food or drink going into the lungs (aspiration), prolonged dependence on immature food textures and on being fed by others. Mealtimes may be lengthy and sometimes unhappy for the child or young person and their family.

Appropriate management of eating, drinking and swallowing difficulties is important for maintaining respiratory health, optimising nutritional status, maximising independence and supporting social participation. The Committee was interested in reviewing the evidence relating to interventions that are commonly suggested by professionals who are supporting families in this area of everyday functioning. These included postural management, modification of food and fluid textures, feeding techniques and equipment, therapies aimed at improving oral-motor skills and reducing the risk of aspiration.

The aim of this review is to identify clinical and cost effective interventions for managing difficulties with eating, drinking and swallowing in children and young people with cerebral palsy.

13.2 Description of clinical evidence

Four randomised trials (Gisel 1995; Gisel 1996; Ottenbacher 1981; Sigan 2013) and 4 observational studies (Adams 2011, Baghbadorani, Clawson 2007, Gisel 2001) were included in the review.

Evidence from these studies is summarised in the clinical GRADE evidence profile below (Table 50, Table 51, Table 52, Table 53, Table 54, and Table 55). See also the review protocol in Appendix E, the study selection flow chart in Appendix F, forest plots in Appendix I, study evidence tables in Appendix J and exclusion list in Appendix K.

Studies were carried out in Bangladesh, Canada, Iran, Turkey and USA. Duration of studies ranged from 5 weeks to 12 months.

With regard to the population considered, 1 study population was diagnosed with moderate impairment (Gisel 2001), whereas the populations in the other included studies were diagnosed with moderate to severe impairment (Adams 2011, Baghbadorani, Clawson 2007, Gisel 1995, Gisel 1996, Ottenbacher 1981, Sigan 2014). One study considered mixed populations of participants with cerebral palsy and other neurological conditions, but this study was included as more than 2/3 of the population had cerebral palsy (Ottenbacher 1981).

With regard to the interventions, 4 randomised studies looked at participants who received oral sensorimotor therapy compared with routine therapy in children and young people with cerebral palsy (Gisel 1995, Gisel 1996, Ottenbacher 1981, Sigan, 2014). One cohort study looked at children with cerebral palsy who received the ISMAR intra-oral appliance compared to children who had no ISMAR appliance (Gisel 2001). One cohort study looked at oral sensorimotor treatment (Baghbadorani 2014) in children with cerebral palsy. One cohort looked at a training programme delivered to children and their caregivers (Adams 2011). One cohort study looked at a multicomponent intervention, including carer training, behavioural interventions and Beckman oral motor exercises in children with cerebral palsy (Clawson 2007).

No evidence was retrieved for the following interventions: postural management, feeding techniques (such as jaw support, food placement and pacing), feeding equipment, or pharmacological interventions.

Of the outcomes listed in the protocol and agreed by the Committee, studies reported critical outcomes including weight and height as mean percentiles and mean kilograms/pounds or centimetres (Adams 2011, Clawson 2007, Gisel 1995, Gisel 1996, Gisel 2001, Ottenbacher 1981). Duration of meal times was reported by 2 randomised studies and 1 non-comparative study (Gisel 1995, Gisel 1996, Clawson 2007). One non-comparative study reported the frequency of chest illness once every 3 months, but only the p value was reported (Adams 2011). Eating times of standard food textures were reported by 2 randomised studies (Gisel 1995, Gisel 1996). Outcomes including oral-motor function or competency in feeding was reported by 1 randomised study and 1 non-comparative study using the modified Functional Feeding Assessment (FFAm) and Oral Motor Assessment Scale (OMAS) respectively (Sigan 2014, Baghbadorani 2014).

13.2.1 Summary of included studies

A summary of the studies that were included in this review are presented in Table 49.

Table 49: Summary of included studies

Study	Intervention/comparator	Population	Outcomes	Comments
Adams 2011	Six sessions of training programme: consisted of education on dietary intake, ease and efficiency of eating, utensils, behaviour of caregiver towards feeding child, postural and physical support for positioning and self-feeding. Each training session included educational content as well as supervised feeding. Teaching methods included traditional pedagogy, discussion, participation and experimental activities, use of visual aids including a 20 minute video drama created especially for the programme.	Children with moderate to severe (levels III-V on GMFCS) cerebral palsy and their caregivers N: 37 caregivers and their children Age of children (range):19 to 129 months	Weight for age (WAZ score) Frequency of chest related illness (n)	Study was conducted in slums of Dhaka, Bangladesh for 4 to 6 months Cohort study
Baghbadorani 2014	Oral sensorimotor stimulation: focussed on tongue lateralisation, lip control, and vigour of chewing. Treatment lasted 15 minutes daily, 3 days a week. Assessments were carried out at 4 and 8 weeks.	Children with moderate to severe motor impairment who scored at or below 10 scores on	Effect of oral motor stimulation on oral- motor skills	Baseline, 4 and 8 weeks Cohort study

Study	Intervention/comparator	Population	Outcomes	Comments
	-tongue lateralisation: A small amount of jam was placed on 4 corners of the lips alternatively (left and right corner and middle of upper and lower lips so the tongue had to remove the stimulus from outside the oral cavity). In order to stimulate the tongue in the mouth, the stimulus was placed in the cheek pocket so that the tongue had to remove it from the cheek in order to swallow.	an initial assessment of the Oral Motor Assessment Scale N:12 Age of children (range): 2 to 7 years		
Clawson 2007	A hospital-based 6 hour-per day programme, Monday through Friday , for an average of 29 treatment days (5.8 weeks) The focus of the study was behavioural interventions and parent education in addition to an oral-motor exercise component, to address the child's food refusal. • Behavioural interventions: presentation of food near child's lips until child opened and accepted the bite into their mouth (accepting food, chewing, swallowing). • Parent training: involved training in food preparation and calorie boosting (puree, texture grading, and food allergies). • Beckman oral motor exercise: each therapeutic meal included oral motor exercises followed by oral feeding. The day programme was provided by the MDT. Beckman oral motor exercises were performed (by the same staff members throughout admission) for 20-30 minutes before each oral feeding. The aim was to increase functional response to pressure and movement (increase range, strength, variety and control of movement for lips, cheeks, jaw and tongue). Caregivers fed the child in the room alone and were observed by the therapist via video and instructed the parent via a	The diagnosis was moderate to severe feeding difficulties, all children had spastic quadriplegic CP. There is no information about the severity of the CP (no GMFCS level). N: 8 Age of children (range): 18 months to 4.7 years	Mean height and weight (percentiles) Patients were scheduled to return for assessment at 1, 4, 7, and 12 months following discharge from the day of the feeding programme. Other measures were reported at Discharge, but not follow up for example food acceptance, mouth clearance, inappropriate behaviours, duration of meal, grams per meal, calories consumed, percent tube fed	Cohort study

Study	Intervention/comparator	Population	Outcomes	Comments
	wireless communication system.			
Gisel 1995	Oral sensorimotor therapy versus routine therapy: Based on children's performance on the modified Functional Feeding Assessment (tailored to children's individual needs). Treatment lasted 5-7 minutes daily, before lunch or snack. Tongue lateralisation, lip control and vigour of chewing were the main focus of oral-motor functioning. Small food stimuli were used to elicit a natural eating reaction. Demonstrations of sucking motions were given and children were encouraged to imitate the motion and to suck a liquid. Children with poor sucking control were given thickened liquids. Vigour of chewing: Children were encouraged to chew by the therapist placing small pieces of biscuit (medium to strong resistance) over the molars (alternatively right and left).	Children with a diagnosis of cerebral palsy with moderate to severe motor impairment N: 27 Age of children (mean, SD): Group 1: 4.8 (1.4); group 2: 5.0 (1.9)	Mean weight (percentiles for age) Duration of lunch/snack at school Time taken to eat foods of standard texture	Open label trial Outcome data reported at 10 weeks
Gisel 1996	Oral sensorimotor therapy versus routine therapy: Based on children's performance on the modified Functional Feeding Assessment (tailored to children's individual needs).	Children with a diagnosis of cerebral palsy with moderate to severe motor impairment N: 35 Age of children (range): 4.3 to 13.3 years	Weight in kg and percentiles for age Eating time for 3 standard food textures Duration of lunch at school	Open label study Outcome data reported at 10 weeks
Gisel 2001	ISMAR appliance versus no ISMAR appliance: ISMARs were fabricated and if satisfactory, were then fitted on the child in school environment, in the presence of caregivers. Care and written wear instructions were provided. During the first week, the research assistant contacted caregivers to ensure safety and correct wear. -Treatment phase I: Onset of phase I was determined by ISMAR wear for 20 minutes of wear daily.	Children had a diagnosis of cerebral palsy with tetraparesis and moderate motor impairment N: 17 Age of children (range): 6.6 to 15.4 years	Weight and height Competency in feeding: spoon feeding, biting, chewing, cup drinking, straw drinking, swallowing, clearing	Follow up study (cohort study)

Study	Intervention/comparator	Population	Outcomes	Comments
	-Treatment phase II: children were evaluated for mobilisation of oral structures, and goals were determined for each child according to their needs. Grooves were drilled into the lingual part of the occlusal shelves or heads attached to different loci on the ISMAR appliance to stimulate tongue movement.			
Ottenbacher 1981	Oral motor therapy: Each participant received 30 to 40 minutes of therapy daily, 5 days a week for 9 weeks. Some participants received therapy just prior to or in conjunction with their meals, and others were scheduled for therapy at various times during the day. There were 3 major components to the treatment: 1. inhibition of abnormal oral and postural reflexes 2. facilitation of normal muscle tone 3. desensitisation of the oral region Control group: Participants received their regular programme of therapy and education. No specific treatment of oral-motor dysfunction or feeding disorders was administered.	Children with profound or severe neuromotor disorder, with dependency in most areas of self-care and feeding N=18/20 participants with cerebral palsy Age of children (mean, SD): 11.5 (4.38)	Weight at pre-therapy and post-therapy	Randomised controlled trial 9 weeks
Sigan 2013	Multi-component intervention: Postural management, texture modification, feeding techniques and oral sensorimotor treatment versus routine physiotherapy: Feeding therapy group: 1 hour therapy sessions with a physiotherapist once a week for 6 months (12 sessions in total).Parents continued techniques between therapy sessions Routine treatment group: Children diagnosed with CP and oral motor dysfunction were called for the first evaluation and then for and evaluation at 6 months. During this time, routine physiotherapy was continued. All patients attended routine	Children with cerebral palsy (Bilateral UL=LL and LL>UL; unilateral CP, hypotonia, and ataxic) N: 81 (consecutively chosen) Age of children (range): 12-42 months	Physical function (spoon feeding, drinking and swallowing subscales of the modified Functional Feeding Assessment)	Single centre RCT conducted in Turkey, for 6 months duration

Study	Intervention/comparator	Population	Outcomes	Comments
	physiotherapy according to the established programme during the 6 months			

1 *CP cerebral palsy, RCT randomised controlled study, SD standard deviation, GMFCS gross motor function*
2 *classification system, ISMAR Innsbruck sensorimotor activator and regulator.*

13.33 Clinical evidence profile

4 The clinical evidence profiles for this review question are presented in Table 50, Table 51,
5 Table 52, Table 53 , Table 54 and Table 55.

6 **Table 50: Oral sensorimotor therapy versus routine treatment**

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Control	Oral sensorimotor treatment versus routine treatment (randomised trials)		
Anthropometric measure-mean weight kg percentiles for age (final) Follow-up: 10 weeks	The mean anthropometric measure-mean weight kg percentiles for age (final) in the control groups was weight percentiles for age	The mean anthropometric measure-mean weight kg percentiles for age (final) in the intervention groups was 8.45 lower (11.91 to 5 lower)	43 (2 studies[1])	very low[2,3,4]
Anthropometric measure- mean weight (kg) (final)	The mean anthropometric measure- mean weight (kg) (final) in the control groups was 19.44 kilograms	The mean anthropometric measure- mean weight (kg) (final) in the intervention groups was 2.47 lower (6.79 lower to 1.85 higher)	23 (1 study)	very low[2,4]
Anthropometric measure-mean weight (pounds, SD) (final at 9 weeks)		The mean anthropometric measure-mean weight (pounds, SD) (final at 9 weeks) in the intervention groups was 9.56 lower (18.65 to 0.47 lower)	20 (1 study)	very low[4,5]
Duration of mealtime (lunch or snack) - Lunch Follow-up: 10 weeks		The mean duration of mealtime (lunch or snack) - lunch in the intervention groups was 4.2 higher (0.24 lower to 8.16 higher)	43 (2 studies[1])	very low[2,4,6]
Duration of mealtime (lunch or snack) -		The mean duration of mealtime (lunch or	20 (1 study[1])	very low[2,4]

Snack Follow-up: 10 weeks		snack) - snack in the intervention groups was 2.5 lower (6.35 lower to 1.35 higher)		
Eating time of different food textures (mean seconds, SD, final) - Puree (Apple sauce) Follow-up: 10 weeks		The mean eating time of different food textures (mean seconds, SD, final) - puree (apple sauce) in the intervention groups was 0.4 lower (2.2 lower to 1.4 higher)	20 (1 study[1])	very low[2,7]
Eating time of different food textures (mean seconds, SD, final) - Viscous (Raisin) Follow-up: 10 weeks		The mean eating time of different food textures (mean seconds, SD, final) - viscous (raisin) in the intervention groups was 1.3 lower (5.79 lower to 3.19 higher)	20 (1 study[1])	very low[2,7]
Eating time of different food textures (mean seconds, SD, final) - Viscous (gelatine)		The mean eating time of different food textures (mean seconds, SD, final) - viscous (gelatine) in the intervention groups was 3.2 higher (1.73 lower to 8.13 higher)	20 (1 study[1])	very low[2,4]
Eating time of different food textures (mean seconds, SD, final) - Solid (Biscuit) Follow-up: 10 weeks		The mean eating time of different food textures (mean seconds, SD, final) - solid (biscuit) in the intervention groups was 2.2 higher (1.53 lower to 5.93 higher)	20 (1 study[1])	very low[2,4]
Eating time of different food textures (mean seconds, SD, final) - Solid (Cereal ring) Follow-up: 10 weeks		The mean eating time of different food textures (mean seconds, SD, final) - solid (cereal ring) in the intervention groups was 9.9 lower (13.27 to 6.53 lower)	20 (1 study[1])	very low[2,7]
Eating time of different food textures (mean seconds, SD, change) - Puree		The mean eating time of different food textures (mean seconds, SD, change) - puree in	23 (1 study[1])	very low[2,7]

Follow-up: 10 weeks		the intervention groups was 9.79 higher (7.15 to 12.44 higher)		
Eating time of different food textures (mean seconds, SD, change) - Viscous Follow-up: 10 weeks		The mean eating time of different food textures (mean seconds, SD, change) - viscous in the intervention groups was 0.35 lower (4.58 lower to 3.88 higher)	23 (1 study)	very low[2,7]
Eating time of different food textures (mean seconds, SD, change) - Solid Follow-up: 10 weeks		The mean eating time of different food textures (mean seconds, SD, change) - solid in the intervention groups was 1.1 higher (4.95 lower to 7.14 higher)	23 (1 study)	very low[2,7]

CP cerebral palsy, RCT randomised controlled study, SD standard deviation.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 open label randomised trial
2 the evidence was downgraded by 2 due to selection bias and performance bias
3 the evidence was downgraded by 2 due to very serious heterogeneity (Chi-squared p <0.1, I-squared inconsistency statistic of 75%) and no plausible explanation was found with subgroup analysis
4 evidence was downgraded by 1 due to 95% confidence interval crossing 1 default MID (-0.5 to +0.5 SD)
5 majority of evidence has only 1 indirect aspect of PICO (population)
6 evidence was downgraded by 1 due to serious heterogeneity (chi-squared p<0.1, I-squared inconsistency statistic of 50%-74.99%) and no plausible explanation was found with sensitivity analysis.
7 the evidence was downgraded by 2 due to 95% confidence interval crossing 2 default MIDs -0.5 and +0.5 SDs
8 the evidence was downgraded by 1 due to performance bias

Table 51: ISMAR versus no ISMAR treatment

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk			
	No ISMAR	ISMAR			
Weight (kg)	-	The mean change in weight in the intervention group was MD 0.87 higher (0.2 to 1.54 higher)	17 (1 study)	very low[1,2,3]	Change at 6 months Cohort study
Weight (kg)	-	The mean change in weight in the intervention group was MD 1.44 lower (1.89 to 0.99 lower)	17 (1 study)	very low[1,2,3]	Change at 12 months Cohort study
Height (cm)	-	The mean height in	17	very low[1,2,3]	Final at 6

		the intervention group was MD 0.15 lower (2.06 lower to 1.76 higher)	(1 study)		months Cohort study
Height (cm)	-	The mean height in the intervention group was MD 2.68 higher (1.21 to 4.15 higher)	17 (1 study)	very low[1,2,3]	Final at 12 months Cohort study
Competency in feeding (%)- Spoon feeding	-	The mean percentage competency in the intervention group was MD 5.8 lower (16.64 lower to 5.04 higher)	17 (1 study)	very low1,2	Final at 12-18 months Cohort study
Competency in feeding (%)- cup drinking	-	The mean percentage competency in the intervention group was MD 1.9 lower (10.09 lower to 6.29 higher)	17 (1 study)	very low[1,2,3]	Final at 12-18 months Cohort study
Competency in feeding (%)- swallowing	-	The mean percentage competency in the intervention group was MD 16 lower (32.08 lower to 0.08 higher)	17 (1 study)	very low[1,2,3]	Final at 12-18 months Cohort study
Competency in feeding (%)- clearing	-	The mean percentage competency in the intervention group was MD 15.5 lower (31.03 lower to 0.03 higher)	17 (1 study)	very low[1,2,3]	Final at 12-18 months Cohort study
Competency in feeding (%)-spoon feeding	-	The mean percentage competency in the intervention group was MD 2.5 lower (14.97 lower to 9.97 higher)	17 (1 study)	very low[1,2,3]	Final at 18-24 months Cohort study
Competency in feeding (%)-cup drinking	-	The mean percentage competency in the intervention group was MD 2.5 lower (14.97 lower to 9.97 higher)	17 (1 study)	very low[1,2,3]	Final at 18-24 months Cohort study
Competency in feeding (%)- swallowing	-	The mean percentage competency in the intervention group was MD 19 lower (32.66 to 5.34 lower)	17 (1 study)	very low[1,2,3]	Final at 18-24 months Cohort study

Competency in feeding (%)-clearing	-	The mean percentage competency in the intervention group was MD 13.9 lower (24.27 to 3.53 lower)	17 (1 study)	very low[1,2,3]	Final at 18-24 months Cohort study
Competency in feeding (%)-spoon feeding	-	The mean percentage competency in the intervention group was MD 2.7 higher (2.85 lower to 8.25 higher)	17 (1 study)	very low[1,2,3]	Change at 12-18 months Cohort study
Competency in feeding (%)-cup drinking	-	The mean percentage competency in the intervention group was MD 3.3 higher (6.26 lower to 12.86 higher)	17 (1 study)	very low[1,2,3]	Change at 12-18 months Cohort study
Competency in feeding (%)-swallowing	-	The mean percentage competency in the intervention group was MD 3.5 lower (15.62 lower to 8.62 higher)	17 (1 study)	very low[1,2,3]	Change at 12-18 months Cohort study
Competency in feeding (%)-clearing	-	The mean percentage competency in the intervention group was MD 4 lower (15.89 lower to 7.89 higher)	17 (1 study)	very low[1,2,3]	Change at 12-18 months Cohort study
Competency in feeding (%)-spoon feeding	-	The mean percentage competency in the intervention group was MD 0.8 higher (6.96 lower to 8.56 higher)	17 (1 study)	very low[1,2,3]	Change at 18-24 months Cohort study
Competency in feeding (%)-cup drinking	-	The mean percentage competency in the intervention group was MD 9.6 lower (14.23 to 4.97 lower)	17 (1 study)	very low[1,2,3]	Change at 18-24 months Cohort study
Competency in feeding (%)-swallowing	-	The mean percentage competency in the intervention group was MD 2.2 lower (11.43 lower to 7.03 higher)	17 (1 study)	very low[1,2,3]	Change at 18-24 months Cohort study
Competency in feeding (%)-clearing	-	The mean percentage competency in the	17 (1 study)	very low[1,2,3]	Change at 18-24 months

		intervention group was MD 3.6 higher (7.96 lower to 15.16 higher)			Cohort study

CP cerebral palsy, RCT randomised controlled study, SD standard deviation, MD mean difference, GMFCS gross motor function classification system, ISMAR Innsbruck sensorimotor activator and regulator.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 the evidence was downgraded by 1 due to performance bias
2 the evidence was downgraded by 1 due to 95% confidence interval crossing 1 default MID (-0.5 to +0.5 SDs)
3 the evidence was downgraded by 2 due to 95% confidence intervals crossing 2 default MIDs (-0.5 to +0.5 SDs)

Table 52: Multi-component intervention compared to routine physiotherapy

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Routine physiotherapy	Multi-component intervention		
Physical function - Spoon feeding mFFA Follow-up: 6 months	-	The mean physical function - spoon feeding in the intervention groups was 8.85 higher (1.55 to 16.15 higher)	81 (1 study)	low[1,2]
Physical function - Swallowing mFFA Follow-up: 6 months	-	The mean physical function - swallowing in the intervention groups was 8.4 higher (1.54 to 15.26 higher)	81 (1 study)	low[1,2]
Physical function - Drinking mFFA Follow-up: 6 months	-	The mean physical function - drinking in the intervention groups was 4.13 higher (1.12 to 7.14 higher)	81 (1 study)	low[1,2]

FFA Functional Feeding Assessment
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 the evidence was downgraded by 1 due to performance bias
2 evidence was downgraded by 1 due to 95% confidence interval crossing 1 default MID (-0.5 to +0.5 SD)

Table 53: Parent/carer Training sessions

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Frequency/mean			
	Placebo	Training session			
Frequency of chest related illnesses at least once every 3 months	-	6	22 (1 study)	very low[1,2,3,4]	Outcome at 4-6 months
Weight for age (WAZ score)	-	mean 4.07 (SD 2.45)	22 (1 study	very low[1,2,3,4]	Final Outcome at 4-6 months

WAZ weight for age, SD standard deviation.

The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).
1 the evidence was downgraded by 2 due to performance, attrition and detection bias
2 the evidence was downgraded by 1 due to study setting in Bangladesh
3 not calculable
4 the absolute risk could not be calculated as there was no comparator group in the study.

Table 54: Multi-component intervention (including Beckman oral exercise training, behavioural intervention and parenting training)

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Control	Multi-component intervention		
Height Percentile Follow-up: 1 years	The mean height in the control groups was measured using an Infantometres height board	The mean (SD) height in the intervention groups was 16.13 higher (17.08)	8 (1 study)	very low[1,2]
Weight Percentile Follow-up: 1 years	-	The mean (SD) weight in the intervention groups was 10.28 higher (15.41)	8 (1 study)	very low[1,2]
Length of food time/time taken to feed Minutes Follow-up: 5.8 weeks	-	The mean (SD) length of food time/time taken to feed in the intervention groups was 17.83 higher (2.06)	8 (1 study)	very low[1,2]

SD standard deviation
The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).
1 the evidence was downgraded by 1 due to performance bias.

Table 55: Oral sensorimotor stimulations

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk			
	Control	Oral motor assessment			
Mouth closure	-	mean 1.33 (SD 1.15)	12 (1 study)	very low[1]	Change at 2 months
Lip closure onto utensil	-	mean 0.66 (SD 0.77)	12 (1 study)	very low[1]	Change at 2 months
Lip closure during deglutition	-	mean 0.5 higher (SD 0.67)	12 (1 study)	very low[1]	Change at 2 months
Control of food during deglutition	-	mean 1 (SD 0.73)	12 (1 study)	very low[1]	Change at 2 months
Straw suction	-	mean 0.41 (SD 0.51)	12 (1 study)	very low[1]	Change at 2 months
Control of liquid during deglutition	-	mean 0.75 (SD 0.45)	12 (1 study)	very low[1]	Change at 2 months

Mastication	-	mean 1 (SD 0.85)	12 (1 study)	very low[1]	Change at 2 months
Mouth closure	-	mean 2.41 (SD 0.51)	12 (1 study)	very low[1]	Final at 2 months
Lip closure onto utensil	-	mean 1.75 (SD 0.62)	12 (1 study)	very low[1]	Final at 2 months
Lip closure during deglutition	-	mean 1.66 (SD 0.49)	12 (1 study)	very low[1]	Final at 2 months
Control of food during deglutition	-	mean 1.91 (SD 0.28)	12 (1 study)	very low[1]	Final at 2 months
Straw suction	-	mean 0.83 (SD 0.93)	12 (1 study)	very low[1]	Final at 2 months
Control of liquid during deglutition	-	mean 1.5 (SD 0.52)	12 (1 study)	very low[1]	Final at 2 months
Mastication	-	mean 1.91 (SD 0.28)	12 (1 study)	very low[1]	Final at 2 months
Overall score	-	mean 12 (SD 1.59)	12 (1 study)	very low[1]	Final at 2 months

SD standard deviation
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 the evidence was downgraded by 1 due to performance and detection bias

13.4 Economic evidence

No economic evaluations of interventions relevant to managing eating, drinking or swallowing difficulties were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

This review question was not prioritised for de novo economic modelling. To aid consideration of cost-effectiveness, relevant resource and cost use data are presented in Appendix G.

13.5 Evidence statements

13.5.1 Oral sensorimotor therapy versus routine treatment

13.5.1.1 Nutritional status/changes in growth (weight)

Very low quality evidence from 2 randomised studies with 43 children showed that there was no clinically significant difference between oral sensorimotor therapy and routine therapy for the outcome of weight (kg) in percentiles for age at10 weeks follow-up.

Very low quality evidence from 1 randomised study with 20 children that there was no clinically significant difference between oral sensorimotor therapy and routine therapy for the outcome of weight (pounds) at 9 weeks follow-up.

13.5.1.21 Duration of meal times (lunch or snack)

Very low quality evidence from 2 randomised studies with 43 children showed that there was no clinically significant difference between oral sensorimotor treatment and routine treatment for the outcome of lunch duration in patients with cerebral palsy at 10 weeks follow-up.

Very low quality evidence from 1 randomised study with 20 children showed that that there was no clinically significant difference between oral sensorimotor treatment and routine treatment for the outcome of snack duration in patients with cerebral palsy at 10 weeks follow-up.

13.5.1.39 Eating time of different food textures/change in diet consistency a child is able to consume

Very low quality evidence from 1 study with 20 children showed that there was no clinically significant difference between oral sensorimotor treatment and routine treatment for the outcome of eating time of pureed food texture in patients with cerebral palsy at 10 weeks follow-up.

Very low quality evidence from 1 study with 20 children showed that there was no clinically significant difference between oral sensorimotor treatment and routine treatment for the outcome of eating time of viscous (raisin or gelatine) food texture in patients with cerebral palsy at 10 weeks follow-up.

Very low quality evidence from 1 study with 20 children showed that there was no clinically significant difference between oral sensorimotor treatment and routine treatment for the outcome of eating time of solid (cereal ring or biscuit) in patients with cerebral palsy at 10 weeks follow-up.

Very low quality evidence from 1 study with 23 children showed that there is a clinically significant beneficial effect of oral sensorimotor treatment compared with routine treatment for the outcome of eating time of pureed food texture in patients with cerebral palsy at 10 weeks follow-up.

Very low quality evidence from 1 study with 23 children showed that there is no clinically significant difference between oral sensorimotor treatment and routine treatment for the outcome of eating time of viscous or solid food textures in patients with cerebral palsy at 10 weeks.

13.5.1.41 Psychological wellbeing of parents/carers

No evidence was retrieved for this outcome.

13.5.1.53 Acceptability of programme

No evidence was retrieved for this outcome.

13.5.1.65 Survival

No evidence was retrieved for this outcome.

13.5.2 Multi-component intervention versus routine physiotherapy

13.5.2.1 Physical function of the oropharyngeal mechanism

Low quality evidence from 1 randomised study with 81 children showed that there is a clinically significant beneficial effect of oral sensorimotor treatment, as part of a programme that also included postural management, texture modification, changes to feeding techniques

and parent education, compared with routine physiotherapy treatment for the outcomes of spoon feeding, drinking and swallowing in patients with cerebral palsy at 6 months (final).

Very low quality evidence from 1 cohort study with 12 children showed that there was a clinically significant beneficial effect of oral sensorimotor treatment for the outcome of mouth closure but not lip closure onto utensil or lip closure, control of food or liquid during deglutition, or straw suction at 2 months follow-up.

13.5.2.2 Psychological wellbeing of parents/carers

No evidence was retrieved for this outcome.

13.5.2.3 Acceptability of programme

No evidence was retrieved for this outcome.

13.5.2.4 Survival

No evidence was retrieved for this outcome.

13.5.3 ISMAR appliance versus no ISMAR appliance

13.5.3.1 Anthropometric measure (weight)

Very low quality evidence from 1 comparative cohort study with 17 children showed that there was a clinically significant beneficial effect of the ISMAR appliance compared with no ISMAR appliance for the outcome of weight in patients with cerebral palsy at 6 or 12 months follow-up.

13.5.3.2 Anthropometric measure (height)

Very low quality evidence from 1 comparative cohort study with 17 children showed that there was no clinically significant difference in change between ISMAR appliance and no ISMAR appliance for the outcome of height in patients with cerebral palsy at 6 months but there is a clinically beneficial effect at 12 months.

13.5.3.3 Respiratory health

No evidence was retrieved for this outcome.

13.5.3.4 Physical function of the oropharyngeal mechanism/Competency in feeding (percentage)

Very low quality evidence from 1 comparative cohort study with 17 children showed that there was no clinically significant difference between ISMAR appliance for the outcome of spoon feeding and cup drinking skills in patients with cerebral palsy at 12-18 months or 18-24 months follow-up.

Very low quality evidence from 1 comparative cohort study with 17 children showed that there may be a clinically significant benefit of no ISMAR appliance compared with ISMAR appliance for the outcome of swallowing and clearing but there is uncertainty around the estimate at 12-18 months. However, low quality evidence from the same study showed that there was a clinically significant beneficial effect of no ISMAR appliance compared with ISMAR appliance for the outcome of swallowing and clearing at 18-24 months (final).

Very low quality evidence from 1 comparative cohort study with 17 children showed that there was no clinically significant difference between ISMAR appliance and no ISMAR

appliance for the outcome of spoon feeding, cup drinking, swallowing, or clearing at 12-18 months, but there was a clinically significant beneficial effect of no ISMAR appliance compared with ISMAR appliance for the outcome of cup drinking at 18-24 months

13.5.3.5 Psychological wellbeing of parents/carers

No evidence was retrieved for this outcome.

13.5.3.6 Acceptability of programme

No evidence was retrieved for this outcome.

13.5.3.7 Survival

No evidence was retrieved for this outcome.

13.5.4 Multi-component intervention, (including Beckman oral exercise training, behavioural intervention and parenting training)

13.5.4.1 Nutritional status/changes in growth (weight and height)

Very low quality evidence from 1 pre- and post-intervention cohort study with 8 children showed that there was a clinical benefit of behavioural intervention (including Beckman oral exercises and parent education) for the outcome of weight and height percentiles in centimetres at 1 year, but the 95% confidence intervals were not reported, therefore, the uncertainty around this effect was unclear.

13.5.4.2 Time taken to feed

Very low quality evidence from 1 pre- and post-intervention cohort study with 8 children showed that children were able to tolerate a longer meal session over the course of treatment after the behavioural intervention (including Beckman oral exercises and parent education), but the 95% confidence intervals were not reported, therefore, the uncertainty around this effect was unclear.

13.5.4.3 Psychological wellbeing of parents/carers

No evidence was retrieved for this outcome.

13.5.4.4 Acceptability of programme

No evidence was retrieved for this outcome.

13.5.4.5 Survival

No evidence was retrieved for this outcome.

13.5.5 Six session training programme

13.5.5.1 Nutritional status/changes in growth (weight)

Very low quality evidence from 1 cohort study with 22 children showed that there was a clinical benefit of 6 session training programme for the outcome of weight z scores at 4-6 months but the 95% confidence intervals were not reported, therefore the uncertainty around this effect was unclear.

13.5.5.2 Respiratory health

Very low quality evidence from 1 cohort study with 22 children showed that there was a clinical benefit of the 6 session training programme in reducing the frequency of chest-related illness occurring at least once every 3 months at 4-6 months.

13.5.5.3 Psychological wellbeing of parents/carers

No evidence was retrieved for this outcome.

13.5.5.4 Acceptability of programme

No evidence was retrieved for this outcome.

13.5.5.5 Survival

No evidence was retrieved for this outcome.

13.5.6 Oral sensorimotor stimulation

13.5.6.1 Physical function of the oropharyngeal mechanism

Very low quality evidence from 1 cohort study with 12 children showed that there was a clinically significant beneficial effect of oral sensorimotor treatment for the outcome of mouth closure but not lip closure onto utensil or lip closure, control of food or liquid during deglutition, or straw suction at 2 months follow-up.

13.5.6.2 Change in diet consistency a child is able to consume

No evidence was retrieved for this outcome.

13.5.6.3 Psychological wellbeing of parents/carers

No evidence was retrieved for this outcome.

13.5.6.4 Acceptability of programme

No evidence was retrieved for this outcome.

13.5.6.5 Survival

No evidence was retrieved for this outcome.

13.6 Evidence to recommendations

13.6.1 Relative value placed on the outcomes considered

The aim of this review was to assess the clinical and cost effectiveness of interventions for managing difficulties with eating, drinking, and swallowing in children and young people with cerebral palsy. The Committee indicated the following to be the critical outcomes of this evidence review: change in height and weight, respiratory health, and duration of meal times/child's participation in meal. All other outcomes were reported as important if retrieved from the search.

13.6.21 Consideration of clinical benefits and harms

The Committee recognised that the results were inconclusive and the majority of the studies were of low and very low quality. The Committee agreed that the interventions included in some of the studies would not be able to be replicated in everyday clinical practice as a very high level of staff training was required; the programmes were of an intensity and duration that would be atypical; and they were mainly conducted in research settings and some used outdated methods (e.g. Ottenbacher 1981). The majority of studies focused on improving oral motor skills, with variation in the attention given to other important outcomes such as growth, weight gain, nutrition, respiratory health, independence skills and the time taken for meals. The Committee noted that some studies focused their analysis on improving physical function, using results such as mouth closure, lip closure onto utensil, lip closure and control of food during eating, drinking and swallowing and straw suction. However, the Committee highlighted this as a possible limitation of the evidence as these outcomes are only clinically meaningful if other aspects of feeding (nutrition and respiratory status) are also improving. Also, they pointed out that improvements in areas of physical function did not necessarily reflect the time taken to eat each spoonful. No studies explored the impact of intervention on the experience of children and young people, or their caregivers.

The Committee discussed that in clinical practice, management of eating and drinking typically involved multiple professionals and addressed several aspects of eating, drinking and swallowing, often simultaneously. Based on the Committee's experience and by consensus they agreed that it was common to address positioning and postural management. Following this, further interventions may be considered including modifying food and fluid textures, feeding techniques and other strategies to reduce the risk of aspiration, to improve the efficiency of eating, drinking and swallowing and to promote the development of oral motor skills. Behavioural and emotional aspects of eating and drinking contribute to the family experience and so require consideration. This could be psychological interventions but the Committee thought it was more about allowing feeding and mealtimes to be a pleasant and sociable experience for the family – not painful, lengthy, disrupted, and stressful.

The Committee recognised that the most relevant training programme in the studies included in the evidence review was the 6 session training programme that addressed many of the aspects listed above. However, the study included only provided 6 sessions and the Committee noted that in clinical practice, a longer duration of professional involvement was likely as a child or young person's abilities and needs will change over time. As a child moves though nursery, school, further education and social care the circle of people supporting an individual's eating and drinking will change, with a need for training.

The Committee noted that the interventions addressed in the studies were often focused on improving specific oral motor skills involved in eating or drinking such as mouth closure or lateral tongue movement, while in clinical practice, multiple aspects of eating, drinking and swallowing are considered. For example, moving a child onto more challenging food textures, through focusing on strategies to improve chewing, may represent progress with regard to oral motor skills, but may increase the length of the mealtime or compromise energy intake as each mouthful will take longer and require more effort.

Based on their clinical experience and by consensus, the Committee unanimously agreed to highlight the importance of working in partnership with children and young people with cerebral palsy, their parents and carers to address skill development, health-related outcomes (growth and weight gain, respiratory health) and improve the mealtime experience. The Committee recognised the risk of faltering growth in the cerebral palsy population, arising from eating, drinking and swallowing difficulties. Monitoring changes in height and weight was noted as a key outcome in management programmes. Based on specific principles retrieved in the evidence and on their clinical experience, the Committee recommended the development of an individualised plan tailored towards the people

involved in the feeding of children and young people with cerebral palsy and eating, drinking and swallowing difficulties and listed a range of management techniques which could be taken into account such as postural management, texture modification, specialised feeding utensils, communication and the training needs of caregivers.

The Committee noted that studies included in the evidence review did not provide clear support for the use of intra-oral devices. Therefore, they agreed that parents and carers should be made aware of this and they agreed a recommendation to that effect. Further to this, the Committee noted that intra-oral appliances such as ISMAR were not widely provided in clinical practice and there was low quality evidence showing that ISMAR was less effective than control (no ISMAR). Additionally, the importance of considering oral-motor skills within the broader context of health and social aspects of eating and drinking was not widely understood.

The Committee considered that there was very limited evidence to guide care. There were few comparisons of interventions and limited data on the natural history of eating and drinking and swallowing disorders. Furthermore, the research on oral-motor therapies was conflicting. Therefore, the Committee agreed to develop a research recommendation on interventions to improve eating, drinking and swallowing in children and young people with cerebral palsy.

13.6.3 Consideration of economic benefits and harms

The Committee were highly concerned that the oral motor sensorimotor regimens used in some trials included in the clinical evidence review were very intensive, involving hospital admission, or taking time out of the school day. These regimens were considered too burdensome to undertake outside of the research setting, especially if they are performed for many months or years. Moreover, the Committee noted that oral motor treatments included in the trials did not aim to manage all aspects of eating, drinking and swallowing difficulties. The Committee agreed that parents, carers or school staff could be trained to use some oral motor techniques, which would reduce the cost of health care professionals, but the efficacy of such training packages has not been assessed. The acceptability to children, families, carers and schools has also not been explored.

It should be noted that the ISMAR intra-operative device is a specific type of intra-oral device, and in the UK the equivalent would be a palatal training aid/device (PTD), which is made individually for each child by the orthodontist or at a specialist centre. The high cost and high skill to fit this device was recognised by the Committee. The SLT and orthodontist would be involved in reviewing PTD (to check functional impact and the fit, approximately every 4-6 months) long term. The study included in the review that looked at ISMAR was conducted over 12 to 24 months, but it is possible that in clinical practice some children may abandon the PTD quickly if it is not comfortable or is not effective, whereas others may use the appliance for a number of years. The Committee agreed that a high proportion of patients who try intra-oral appliances will not tolerate them, consequently, the cost-effectiveness of oral motor devices will depend largely on patient preference. Furthermore, the Committee believed oral motor devices are primarily used to manage saliva control and are not typically used to manage eating, drinking and swallowing difficulties and questioned their cost-effectiveness for this indication.

Overall, the Committee were unable to recommend any specific intervention because any plan would be individualised to the child and young person and may involve several interventions. Despite this, the Committee agreed that factors such as postural management, texture modification and feeding techniques would be considered, before initiating exercise programmes or pharmacological treatment. As a result the least expensive and intensive interventions would be implemented first.

The plan would be reviewed regularly by a health care professional to ensure the child and young person and family/carer were satisfied with the plan and to modify the plan as necessary. Ideally this would take place in the child and young person's home and school environment. Consequently monitoring costs would be incurred regardless of the interventions included in the plan.

The Committee was aware that a plan to manage eating, drinking and swallowing difficulties could not include an intervention if there was no-one there to implement it accurately. For this reason training costs may be incurred by the school/carers/families if the health care professional believes the skills of the people who support the child's eating and drinking are inadequate.

13.6.4 Quality of evidence

Four randomised trials and 4 cohort studies were included in the evidence review. The quality of the evidence for this review ranged from very low to low. Main reasons of bias were: lack of information on the randomisation method used, concealment of allocation unreported or unclear, lack of blinding of investigators and also the blinding of participants due to the type of intervention being administered. The sample sizes of most of the studies was small, except 1 randomised trial which included 81 participants, which increased the uncertainty around the effects of the reviewed interventions In addition, it was not possible to conduct a meta-analysis studies due to the differences in the interventions.

13.6.5 Other considerations

It was noted that the validity of 1 of the outcome measures used in several studies was questioned. The Functional Feeding Assessment is a subscale of the Multidisciplinary Feeding Profile.

The Beckman oral motor exercise programme is not common in UK practice but other oral-motor exercise regimens do exist (for example TalkTools, or individually tailored oral motor programmes developed by speech and language therapists). There is considerable variation in practice across speech and language therapists in the UK with regard to the degree of individualisation, frequency of review, intensity of practice, and duration of such oral motor programmes. Data on compliance with treatment and acceptability of programmes to children, young people and caregivers is lacking.

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

13.6.6 Key conclusions

The Committee concluded that interventions to improve eating, drinking and swallowing in children and young people with cerebral palsy require input from multiple professionals. Studies in this area have largely focused on the development of oral motor skills with limited attention to the impact of interventions on other outcomes such as growth, weight gain, nutritional status, respiratory health, independence, the time taken for meals and the experience of the children and young people and their families and carers. The key areas of postural management, food and fluid modification, environmental adaptations and carer training have received limited consideration to date.

13.7 Recommendations

47. Develop strategies and goals in partnership with the child or young person with cerebral palsy and their parents, carers and other family members for interventions to improve eating, drinking and swallowing.

48. Create an individualised plan for managing eating, drinking and swallowing difficulties in children and young people with cerebral palsy, taking into account the understanding, knowledge and skills of parents, carers and any other people involved in feeding the child or young person. Assess the role of the following:

- postural management and positioning when eating
- modifying fluid and food textures and flavours
- feeding techniques, such as pacing and spoon placement
- equipment, such as specialised feeding utensils
- optimising the mealtime environment
- strategies for managing behavioural problems associated with eating and drinking
- strategies for developing oral motor skills
- communication strategies
- modifications to accommodate visual or other sensory impairments that affect eating, drinking and swallowing
- the training needs of the people who care for the child or young person particularly outside the home.

49. Advise parents or carers that intra-oral devices have not been shown to improve eating, drinking and swallowing in children and young people with cerebral palsy.

50. Use outcome measures important to the child or young person and their parents or carers to review:

- whether individualised goals have been achieved
- the clinical and functional impact of interventions to improve eating, drinking and swallowing.

13.8 Research recommendations

3. What is the clinical and cost effectiveness and safety profile of interventions to improve eating, drinking and swallowing in children and young people with cerebral palsy?

Table 56: Research recommendation rationale

Research question	What is the clinical and cost effectiveness and safety profile of interventions to improve eating, drinking and swallowing in children and young people with cerebral palsy?
Why this is needed	
Importance to 'patients' or the population	Children and young people with cerebral palsy may have eating, drinking and swallowing (EDS) difficulties leading to poor nutritional status, aspiration, respiratory infections, hospital admissions and reduced life expectancy. This can impact significantly on families and carers, although they are often keen to maintain oral intake.
Relevance to NICE guidance	The research is essential to inform future updates of key recommendations in the areas of eating, drinking and swallowing, optimising nutrition, and social care needs in the guidance.
Relevance to the NHS	Children and young people with severe swallowing difficulties or inadequate oral intake may require non-oral tube feeding. Surgical placement of

Research question	What is the clinical and cost effectiveness and safety profile of interventions to improve eating, drinking and swallowing in children and young people with cerebral palsy?
	gastrostomy/ jejunostomy carries a level of risk. Behavioural interventions include postural management, modification of food and fluid textures, feeding techniques and equipment, therapies aimed at improving oral-motor skills and reducing the risk of aspiration. Such interventions require specialist input from speech and language therapists and other members of the MDT. Carer/family training and support also requires resources.
National priorities	NHS Outcomes Framework (April 2016). The management of eating, drinking impacts on the following domains: 1. Preventing people from dying prematurely: children and people with learning disability 2. Enhancing quality of life for people with long term conditions: improving functional abilities, and enhancing quality of life for carers
Current evidence base	Very limited evidence is available to guide care. Both surgical and behavioural intervention studies are typically small, short term and with uni-dimensional outcomes. There are few comparisons of interventions and limited data on the natural history of eating and drinking and swallowing disorders. The research on oral-motor therapies is conflicting. No data is available on the impact of behavioural interventions on participation.
Equality	For most children and young people eating and drinking is an enjoyable experience, undertaken several times a day. Meals and snacks serve the purpose of obtaining nutrition and hydration, but also provide a context for social interaction. Difficulties with eating and drinking and swallowing results in medicalisation of an everyday activity and reduces opportunities for participation, with families reporting reluctance to eat in public. Swallowing difficulties contribute to health inequalities.
Feasibility	Longer term, comprehensive case series and prospective cohort studies exploring the impact of behavioural as well as surgical interventions are required. Multidimensional outcomes should explore changes in nutritional status, respiratory health, and psychosocial impact on children or young people and families. Multi-site, school-based studies, with carer/family involvement, may be more feasible than studying outpatient feeding clinic populations. The main ethical issue would be no or delayed treatment for children and young people at risk of respiratory compromise or under-nutrition.
Other comments	The NIHR Research for Patient Benefit Programme has supported the development of an Eating and Drinking Abilities Classification System in cerebral palsy, and a study on how services meet the psychosocial support needs of children and young people with feeding difficulties and their families is currently funded.

1 **Table 57: Research recommendation statements**

Criterion	Explanation
Population	Children and young people with cerebral palsy
Intervention	Change from background MDT input to individualised, targeted programmes including a variety of the following: Behavioural interventions include postural management, modification of food and fluid textures, Feeding techniques and equipment, Specific dysphagia therapies used in current clinical practice aimed at improving oral-motor skills and reducing the risk of aspiration. Pharmacological
Comparator	Population without the above

Criterion	Explanation
Outcome	Anthropometrics (including linear growth, weight, skin fold thickness) and developmental outcome Reduced risk of aspiration Change in diet consistency a child is able to consume QoL including enjoyment of eating and drinking and swallowing Child's level of participation in mealtime Psychological wellbeing of parents or carers Acceptability of programme
Study design	Comparative cohort
Timeframe	2 years

1

2

14 Optimising nutritional status

Review question: In children and young people with cerebral palsy, what interventions are effective at optimising nutritional status?

14.1 Introduction

Children and young people with cerebral palsy are at risk of nutritional problems associated with altered intakes of food and drink due to eating and drinking difficulties. Up to 90% of children and young people with cerebral palsy experience difficulties in chewing or swallowing, and/or eating or drinking independently. Factors that commonly affect intake and nutritional requirements include neuromuscular dysfunction, medication side effects, epilepsy and gastrointestinal disturbances such as constipation or gastro-oesophageal reflux.

Nutritional problems affecting the health and wellbeing of children and young people with cerebral palsy include being overweight or underweight, and vitamin and mineral deficiencies. Optimising nutritional status includes addressing all of these problems. However, this guideline focuses on interventions related to the common problem of protein-energy malnutrition - i.e. undernutrition caused by inadequate energy and protein intake. Protein-energy malnutrition is associated with overall poor health and wellbeing, and may impact negatively on movement, communication and other functional skills, and prolonged dependence on carers.

Children and young people with cerebral palsy who are identified with signs of protein-energy malnutrition - faltering growth or being underweight - are typically offered tailored nutritional assessment and support from a dietitian. This may include: oral nutrition support - fortifying or modifying food intake to increase its calorie and protein content; the addition of specific oral nutritional supplements or referral on for tube feeding via nasogastric (NG) or gastrostomy tubes, including percutaneous endoscopic gastrostomies (PEG). There is wide variation across the UK in the availability of dietetic service provision for children and young people with cerebral palsy

The aim of this review is to identify clinical and cost effective interventions for optimising nutritional status in children and young people with cerebral palsy.

14.2 Description of clinical evidence

One randomised controlled trial (RCT) (Patrick 1986) and 3 observational studies (Fung 2002; Kong and Wong 2005; Sullivan 2006) were included in the review.

With regard to the population, all studies examined children with cerebral palsy. One study (Kong and Wong 2005) reported evidence from children with quadriplegic (Bilateral UL≥LL) and dyskinetic cerebral palsy, 1 study focused on children with spastic quadriplegic (Bilateral UL≥LL) cerebral palsy (Sullivan 2006), 1 study (Fung 2002) included children with moderate to severe cerebral palsy, classified by GMFCS level III to V, and 1 study (Patrick 1986) examined undernourished participants with cerebral palsy who had skinfold thickness below fifth percentile for age and failure to gain weight during the previous year.

Only 1 RCT (Patrick 1986) provided evidence relating to the protocol and was included in the evidence review. In this trial, participants in the intervention group received an immediate high-energy feeding programme through a nasogastric tube and aimed to re-establish normal metabolism, energy intake and feeding, while participants in the control group received standard oral feeding.

Observational evidence was searched for the interventions where no RCT evidence was retrieved. Subsequently, the remainder of the studies were observational and examined tube

fed children and young people with cerebral palsy compared to orally fed. Of these 3 observational studies, 2 (Sullivan 2006; Fung 2002) that assessed tube feeding specified gastrostomy whilst the remaining study (Kong and Wong 2005) did not specify the type of tube feeding. One of these (Sullivan 2006) was a prospective cohort study with a follow-up period of 12 months and 2 (Kong and Wong 2005; Fung 2002) were cross-sectional studies with no follow-up period.

No evidence was found for the following interventions:

- Jejunostomy tube feeding
- Lifestyle changes
- Antiemetics

Of the outcomes listed in the protocol, all the studies provided weight as an outcome measure. Two studies (Sullivan 2006; Fung 2002) measured weight in z scores and 2 studies (Kong and Wong 2005; Patrick 1986) measured weight in kilograms. One study (Fung 2002) reported Health-Related Quality of Life (HRQoL) outcomes, by asking parent's to complete the Child Health Questionnaire (CHQ) on behalf of the child or young person with cerebral palsy they cared for.

In terms of setting, 1 study (Sullivan 2006) recruited patients from a tertiary feeding clinic for children with neurological impairment, 1 study (Patrick 1986) conducted the study in a child neurology centre, 1 study conducted the study at a hospital unit (Kong and Wong 2005) and 1 study (Fung 2002) recruited patients through multiple methods including clinics, volunteer organisations and schools and did not report where the study was conducted.

Evidence from these are summarised in the clinical GRADE evidence profiles below (Table 59 and Table 60). See also the study selection flow chart in Appendix F, forest plots in Appendix I, study evidence tables in Appendix J and exclusion list in Appendix K.

14.2.1 Summary of included studies

A summary of the studies that were included in this review are presented in Table 58.

Table 58: Summary of included studies

Study	Intervention/Comparison	Population	Outcomes	Comments
Fung 2002	Gastrostomy fed vs orally fed	230 children with cerebral palsy (GMFC III to V) aged 2 to 18 years.	1. Anthropometric measures: weight (z score) 2. Health related quality of life: - CHQ Global Health Score: assessed the parent's perception of child's overall health - CHQ Physical Summary Score: assesses physical function, societal role and participation, general health and body pain - 2 subsets of	

Study	Intervention/Comparison	Population	Outcomes	Comments
			CHQ: parent-time and parent-emotion designed to asses impact of child's health on the parent's emotional health and societal role.	
Kong and Wong 2005	Tube fed vs orally fed	110 patients with cerebral palsy aged 2.4 to 17.7 years. Of these, 9 had dyskinetic cerebral palsy.	1. Anthropometric measure: weight (kg)	
Patrick 1986	Immediate high-energy feeding through nasogastric tube.	10 children and infants with cerebral palsy aged 2.8 to 15.8 years who were undernourished defined by a skinfold thickness below fifth percentile for age and failure to gain weight during the previous year.	1. Anthropometric measures: weight (kg).	The control group (standard feeding regimen) were tube fed after 5 weeks of study initiation and labelled 'delayed intervention'.
Sullivan 2006	Gastrostomy fed vs orally fed	40 children with spastic quadriplegic cerebral palsy (Bilateral UL≥LL) aged 1.4 to 18.11 years	1. Anthropometric measures: mean difference in weight (z-score).	

CHQ child health questionnaire, GMFCS Gross Motor Function Classification System.

14.32 Clinical evidence profile

The clinical evidence profiles for this review question (nutritional status in cerebral palsy) are presented in Table 59 and Table 60.

Table 59: High energy tube feeding versus control

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Control	High energy feeding		
Weight kg	The mean weight in the control groups was -0.1 kg	The mean weight in the intervention groups was 6.1 higher[1]	10 (1 study)	very low[2,3]

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 unable to calculate 95% ci as standard deviation for intervention group not available.
2 evidence downgraded by 2 due to no information on randomisation process, blinding or allocation concealment given. Attrition bias due to missing data.
3 imprecision not calculable: standard deviation for intervention group not reported.

Table 60: Tube fed versus orally fed

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Orally fed	Gastrostomy		
Weight z score Follow-up: 12 months	-	The mean weight in the intervention groups was 0.002 higher (0.64 lower to 0.65 higher)	40 (1 study)	very low[1,2]
Weight z score	The mean weight in the control groups was -2.77 z-score	The mean weight in the intervention groups was 0.62 higher (0.24 lower to 1.48 higher)	119 (1 study)	very low[3]
Weight kg	-	The mean weight in the intervention groups was 0.51 higher (1.79 lower to 2.8 higher)	110 (1 study)	low
Health related quality of life (CHQ) CHQ: Global Health Score	The mean health related quality of life (CHQ) in the control groups was -0.46	The mean health related quality of life (CHQ) in the intervention groups was 1.38 lower (1.79 to 0.97 lower)	119 (1 study)	low
Health related quality of life (CHQ) CHQ: Physical Summary Score	The mean health related quality of life (CHQ) in the control groups was 38.1	The mean health related quality of life (CHQ) in the intervention groups was 14.5 lower (19.35 to 9.65 lower)	119 (1 study)	low
Health related quality of life (CHQ) - Impact on Parent-Time: z score	The mean health related quality of life (CHQ) - impact on parent-time: z score in the control groups was -0.91	The mean health related quality of life (CHQ) - impact on parent-time: z score in the intervention groups was 0.47 lower (1.11 lower to 0.17 higher)	119 (1 study)	very low[4]
Health related quality of life (CHQ) - Impact on Parent-Emotion: z-score	The mean health related quality of life (CHQ) - impact on parent-emotion: z-score in the control groups was -0.07	The mean health related quality of life (CHQ) - impact on parent-emotion: z-score in the intervention groups was 0.11 higher (0.47 lower to 0.69 higher)	119 (1 study)	low

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*

1 evidence was downgraded by 1 due to attrition bias: Dropout rate at follow-up not given.

2 evidence was downgraded by 2 due to very serious imprecision as 95%CI crossed 2 default MID

3 evidence was downgraded by 1 due to serious imprecision as 95%CI crossed 1 default MID

4 evidence was downgraded by 1 due to serious imprecision as 95%CI crossed 1 default MID

14.4 Economic evidence

No economic evaluations of interventions relevant to optimising nutritional status were identified in the literature search conducted for this guideline. Full details of the search and

economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

This review question was not prioritised for de novo economic modelling. To aid consideration of cost-effectiveness relevant resource and cost use data are presented in Appendix G.

14.5 Evidence statements

14.5.1 Immediate high energy feeding versus control

Anthropometric measures

Very low quality evidence from 1 RCT with 10 participants showed that immediate high-energy feeding is effective at improving weight in undernourished cerebral palsy patients after 5 weeks follow-up. However, evidence reported was incomplete and confidence intervals were not calculable.

Adverse events

No evidence was retrieved for this outcome.

Dietary intake

No evidence was retrieved for this outcome.

Health related quality of life

No evidence was retrieved for this outcome.

14.5.2 Tube feeding versus oral feeding

Weight

Very low to low quality evidence from 3 observational studies with 269 participants showed no difference in weight between tube fed group and control group, measured in kilogram and Z-scores.

Adverse events

No evidence was retrieved for this outcome.

Dietary intake

No evidence was retrieved for this outcome.

Health related quality of life

Very low to low quality evidence from 1 observational study with 119 participants which used the CHQ and showed no difference between gastrostomy fed and orally fed groups in parent-time score and parent-emotion score, while the orally fed group had a better global health score and physical summary score.

14.6 Evidence to recommendations

14.6.1 Relative value placed on the outcomes considered

The aim of this review was to assess the clinical and cost effectiveness of interventions for optimising adequate nutritional status in children and young people with cerebral palsy. The

Committee indicated the following to be the critical outcomes of this review: anthropometric measures including weight, adverse events and dietary intake.

14.6.23 Consideration of clinical benefits and harms

The Committee recognised a number of inherent barriers to carrying out high quality research to ascertain effective strategies for optimising the nutritional status of children and young people with cerebral palsy:

- It would be unethical to conduct research whereby a control group was not given adequate nutrition
- There is a lack of consensus as to how to measure nutritional status in children with cerebral palsy and standard measures may be problematic for a number of reasons:
  - It can be challenging to obtain reliable anthropometric measures such as height and length in non-ambulatory children and young people
  - Anthropometric reference ranges (such as growth charts and mid-upper arm or waist circumference ranges) are typically designed for healthy and typically developing populations and may not be applicable to those with cerebral palsy who may have significantly different body composition
  - Growth charts that have been specifically developed for children and young people with cerebral palsy included those with poor nutritional status and therefore do not represent 'ideal growth'.

The Committee agreed that the included evidence was limited in terms of the outcomes used to assess the clinical effectiveness of optimising nutritional status, for example obtaining individual measures such as weight rather than combined measures.

Additionally, the Committee highlighted that the 3 included studies that compared oral and tube feeding lacked detail on the 2 diets they compared – for example whether the initiation of tube feeding resulted in an increased or comparable nutritional intake.

The Committee recognised that optimising nutritional status in children and young people with cerebral palsy involved preventing and treating a number of nutritional issues including vitamin and mineral deficiencies, overweight and obesity, however the treatment and prevention of protein-energy malnutrition via a high calorie and protein diet was prioritised as the main focus of this review.

The Committee raised that it was important to recognise that in children and young people with cerebral palsy nutritional issues can be common. This can range from malnutrition to excess weight or obesity, all with resulting impacts on physical and mental wellbeing. The Committee were also aware from their own experience that access to nutritional services for children and young people with cerebral palsy was suboptimal and showed high degree of variation across the UK. The Committee considered it was important to ensure that children and young people with cerebral palsy had access to at least the same level of nutritional monitoring and support currently provided to their peers in the general population. Based on their experience they agreed by consensus to develop a recommendation for regular review and to ensure anthropometric measurements were taken regularly and dietetic advice was sought in a way equitable to children and young people in the rest of the population. Due to the compounding effects of poor nutrition on other health issues and quality of life, it was considered that it should be made clear that access to support in the form of assessment by dietitians and optimising nutritional interventions was available in a time frame appropriate to the child or young person, particularly under the age of 2 years.

The Committee agreed that each child and young person with cerebral palsy will have their own individual, specific nutritional needs which where necessary, should be assessed by a specialist dietitian in order to meet their nutritional requirements, as part of their standardised multidisciplinary review. In children where there is concern about growth, regular review is necessary.

The Committee recognised the need to recommend tube feeding for some children and young people with cerebral palsy and wanted to ensure that this was implemented only following appropriate assessment, in partnership with the child, young person and their family and carers, and should be directly related to concerns over serial anthropometric measures or health issues. The Committee discussed 1 study which reported Health-Related Quality of Life (HRQoL) showing no difference in the impact on parental emotion if their child was orally or tube fed and considered that this was invalid as it was comparing different groups of children and young people and different forms of nutritional support. The Committee recognised that although the reported experience of tube feeding in most children, young people and families is positive, multidisciplinary support is key to preventing some potential drawbacks such as overfeeding, and feeling less involved with family mealtimes.

Given the limited evidence that high calorie and high protein diets improved weight and other outcomes in children with cerebral palsy, and due to the large proportion of children with clinically significant oral motor dysfunction and who are undernourished, the Committee agreed that assessing the clinical and cost effectiveness of early interventions for optimising protein, energy and micronutrient nutritional status would be prioritised as a research recommendation.

14.6.3 Consideration of economic benefits and harms

The high upfront cost of the procedure and initial monitoring schedule for tube feeding was recognised by the Committee. They also iterated that tube feeding is associated with adverse effects (incurring a treatment cost and disutility) and can negatively impact social interactions during meal times (incurring a disutility). However they considered a role for tube feeding if oral intake is insufficient to provide adequate nutrition after assessment and nutritional interventions, as in such cases, the benefits of tube feeding could outweigh the costs.

Overall the Committee were unable to recommend any specific intervention because interventions would be individualised to the child or young person with cerebral palsy, and could involve several interventions. Despite this, the Committee agreed that appropriate dietary modification would be considered, before initiating antiemetic drugs or tube feeding. As a result the least expensive and invasive interventions would be implemented first.

The Committee stated that nutritional interventions should be reviewed regularly by a dietitian to take anthropometric measures and to ensure the child or young person with cerebral palsy and their family and carers are satisfied with their plan. However, the Committee was aware that access to nutritional services for children and young people with cerebral palsy are sometimes suboptimal. For this reason training costs may be incurred by the NHS to ensure access to dietitians with the necessary competencies to recognise, treat and monitor nutritional issues in children and young people with cerebral palsy is sufficient, especially for those patients who are considered eligible for tube feeding.

The Committee acknowledged that oral solution preparations of antiemetic drugs can cost substantially more than capsules or tablets. Despite this the Committee noted that most patients who require antiemetic drugs would be unable to take capsules or tablets due to their inability to swallow. However, the Committee acknowledged that when capsules or tablets can be tolerated (or grounded to a powder) they should be offered instead of oral solutions because they are cheaper and there is no evidence to suggest they are any less effective.

14.6.4 Quality of evidence

The evidence from 1 RCT and 3 observational studies were of low to very low quality as assessed by GRADE. The predominant reasons included no information on randomisation or allocation for the RCT and attrition bias due to missing data and imprecision in the 3 observational studies.

14.6.5 Other considerations

The Committee noted that oral nutritional support including food intake and monitoring vitamins and minerals and enteral tube feeding were covered in detail by the NICE guideline on nutrition support in adults, and that it would be relevant to refer to this guideline as part of the guideline recommendations for young people over 18 years of age. The Committee also noted the NICE guideline currently under development (due for publication in November 2017) on faltering growth. The Committee also considered that aspects of various conditions which can affect nutritional status can be found in the NICE guidance on Constipation in children and young people, Obesity prevention, Obesity, Vitamin D: increasing supplement use in at-risk groups, Gastro-oesophageal reflux disease in children and young people and Gastro-oesophageal reflux disease and dyspepsia in adults.

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

14.6.6 Key conclusions

The Committee concluded that the studies included in the clinical evidence review were not adequate in assessing the clinical effectiveness of interventions to optimise the nutritional status in children and young people with cerebral palsy. However, given the Committee's awareness of issues in the access to nutritional services for children and young people with cerebral palsy, consensus based recommendations highlighted the need for regular review of nutritional status, referral to dietetics and a multi-disciplinary team if there were concerns regarding growth and nutritional status. Given the paucity of evidence in terms of the clinical effectiveness of interventions to optimise the nutritional status, the Committee agreed to prioritise a research recommendation in this area.

14.7 Recommendations

51. Regularly review the nutritional status of children and young people with cerebral palsy, including taking anthropometric measurements.

52. Provide timely access to assessment and nutritional interventional support from a dietitian if there are concerns about oral intake, growth or nutritional status.

53. If oral intake is still insufficient to provide adequate nutrition after assessment and nutritional interventions, refer the child or young person to be assessed for enteral tube feeding by a multidisciplinary team with relevant expertise.

54. For guidance on nutritional interventions and enteral tube feeding in over 18s, see the NICE guideline on nutrition support for adults.

14.8 Research recommendations

4. What is the clinical and cost effectiveness of early interventions for optimising protein, energy and micronutrient nutritional status in children with cerebral palsy?

Table 61: Research recommendation rationale

Research question	What is the clinical and cost effectiveness of early interventions for optimising protein, energy and micronutrient nutritional status in children with cerebral palsy?
Why this is needed	
Importance to 'patients' or the population	More than 90% of children with cerebral palsy have clinically significant oral motor dysfunction and a large proportion (20%) of children with cerebral palsy (40% of those with GMFCS of IV or V) are undernourished (z-scores for weight and/or height below -2 SD). Studies have also shown low micronutrient intakes and status in children and young people with cerebral palsy. Adequate nutrition is essential for wellbeing, growth and development in all children. Provision of high calorie and high protein diets either orally or via tube feeding is well established to improve weight however supplementation of micronutrients is also necessary to ensure nutritional adequacy and prevent deficiencies.
Relevance to NICE guidance	High priority: There is an urgent need for evidence to inform the timing and type of nutritional intervention that would optimise nutritional status in children and young people with cerebral palsy.
Relevance to the NHS	Early intervention could improve long term outcomes for children and young people with cerebral palsy. Hence any nutritional interventions would be offset by improved quality of life and health.
National priorities	N/A
Current evidence base	There is limited low level evidence that high calorie and high protein diets improve weight and other outcomes in children with cerebral palsy.
Equality	There is a clear evidence that socio-economic and environmental factors influence nutritional status.
Feasibility	The proposed research would not needs large numbers or duration to demonstrate efficacy and would be relatively straight forward to carry out.
Other comments	Early intervention could improve long term outcomes for children and young people with cerebral palsy. Hence any nutritional interventions would be offset by improved quality of life and health.

Table 62: Research recommendation statements

Criterion	Explanation
Population	Infants and Children (under 2 years) with a non-progressive lesion of their brain who have problems with movement and posture picked up through enhanced screening of the high risk population.
Intervention	Dietetic support in the first 2 years of life and provision of adequate protein, energy and micronutrient intake.
Comparator	Usual care
Outcome	Anthropometrics including linear growth, weight, skin fold thickness. Developmental functioning in the areas of gross motor, fine motor, communication, self-care, cognitive abilities. Clinical aspects focusing on chest health, gastrointestinal motility (prevalence and severity of vomiting, regurgitation and reflux and constipation). Quality of life for children and young people with cerebral palsy and their families
Study design	Multicentre randomised controlled trial

Criterion	Explanation
Timeframe	2-5 years

1

15 Improving speech, language and communication: Speech intelligibility

Review question: In children and young people with cerebral palsy, what interventions are effective in improving speech intelligibility?

15.1 Introduction

Motor speech disorders are common in cerebral palsy, resulting in problems with speech intelligibility. There is an association between the overall severity of the movement difficulty and the level of intelligibility. Children and young people with little or no speech often have multiple challenges, including learning disability, epilepsy, vision or hearing impairments, and feeding difficulties. Speech disorders are more prevalent in the dyskinetic forms of cerebral palsy, including children and young people with unilateral spastic cerebral palsy.

A lack of intelligibility can be a barrier to social engagement, education, employment and impact on self-esteem and quality of life for an individual. Even when intelligibility difficulties are present, speech is still often the quickest and most effective way for children and young people to communicate, particularly within families. Interventions aimed at improving speech intelligibility are therefore important to consider.

Speech production is a challenging area to study as its development is prolonged and varied in a child's early years. Speech development is also influenced by other factors such as cognition, so a child's potential for speech may be difficult to determine. Consequently the same intervention in different children may have very different outcomes.

The clinical guidelines group not only looked at areas such as speech production, intelligibility and expressive language but also quality of life, participation and self-confidence. These areas were identified based on existing guidelines, published reviews and personal experience. Those then felt to be most important were prioritised for detailed systematic review.

The objective of this review was to assess the clinical and cost effectiveness of interventions in improving speech intelligibility in children and young people with cerebral palsy.

Systematic reviews of randomised controlled trials or single experimental trials were considered the most appropriate study designs to answer the review question. Where possible, we identified the most recent systematic review available and updated it with the latest studies that matched the criteria specified in the review.

15.2 Description of clinical evidence

One Cochrane review was identified on speech and language therapy in children with cerebral palsy (Pennington 2004). The Cochrane review aimed to assess the effectiveness of speech and language therapy to improve the communication skills of children with cerebral palsy including, but not limited to speech intelligibility. Although the focus of this review was on speech, the results presented address wider communication skills. Both group and single case experimental designs were included. Single case experimental designs were included if communication behaviours were allocated to treatment or control and both behaviours were measured at baseline, intervention and follow-up phases in order to allow for causal inference. The review looked at any child or individual under 20 years of age with any communication disorder associated with cerebral palsy, including dysarthria, dyspraxia and mixed syndromes; or their communication partners. Similarly, the review studied both interventions given directly to the child with the aim of developing the child's communication skills, and those therapies given to familiar communication partners (families, teachers,

teaching assistants, peers) with the aim of changing the communication partners' conversation style to help them children's communication. The outcome measures considered were:

- Measures of communication
- Measures of family stress and coping
- Children's quality of life
- Children's participation
- Satisfaction of patient and family with treatment
- Non-compliance with treatment.

Of the 17 papers included by this review, the 9 papers focusing on therapies given directly to children (8 single case studies and 1 interrupted time series study) have been considered in order to address the current review question.

Four additional studies have been found (Miller 2013; Ward 2014; Pennington 2013; Fox 2012)) that looked at speech and language therapy interventions in children and young people with cerebral palsy. Miller and colleagues used a group design pre- versus post-intervention and looked at change in voice quality, whereas the paper by Ward used a single-subject A1BCA2 multiple baseline design to study effects on speech production accuracy. Fox et al. conducted a study to examine the effect of intensive voice treatment (LSVT LOUD) in 5 children with spastic cerebral palsy, measuring results at baseline, post-treatment and 6-week follow up. Finally, Pennington et al. conducted a study in 15 children with dysarthria and cerebral palsy who received 3 sessions of therapy per week for 6 weeks. Results have been compared at baseline, and 1, 6, and 12 weeks after therapy. For the detailed description of the included studies see Table 63.

As GRADE was not performed for this question, the quality of the evidence was reported by study based on the study design and risk of bias. Included studies have all been assigned a very low quality evidence status, as their study design does not allow for generalisation of the results (RCT would have been the most appropriate design for this intervention review). For more details, please see section 15.5.4 on the quality of the evidence.

Given the very wide range of communication aspects targeted, interventions used in the review, and the methodology employed by the Cochrane Review, a narrative summary of the evidence has been used in this evidence review.

For full details see protocol in Appendix E. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

15.2.1 Summary of included studies

A summary of the studies that were included in this review are presented in Table 63 and Table 64.

Table 63: Summary of included studies (Cochrane review)

Study	Study design	Population	Intervention	Outcomes	Conclusions
Cochrane Review					
Pennington 2004	Systematic review	Any child or individual under 20 years of age with any communication	1. Therapies given directly to the child with the aim of developing the child's communication skills.	• Measures of communication • Family stress and coping	• The Cochrane review addressed a clearly focused question. • RCTs would have been the most appropriate study design for this type of question (intervention), but

Study	Study design	Population	Intervention	Outcomes	Conclusions
Cochrane Review					
		disorder associated with CP, including dysarthria, dyspraxia, ataxia, and mixed syndromes.	2. Therapies given to familiar communication partners with the aim of changing the communication partners' conversation style to help them facilitate children's communication development.	• Children's QoL • Children's participation • Satisfaction of patients and family with treatment • Non-compliance with treatment	since RCTs were not available the authors included controlled studies including group and single case experimental design. • The overall results of the review suggest that it is not possible to conclude that SALT focusing on children with CP is more effective than no intervention at all. • Given the study design considered, it is not possible to tell whether the results can be applied to a local population. • Because of the heterogeneity of children with cerebral palsy, their conversational partners and communication environments the authors suggest that a broad evaluation of the effectiveness of SALT will not be possible, and evaluations should focus on the effectiveness of interventions addressing particular areas and stages of speech, language and communication, with emphasis on facilitating the participation of children and families in chosen life situations. • All the important outcomes have been considered by this review; however, evidence wasn't retrieved for the following outcomes: Children's QoL Family stress and coping Satisfaction of patients and family with treatment Non-compliance with treatment

1 *CP cerebral palsy, QoL quality of life, RCTs randomised controlled trial, SALT Speech and Language Therapy.*

2 **Table 64: Summary of included studies**

Study	Study design	Population	Intervention	Outcomes	Risk of bias
Studies included in Cochrane Review					
Campbell 1982	Single case experim	One boy aged 10 years with	Correct production of "is/are" in 3	Expressive language: frequency of	Selection bias: random sequence generation not used – unclear risk.

Study	Study design	Population	Intervention	Outcomes	Risk of bias
Studies included in Cochrane Review					
	ental design	CP and moderate language delay.	syntactic structures was reinforced using behaviour modification techniques. Two 15 minutes sessions/school day (155 sessions in total)	correct "is/are" [production was recorded online by an unblinded observer in each training session, and by an assessor in 175 of sessions	Detection bias: reliability between 2 unblinded raters on 17% of sessions ranged from 68-90% - high risk. Attrition bias: no missing data – low risk. Reporting bias: all expected outcomes reported - unclear risk.
Dada 2009	Single case experimental design	Three children with CP who had fewer than 15 spoken words, aged 8-12 years	Aided language stimulation; 1 set of 8 words taught in a week, same activity repeated each day for 5 days. Duration = 15-25 min per session. Three week intervention. Total of 24 vocabulary items taught. Intervention was provided in English, but English was not the children's first language.	Receptive vocabulary: Number of objectives correctly selected when named.	Selection bias: random sequence generation not used – unclear risk Detection bias: coding from videotaped recordings. Unclear if outcome assessor was blinded to time of recording. High agreement between raters (>90%) - high risk. Attrition bias: no missing data – low risk.
Davis 1998	Single case experimental design	One boy with CP aged 15 years who communicated using vocalisation, gesture and word phrases via AAC. Communication partners: 2 female graduate students and a male personal care attendant.	Child was thought to produce responses to statements made by others in conversation. Communication partners trained to use non-obligatory requests in conversation to promote responses. Treatment 2-3 times per week at home. 36 sessions in	Communicative functions: Percentage responses of blocks of 5 elicitation sequences was recorded by unblinded assessor	Selection bias: random sequence generation not used – unclear risk. Detection bias: online, live coding of interactions. Inter-rater agreement >94% - Unclear risk. Attrition bias: no missing data – low risk. Reporting bias: all expected outcomes reported - low risk.

Study	Study design	Population	Intervention	Outcomes	Risk of bias
Studies included in Cochrane Review					
			total.		
Hunt 1986	Single case experimental design	One girl aged 7 years with CP, severe intellectual impairment and multiple disabilities. Communicated via vocalisation, 1 gesture, 2 manual signs, and by touching the listener.	The child was thought to request 4 objects or events by eye pointing to line drawings symbolising the object or action. Interrupted chain training of 4 requests. Treatment given twice daily in familiar routines, with 55 sessions in total.	Communicative functions: Probes were made daily of the request currently under investigation. Content, form and function of communicative behaviour was assessed by a therapist.	Selection bias: random sequence generation not used – unclear risk. Detection bias: online, live coding of interactions. Second independent rater coded 20% of sessions. Inter-rater agreement >92% - High risk. Attrition bias: no missing data – low risk. Reporting bias: all expected outcomes reported - low risk.
Hurlburt 1982	Single case experimental design	Three teenage boys aged 14, 16, 18 years with severe CP and cognitive impairments.	The children were taught to label objects using Blissymbols or iconic line drawings using micro-teaching strategies. Frequency and duration of the therapy was not stated.	Proportions of Blissymbols and iconic symbols used to label taught and untaught items was calculated before and throughout training.	Selection bias: random sequence generation not used – unclear risk. Detection bias: online, live coding of interactions. Mean Inter-rater agreement 98% - Low risk. Attrition bias: no missing data – low risk. Reporting bias: all expected outcomes reported - low risk.
Pennington 2010	Interrupted time series	15 children with CP, 1 with Worster Drought, aged 12-18 years (mean=14, SD=2). Dysarthria rated mild-severe by referring therapists. All children able to comprehend simple instructions.	Individual therapy focused on stabilising respiratory and phonatory effort and control, speech rate and phrase length/syllables per breath.	Speech production: Percentage of words intelligible in single words and connected speech to familiar and unfamiliar listeners.	Selection bias: participants acted as own controls – unclear risk. Detection bias: listeners blind to time of recording - Low risk. Attrition bias: 1 child's data missing at Time 1 – low risk. Reporting bias: all expected outcomes reported - low risk.
Pinder 1995	4 Single cases experimental	Four children with CP (2 males and 2 females),	Children were taught to produce either requests for	Communicative functions: Requests for	Selection bias: not used, single case experimental design – unclear risk.

Study	Study design	Population	Intervention	Outcomes	Risk of bias
Studies included in Cochrane Review					
	design	aged 11.5-13.5 months who had difficulty grasping and releasing objects and did not sit independently	objects or requests for more of an activity using micro teaching techniques. Therapy was given twice a week for up to 12 weeks.	more and requests for objects were probed once per week in play with toys (experimental conditions) and at snack times (control condition).	Detection bias: coding of interaction from videotapes, primary rater not blind to data collection point. Second rater independently coded 22% of all data, k>0.69 – high risk. Attrition bias: no missing data – low risk. Reporting bias: all expected outcomes reported - low risk.
Richman 1977	Single case experimental design	One girl aged 9 years old with CP and severe cognitive impairment.	Interventions to produce pre-intentional communication skills: maintaining eye contact and head control and increasing vocal imitations. 10 minute therapy sessions given 4 days/week for 40 weeks. Ten minutes were sampled for the presence of the 3 behaviours.	Pre-intentional communication: percentage of time eye contact and head control were maintained during each training session. Vocal imitation was requested 30 times in each session, percentage response recorded.	Selection bias: not used, single case experimental design – unclear risk. Detection bias: online, live coding. Inter-rater agreement >80% - unclear risk. Attrition bias: 3/80 sessions missed – low risk. Reporting bias: all expected outcomes reported - low risk.
Sigafoos 1995	Single case experimental design	Boy aged 6 years with severe CP of unspecified type, who had moderate cognitive impairment and required assistance for all activities of daily living. Participant was reported to understand various spoken commands and communicated using eye	Child was taught to request objects by using micro-teaching strategies in 19 sessions over 8 weeks.	Communicative functions: Therapist registered percentage of trials in which object requested.	Selection bias: not used, single case experimental design – unclear risk Detection bias: online, live coding. Inter-rater agreement >83% - low risk. Attrition bias: child absent from school for replication phase – high risk. Reporting bias: all expected outcomes reported - low risk.

Study	Study design	Population	Intervention	Outcomes	Risk of bias
Studies included in Cochrane Review					
		gaze.			
Relevant published studies since 2011					
Fox 2012	Multiple baseline single-subject design	5 children with spastic CP between the ages of 5 and 7 years with dysarthria.	LSVT LOUD treatment consisted of 16 individual 1-hr sessions delivered on 4 consecutive days each week for 4 consecutive weeks.	Measures obtained: Auditory-perceptual analysis of speech Acoustic measures of vocal functioning Perceptual ratings by parents and participants	Selection bias: not used – unclear risk. Detection bias: online, live coding. Inter-rater agreement 74%-89% - unclear risk. Attrition bias – low risk. Reporting bias: all expected outcomes reported - low risk.
Miller 2013	Group design pre-post intervention	16 individuals with CP and dysarthria (9 F, mean age = 14 years SD = 2).	All participants received 6 weeks of speech therapy at schools, comprising 3, 35-40 minute individual sessions per week, delivered by a SLP. Therapy focused on achieving and maintaining a suitable posture for breathing and phonation, stabilising students' respiratory and phonary effort and control, speech rate and phrase length/syllables per breath. Articulation was not directly targeted.	Speech production: Change in voice quality: grade, breathiness, asthenia, roughness, strain. Association between change in voice quality and speech intelligibility (mean intelligibility scores for each patient reported).	Selection bias: not used– unclear risk. Detection bias: 16 experienced SLP rated voice quality using GRBAS scales; therapists were blind to all speaker and time point information - low risk. Attrition bias: no missing data - low risk. Reporting bias: all expected outcomes reported - low risk.
Pennington 2013	Group design pre-post	15 children with cerebral palsy and	Three sessions of individual	Intelligibility of single words and	Selection bias: not used– unclear risk. Detection bias: - low risk.

Study	Study design	Population	Intervention	Outcomes	Risk of bias
Studies included in Cochrane Review					
	intervention	dysarthria (age range 5-11 years).	therapy per week for 6 weeks.	speech. Participation in communicative interactions was measured using the FOCUS tool.	Attrition bias: 1 child received 10 sessions only owing to illness (all the others received 14-16 sessions) - low risk. Reporting bias: all expected outcomes reported - low risk.
Ward 2014	Single-subject A1BCA2 multiple baseline design	6 children with CP (age range 3 - 11 years) with moderate to severe speech impairment	Tactile-kinesthetic motor-speech intervention program (Prompts for Restructuring Oral Muscular Phonetic Targets) Phase A1 = baseline (5-8 weeks) Phase B targeted each participant's intervention priority Phase C targeted 1 level higher (B and C together = 10 weeks) Phase A2 = follow-up data collection at 12 weeks post phase C.	Speech production: accuracy assessed for both attainment of the targeted motor-speech movement pattern and perceptual accuracy using weekly probes.	Selection bias: not used– unclear risk. Detection bias: an independent PROMPT trained SLP blinded to the phases of the study and the participants completed the scoring of the speech data - low risk. Attrition bias: no missing data - low risk. Reporting bias: all expected outcomes reported - low risk.

CP cerebral palsy, SD standard deviation, SLP speech and language pathologist, SD standard deviation, AAC alternative augmentative communication, GRRBAS scale Grade, Roughness, Breathiness, Asthenia, Strain scale, SLP speech and language pathologist, FOCUS focus on the outcomes of communication under six, LSVT LOUD Lee Silverman Voice Treatment.

15.3 Economic evidence

No economic evaluations of interventions relevant improving speech intelligibility were identified in the literature search conducted for this guideline and this review question was not prioritised for additional economic analysis. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

15.4 Evidence statements

15.4.1 Speech production and Intelligibility

There is very low quality evidence from 1 pre-post intervention study with 16 participants with cerebral palsy (Miller 2013) that observed differences pre- versus post-intervention in speech intelligibility. The study focused on examining the correlation between voice quality (grade, roughness, breathiness, asthenia and strain) and speech intelligibility, but mean intelligibility scores for each participant were also reported. Intelligibility scores were based on the mean percentage intelligibility score per participant from the single word and connected speech (cartoon strip) results obtained from the multiple unfamiliar listeners. An overall improvement in speech intelligibility was observed, as the mean score increased from 29.70 pre-intervention to 45.70 post-intervention.

There is very low quality evidence from 1 study with interrupted time series design (Pennington 2010) to suggest an overall improvement in speech production in 15 children aged 12-18 years (mean=14, SD=2) and able to comprehend simple instructions, who received intervention focusing on respiratory and phonatory control, and control of speech rate and phrase length. No changes in speech production that were understandable to familiar and unfamiliar adults were observed at baseline (6 weeks and 1 week prior to treatment). Following treatment the estimated increase in intelligibility to familiar listeners was 14.7% (95% CI 9.8-19.5) for single words and 12.1% (95% CI 4.3-20.0) for connected speech. For unfamiliar listeners the immediate post-intervention estimated increase was 15.0% (95% CI 11.73-18.17) for single words and 15.9% (95% CI 11.8-20.0) for words in connected speech. No differences were observed between post-intervention scores and follow-up scores taken at 1 and 6 weeks after intervention completion for either single words or connected speech when heard by either a familiar or unfamiliar listener.

There is low quality evidence from another single-case multiple baseline study (Ward 2014) with 6 children with cerebral palsy who received speech and language therapy using a tactile-kinethetic therapy programme (PROMPT) to suggest a significant change in performance level post-intervention. Weekly speech probes containing trained and untrained words were administered individually to each participant. The speech probes were used to analyse motor-speech movement pattern (MSMP) and perceptual accuracy (PA). Data on MSMP showed that between phases A1-B and B-C 6/6 and 4/6 children, respectively, recorded a significant increase; 5 participants achieved a significant increase at phase A2 (12 weeks follow-up) as compared to phase A1. Data on PA showed that between phases A1-B and B-C 4/6 and 1/6 children, respectively, recorded a significant change in performance; all participants achieved a significant increase at phase A2 as compared to phase A1.

There is very low quality evidence from 1 multiple baseline single-subject design study (Fox 2012) with 5 children with spastic cerebral palsy and dysarthria that showed that changes in acoustic measures of vocal functioning after LSVT LOUD treatment were not consistent across participants. Although an improved perception of vocal loudness immediately after treatment was reported by parents, maintenance of such changes at 6-week follow-up varied across participants.

There is very low quality evidence from 1 study (Pennington 2013) with 15 children with cerebral palsy and dysarthria that showed that children's mean speech intelligibility (both single words and connected speech) improved post-treatment when rated by both familiar listeners and unfamiliar listeners.

15.4.2 Pre-intentional, non-verbal communication

There is very low quality evidence from 1 single case study (Richman 1977) to suggest an increase in pre-intentional communication in 9 year old child with severe cognitive

impairment who received intervention aimed to increase her amount of eye contact, time she kept her head in upright position, and her imitative vocalisations. Wide variation was observed at baseline in each of the 3 behaviours. Increases were observed during the intervention phase. Behaviours reduced during the reversal phase, and increased again once the treatment was recommenced. Increased scores were also observed at 12 month follow up.

15.4.37 Expressive language

There is very low quality evidence from 1 single case study (Campbell 1982) to suggest an improvement in expressive language in 1 child aged 10 years with CP and moderate language delay who received intervention aimed to teach the use of “is/are” in 3 linguistic structures: ‘wh’ questions (what, why, who, where, etc.), ‘yes/no’ reversal questions and statements). Training criterion was established at 80% correct in each of 2 consecutive 5-session blocks for’ is/are’ use in each of the syntactic structures. At baseline measurement, “is/are” were produced correctly in 0-10% of ‘wh’ questions, 0-10% of yes/no reversal questions and 0-35% of statements. During intervention, the percentage of correct productions rose steeply for all 3 targeted structures. However, the number of training sessions required to reach criterion performance on ‘is/are’ use for a given syntactic structure varied: the child required 70 sessions to reach criterion on ‘wh’ questions and 45 session on the ‘yes/no’ reversal questions. Because the participant transferred to a different school system prior to the completion of training, is/are use in statements was not trained. Level showed considerable variations during the maintenance phase. Generalisation to use in spontaneous speech showed increases from baseline for ‘yes/no’ questions, but much lower levels than observed with intervention.

15.4.44 Expressive communication (Augmentative and Alternative Communication)

There is very low quality evidence from 5 single case studies that focused on the production of nonverbal messages, teaching children to use individual communication functions.

One study (Hunt 1986) observed one 7 year old child with severe intellectual impairment and multiple disabilities who communicated via vocalisation, 1 gesture, 2 manual signs, and by touching the listener. The child was taught to request 4 objects or events by eye pointing to line drawings symbolising the object or action. Baseline measurements of interactions were stable, showing infrequent use of any of the requests. The first request showed a steady increase and reached criterion (3 successive correctly produced requests) in 16 sessions; the second request was produced without direct teaching; the third request also increased steadily during the intervention phase and reached criterion in 13 sessions; the final request also generalised without direct teaching.

One study (Pinder 1995) observed 4 children with cerebral palsy who were taught to request either an object or ‘more’ by looking at the adult and the object, the untaught request acted as a control. Baseline measurements were stable for 3 of the children with requests made to less than 20% of probes. For all children, increases in the production of both taught and untaught requests were observed during intervention across both treatment and generalisation situations. Levels of requests were maintained for 4 weeks after therapy had been withdrawn.

One study (Sigafoos 1995) observed a 6 year old child with severe cerebral palsy of unspecified type, who had moderate cognitive impairment and required assistance for all activities of daily living, and who was taught to use 3 requests for objects by using micro-teaching strategies. Baseline percentages of correct production of the 3 requests (not separated) ranged from 0% to 35%. For the first request, correct production increased from 35% to 60% with verbal prompting and to 80% to 100% when expectant delay was used and verbal prompts were faded. Although requests increased from the first to the second phase of intervention, they showed a downward trend in the latter part of the second phase. The

other target requests (tested after intervention for the first one) were correct for 65% and 30% of 17 trials.

One study (Davis 1998) observed a child aged 15 years who communicated using vocalisation, gesture and word phrases via alternative and augmentative communication (AAC), who was taught to produce conversational responses to statements made by 3 communication partners. The participant communicated by yes/no responses only but had access to a voice output communication device with pre-stored phrases and spelling for novel words. At baseline, responses to statements were rare, being produced following 0% to 20% of statements by each of the 3 partners in communication (means = 1.8%; 2.5%; 4.0%). During the intervention phase the percentage of responses immediately increased, following an average of 41.7% and 52% of statements by the first 2 partners. However, considerable variation was observed in the frequency of responses during intervention, ranging from 0% to 60% and from 20% to 80% with each partner. As intervention with the third partner was not carried out due to child's family moving away from area where research was conducted, it remained at baseline level and used as control.

Finally, 1 study (Hurlburt 1982) observed 3 children with severe cerebral palsy and cognitive impairments who were trained to use Bliss and iconic symbols to name objects. The proportions of Blissymbols and iconic symbols used to label taught and untaught items was calculated before and throughout training. Results showed that the children required approximately 4 times as many trials to acquire Bliss symbols as iconic pictures. All children also produced iconic symbols more frequently than Blissymbols in maintenance and generalisation probes, and named more untaught objects using iconic symbols than Bliss. Finally, participants almost always showed more iconic symbols responses than Bliss responses in daily spontaneous usage.

15.4.5 Receptive vocabulary

There is very low quality evidence from 1 single case study (Dada 2009) to suggest an improvement in the identification of graphic symbols in 3, 8-12 years of age children with cerebral palsy, who had fewer than 15 spoken words. During baseline, 2 children selected 2 out of the 24 items named. During the intervention, the percentage of correct identification rose steeply for all target items. During follow up, children continued to select items from the first 2 sets of vocabulary items. However, follow up was not long enough to show retention of the third set of taught words.

15.4.6 Quality of life

No evidence was retrieved for this outcome.

15.4.7 Self-confidence

There is very low quality evidence from 1 study (Pennington 2013) with 15 children with cerebral palsy and dysarthria that showed that children's communicative participation in interactions at home and school improved post-treatment, when measured by parents and teachers.

15.4.8 Family stress and coping

No evidence was retrieved for this outcome.

15.4.9 Satisfaction of patient and family with treatment

No evidence was retrieved for this outcome.

15.5 Evidence to recommendations

15.5.1 Relative value placed on the outcomes considered

The aim of this evidence review was to assess the clinical and cost effectiveness of interventions in improving speech intelligibility in children and young people with cerebral palsy. The Committee agreed that participation and speech intelligibility were to be the critical outcomes. In addition, quality of life, self-confidence, family stress and coping, and satisfaction of patient and family with the treatment were considered to be important outcomes.

15.5.2 Consideration of clinical benefits and harms

The Committee were aware that despite the fact that a wide range of different interventions were available for children and young people with speech difficulties, good quality evidence was very limited. In addition, evidence was not retrieved for the following outcomes listed in the review protocol: quality of life, self-confidence, family stress and coping, and satisfaction with the treatment.

This review focused specifically on interventions to improve speech intelligibility. Other studies, targeting a broader range of communication skills, were included as intelligible speech may not be a realistic expectation for children and young people with severe functional disability, particularly if accompanied by cognitive impairments. The available evidence suggested there may be benefit from interventions addressing aspects of communication development, such as language understanding, and expressive communication in its widest sense (including functions such as making requests and participating in conversations) using a range of non-verbal methods: eye pointing, gesture, turn-taking, and the use of augmentative and alternative communication. Interventions may also target the skills of the people around the child or young person with cerebral palsy to create an environment that supports communication.

There is wide variation in practice in the UK concerning interventions to improve speech intelligibility. Non-speech oral motor exercises, oral motor therapies and speech articulation therapies targeting specific speech sounds are in use. No evidence was identified to support the use of such interventions in cerebral palsy. Some low quality evidence was found to suggest that therapy focusing on teaching children to produce slower, louder speech may be associated with increased speech intelligibility, voice quality and clarity. There was also low quality evidence to suggest tactile-kinesthetic therapy may benefit some children. Based on this evidence, and their clinical experience, the Committee was confident in making a recommendation in this area. Other recommendations focused more broadly on the risk of speech, language and communication difficulties in children and young people with cerebral palsy, and possible need for augmentative and alternative communication.

The Committee agreed that regular assessments should be carried out in children and young people with cerebral palsy in order to identify concerns regarding speech, language and communication skills. The Committee also agreed that these assessments should be carried out by a multidisciplinary team including a speech and language therapist. This decision was derived by consensus based the Committee's clinical experience.

15.5.3 Consideration of economic benefits and harms

The Committee were unable to recommend any specific intervention because the plan would be individualised to the patient which may involve several interventions. Despite this, if there were concerns about speech, language and communication, including speech intelligibility the Committee agreed that all children with cerebral palsy should be referred to a speech and language therapist. According to NHS Reference Costs 2015 the cost per consultant led

attendance with a Speech and Language Therapist is £101 (WF01B, Non-Admitted Face to Face Attendance, First Attendance, Service Code 652).

15.5.4 Quality of evidence

One systematic review of 8 single case studies and 1 interrupted time series study was included in this evidence review. In addition, 3 pre-versus post-intervention group study and 1 study using single-subject multiple baseline design were retrieved following publication of the included systematic review. The quality of the included studies was very low. Main reasons of bias were that the study design used did not allow for generalisation of the results (randomised controlled trials [RCTs] would have been the most appropriate design for this intervention review) and many of the included studies reported low reliability scores between unblinded raters. In addition, there was a very wide range of communication aspects targeted and interventions used in the review.

15.5.5 Other considerations

In reviewing the evidence it was noted that interventions were often tailored to the communication skills profile of an individual child or small group of children. Communication skills and needs are influenced by a complex interaction of variables including type of cerebral palsy, severity of functional disability, level of cognition, the skills of conversational partners and the opportunities for communication in different environments. The role of skilled assessment in of these variables, as a precursor to choosing appropriate interventions, was recognised by the Committee in the development of the recommendations.

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

15.5.6 Key conclusions

Although the Committee recognised that there was no good quality evidence to support that speech and language therapy interventions for children with cerebral palsy, they believed that on an individual basis certain approaches might be effective for a particular child. For that reason they recommended a specialist assessment where there were concerns and access to interventions, particularly in the areas of speech intelligibility, augmentative and alternative communication, and training for families, carers and professionals in strategies to support communication. They noted that no evidence had been identified to suggest there were likely harmful effects associated with speech and language therapies for these children and young people.

15.6 Recommendations

55. Regularly assess children and young people with cerebral palsy during routine reviews to identify concerns about speech, language and communication, including speech intelligibility.

56. Refer children and young people with cerebral palsy for specialist assessment if there are concerns about speech, language and communication, including speech intelligibility.

57. Specialist assessment of the communication skills, including speech intelligibility, of children and young people with cerebral palsy should be conducted by a multidisciplinary team that includes a speech and language therapist.

58. Offer interventions to improve speech intelligibility, for example targeting posture, breath control, voice production and rate of speech, to children and young people with cerebral palsy:

- who have a motor speech disorder and some intelligible speech **and**
- for whom speech is the primary means of communication **and**
- who can engage with the intervention.

15.7 Research recommendations

None identified for this topic.

16 Improving speech, language and communication: Communication Systems

Review question: In children and young people with cerebral palsy, which communication systems (alternative or augmentative) are effective in improving communication?

16.1 Introduction

Communication involves 2 or more people working together to send and receive messages. It draws on motor, cognitive, linguistic and social skills. In children with cerebral palsy the development of language understanding is particularly influenced by intellectual disability, and expressive speech skills by motor impairment. The association between severe functional disability and motor speech disorders (dysarthria) means that some children and young people do not develop sufficient intelligible speech to meet their communication needs. This has led to the use of augmentative and alternative methods of communication (AAC), often alongside speech.

AAC systems encompass manual signing (usually simplified vocabularies derived from British Sign Language) and graphic systems such as pictures or symbols. Graphic systems can be presented in paper-based books or charts, or on computer-based speech-generating devices operated through a keyboard, touchscreen, switches or eye-gaze technology. AAC can be used to support language understanding and/or expressive skills.

Communication intervention may also be directed at the child or young person's communication partners – families, carers and school staff – focusing on strategies to support communication whether verbal, non-verbal or AAC.

There is considerable variation in clinical practice around the timing of introducing AAC systems to children and young people with cerebral palsy, the types of systems recommended, and the provision of training. There is also variable uptake of AAC by families and carers of children and young people. The Committee therefore felt it important to consider the effectiveness of communication programmes and AAC in this population.

Interventions aimed at increasing speech intelligibility have been addressed separately, although that evidence report also encompasses interventions involving communication systems.

The objective of this review was to assess what is the clinical and cost effectiveness of communication systems to improve communication.

16.2 Description of clinical evidence

Three observational studies were included in this review (Hochstein 2003, McConachie and Pennington 1997, Udwin and Yule 1990). Of these, 1 study is a longitudinal study which assessed the acquisition of 2 AAC methods: Blissymbols (graphic symbols representing words) and Makaton signs (manual signs representing words) in 2 groups of children with cerebral palsy (Udwin and Yule 1990). The results were reported at initial assessment at 10.5 months, and until the end of follow-up at 1.5 years after the initial assessment.

Another study (McConachie and Pennington 1997) focused on training methods ('My Turn to Speak' workshops), compared with no training, given to 33 teachers and assistants in order to improve the facilitation of communication amongst 9 students with cerebral palsy. Change in communication support strategies by the participants was assessed through video recordings of interactions with the target group of children and young people in naturally

occurring situations. A range of strategies that facilitated any form of communication (speech, AAC or non-verbal) were credited, including postural management, use of open questions, responsiveness to the child or young person's attempts to communicate, and repair strategies when communication was unintelligible. Results were available for follow up at 1 month and 4 months.

One case-control study (Hochstein 2003) investigated 2 speech generating devices (SGDs) and had participants below the sample size requirement stated in the protocol of 30 participants and above. The study was included as interventions using SGDs were not found for the sample sizes of 30 participants or more. However, the evidence obtained from this study should be used with caution as the very low sample size (n = 7) could be an unreliable representation of the population and the absolute effect size could not be calculated. This study investigated the error rate amongst 7 children with cerebral palsy when using Dynavox2c, a dual-level display SGD (user selects category of vocabulary and then accesses specific vocabulary represented by pictures) and Alphatalker, a single-level display SGD (all vocabulary, represented by pictures, is visible at all times). The error rates using these SGDs were tested twice. The median error rates and ranges were calculated and reported in this review (but not reported in the study). The study compares results to children without cerebral palsy which is not reported in this review.

A total of n = 56 children and young people with cerebral palsy and n = 33 teachers and assistants were included in this review.

Evidence from these is summarised in the clinical GRADE evidence profile below (Table 66, Table 67, Table 68, and Table 69). See also the study selection flow chart in Appendix F, the complete GRADE profiles in Appendix H, study evidence tables in Appendix J and exclusion list in Appendix K.

16.2.1 Summary of included studies

A summary of the studies that were included in this review are presented in Table 65.

Table 65: Summary of included studies

Study	Intervention/Comparison	Population	Outcomes	Comments
Hochstein 2003	2 SGD were used: Dynavox2c (dual-level display) and Alphatalker (single-level display)	n = 7 CP children with speech impairment between the vocabulary age equivalencies of 3.3 and 8.1 years.	Median value of error rates for both SGDs in 2 tests	
McConachie and Pennington, 1997	N = 19: 'My Turn to Speak' training (in the form of 5 workshops) aimed to improve adult facilitation of AAC user's communication N = 14: no training	CP participants: n = 9, age range: 7 – 17, all using AAC (Rebus or Bliss) Adults (teachers and assistants in schools): n = 33	Quality of facilitation of children's communication taken 1 month prior intervention (Time 1), 1 month after completion (Time 2) and 4 months after (Time 3).	At Time 2, data available for n = 19 adults in intervention and n = 10 in comparison. At Time 3, data available for n = 9 adults in intervention and n = 4 in comparison.
Udwin and Yule 1990	Bliss (Blissymbols) and Makaton signs	n = 40 children aged 3.6 – 9.8 years	At initial assessment (10.5 months) and 1.5	

Study	Intervention/Comparison	Population	Outcomes	Comments
		Bliss (Blissymbolics) group: n = 20, Makaton: n = 20)	years after initial assessment: Number of symbols and signs understood Number of symbols and signs produced	

1 *AAC augmentative and alternative communication, SGD speech generating device, CP cerebral palsy.*

16.32 Clinical evidence profile

3 The clinical evidence profiles for this review question (communication systems) are
4 presented in Table 66, Table 67, Table 68 and Table 69.

5 **Table 66: Blissymbols intervention for improving communication in cerebral palsy**

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Control	Blissymbol		
Number of symbols/signs understood Follow-up: 10.5 months	-	The mean number of symbols/signs understood in the intervention groups was 54.0 higher (47.3 to 0 higher)	20 (1 study)	very low[1,2]
Number of symbol/sign understood Follow-up: 1.5 years	-	The mean number of symbol/sign understood in the intervention groups was 113.7 higher (70.5 to 0 higher)	20 (1 study)	very low[1,2,3]
Number of symbols/signs produced Follow-up: 10.5 months	-	The mean number of symbols/signs produced in the intervention groups was 50.6 higher (42.9 to 0 higher)	20 (1 study)	very low[1,2]
Number of symbols/signs produced Follow-up: 1.5 years	-	The mean number of symbols/signs produced in the intervention groups was 109 higher (69.9 to 0 higher)	20 (1 study)	very low[2,3]

6 **The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The*
7 *corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and*
8 *the relative effect of the intervention (and its 95% confidence interval).*
9 *1 evidence was downgraded by 1 due to participants not comparable at baseline for: 'measures of physical*
10 *handicap, non-verbal IQ and language comprehension and expression'.*
11 *2 not calculable.*
12 *3 evidence was downgraded by 2 due to attrition bias - groups not comparable for availability of outcome data*

13 **Table 67: Makaton intervention for improving communication in cerebral palsy**

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants	Quality of the evidence
	Assumed	Corresponding risk		

	risk		(studies)	(GRADE)
	Control	Makaton		
Number of symbols/signs understood Follow-up: 10.5 months	-	The mean number of symbols/signs understood in the intervention groups was 34.4 (27.9) higher (0 to 0 higher)	20 (1 study)	very low[1,2]
Number of symbols/signs understood Follow-up: 1.5 years	-	The mean number of symbols/signs understood in the intervention groups was 72.1 (46.1) higher (0 to 0 higher)	14 (1 study)	very low[1,2]
Number of symbols/signs produced Follow-up: 10.5 months	-	The mean number of symbols/signs produced in the intervention groups was 28.2 (25.6) higher (0 to 0 higher)	20 (1 study)	very low[1,2]
Number of symbols/signs produced Follow-up: 1.5 years	-	The mean number of symbols/signs produced in the intervention groups was 65.1 (46.2) higher (0 to 0 higher)	14 (1 study)	very low[1,2]

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence downgraded by 1 due to participants not comparable at baseline for: 'measures of physical handicap, non-verbal IQ and language comprehension and expression'.
2 not calculable.

Table 68: 'My Turn to Speak' training vs control group

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	No training	'My Turn to Speak' training (workshops)		
Quality of facilitation of children's communication by adults (teachers and assistants) Follow-up: 1 months	-	The mean quality of facilitation of children's communication by adults (teachers and assistants) in the intervention groups was not calculable[2]	29 (1 study)	very low [3]
Quality of facilitation of children's communication by adults (teachers and assistants) Follow-up: 4 months	-	The mean quality of facilitation of children's communication by adults (teachers and assistants) in the intervention groups was not calculable[4]	13 (1 study)	very low [3,5]

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 facilitation of communication by n = 34 teachers and assistants with n = 9 students who had CP and used AAC (2 used VOCAs)

2 raw data was not available for both groups to calculate mean difference and imprecision.
3 raw data was not available for both groups to calculate mean difference. No significant difference in quality of facilitation of children's communication in participant group reported (Chi squared = 1.62, not significant).
4 evidence was downgraded by 1 due to attrition bias - loss of follow-up in comparison group and unavailability of data in intervention group.
5 raw data was not available for both groups to calculate mean difference. Significant improvement in quality of facilitation of children's communication in participant group reported but no significant difference in comparison group.

Table 69: Dynavox2c vs Alphatalker

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Alphatalker	Dynavox2c			
Error rate in test 1 among 7 CP participants1 errors ÷ number of possible correct responses	Median 0.19 (range 0.09 to 0.44)	Median 0.59 (range 0.22 to 0.78)	Not estimable[2]	7 (1 study[1])	low
Error rate in test 2 among 7 CP participants1 errors ÷ number of possible correct responses	Median 0.19 (range 0.06 to 0.38)	Median 0.50 (range 0.13 to 0.72)	Not estimable[2]	7 (1 study[1])	low

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 case-control (controls were non-CP participants, results not reported here). 7 CP participants used both Dynavox2c and Alphatalker.
2 absolute effect not calculable.

16.4 Evidence statements

16.4.1 Blissymbols and Makaton signs

16.4.1.1 Communication production

Very low quality evidence from 1 study showed that all children made progress with learning signs or symbols for communication, although there was wide variation within each group, and the vocabulary and grammatical structures used by children in both groups remained limited.

16.4.1.2 Change in communication production

No evidence was retrieved for this critical outcome.

16.4.1.3 Change in sign/symbol production

No evidence was retrieved for this outcome.

16.4.1.4 Impact on family: stress, coping

No evidence was retrieved for this outcome.

16.4.1.5 Parental satisfaction

No evidence was retrieved for this outcome.

16.4.1.6 Participation

No evidence was retrieved for this critical outcome.

16.4.1.7 Quality of life

No evidence was retrieved for this outcome.

16.4.2 'My Turn to Speak' training vs no training

16.4.2.1 Communication production

No evidence was retrieved for this outcome.

16.4.2.2 Change in communication production

Very low quality evidence from 1 study reported that teacher training improved the quality of facilitation of communication 4 months after the training among 9 children with cerebral palsy who used AAC. No change was reported for 1 month after the training.

16.4.2.3 Change in sign/symbol production

No evidence was retrieved for this outcome.

16.4.2.4 Impact on family: stress, coping

No evidence was retrieved for this outcome.

16.4.2.5 Parental satisfaction

No evidence was retrieved for this outcome.

16.4.2.6 Participation

No evidence was retrieved for this critical outcome.

16.4.2.7 Quality of life

No evidence was retrieved for this outcome.

16.4.3 Dynavox2c vs Alphatalker

16.4.3.1 Communication production

Low quality evidence from 1 study provided reported error rates produced for both Dynavox2c (a dual-level display) and Alphatalker (single-level display) was available. The median value error rate produced by 7 speech impaired CP children was higher for Dynavox compared to Alphatalker and the range of values overlapped. However, due to the small sample size (n = 7), absolute effect and imprecision could not be calculated and results should be taken with caution.

16.4.3.2 Change in communication production

No evidence was retrieved for this critical outcome.

16.4.3.3 Change in sign/symbol production

No evidence was retrieved for this outcome.

16.4.3.4 Impact on family: stress, coping

No evidence was retrieved for this outcome.

16.4.3.5 Parental satisfaction

No evidence was retrieved for this outcome.

16.4.3.6 Participation

No evidence was retrieved for this critical outcome.

16.4.3.7 Quality of life

No evidence was retrieved for this outcome.

16.5 Economic evidence

16.6 Evidence to recommendations

16.6.1 Relative value placed on the outcomes considered

The Committee agreed that participation and change in communication production were critical outcomes for this evidence review. Important outcomes for this review were: communication production, change in communication production, impact on family: stress, coping, parental satisfaction, participation, and quality of life.

16.6.2 Consideration of clinical benefits and harms

Very low quality evidence was identified from 1 study that was considered to be a proxy for change in communication production. This study reported change in the strategies used to support children's communication by teachers and classroom assistants. In addition, no evidence was identified with regard to impact on family stress, coping, parental satisfaction, participation, quality of life or how the introduction of AAC changes the functional communication skills in children or young people with cerebral palsy.

However, some evidence included in the speech intelligibility evidence review (see section 15) suggested that there may be benefit from interventions addressing aspects of communication development, such as language understanding, and expressive communication in its widest sense (including functions such as making requests and participating in conversations) using a range of non-verbal methods, including augmentative and alternative communication.

The Committee highlighted that AAC systems may have a role in children and young people with low speech intelligibility to support language understanding and to provide a means of expression. The Committee recommended referral of children and young people with cerebral palsy and difficulties in speech, language and communication for specialist assessment in such situations. Factors that impact on communication include sensory,

perceptual and motor skills, intellectual level, language understanding, social interaction abilities, and the environment. For this reason, multidisciplinary assessment would be appropriate. If, based on this assessment, it was thought the children and young people could benefit from an augmentative or alternative communication intervention then the child or young person should be referred on to a specialist AAC service to tailor intervention to the individual's need. The Committee noted that children and young people who were then using AAC systems would need to be monitored to ensure interventions continue to be appropriate for their needs.

The Committee noted that because of the range of factors influencing communication the process of selecting the most appropriate forms of AAC for an individual child or young person was complex. The level of knowledge, skill and receptiveness to AAC in the family, carers, school or other environments was a further consideration in the choice of AAC system and the design of interventions to support the development of effective communication. Collaborative goal setting, with the involvement of families, carers and schools, in this area of clinical practice requires high levels of skill and experience to manage expectations. Multidisciplinary specialist AAC services are best placed to address these complexities. The Committee did not make recommendations on the use of specific AAC interventions as the evidence presented did not allow useful comparisons of different systems. The 1 study that reported on 2 different systems (Makaton signing and Blissymbols) involved groups that differed significantly with regard to functional severity and intellectual ability. It was also noted that Blissymbols are now rarely used in the UK and that other symbols systems that are more compatible with computer based communication programmes are more likely to be used.

The Committee highlighted the importance of training in the use of various AAC interventions for the children and young people, their families, carers and team around the child. This could be a long-term commitment, particularly as children's skills, communication needs, communication partners and environments change over time as they move into adulthood. Children and young people with significant learning disabilities may not benefit from the use of formal systems, such as symbols or speech generating devices, but would require interventions aimed at families, carers and the team around the child to support communication.

It was the Committee's view that many children with cerebral palsy find communication difficult because they have little or no clear speech, resulting in social isolation. Given that research evidence in this area is largely limited to single case studies, with a focus on acquisition of skills (for example, recognising symbols or making requests), the Committee agreed that addressing the clinical and cost effectiveness of early interventions for managing communication difficulties in children with cerebral palsy should be a priority research recommendation for this guideline.

16.6.3 Consideration of economic benefits and harms

The Committee were unable to recommend any specific AAC method because any intervention would be individualised to the child or young person with cerebral palsy and could involve several methods of communication.

To prevent unnecessary referrals to specialist AAC services, the Committee agreed that an initial clinical assessment should be undertaken by a Speech and Language Therapist; and other members of the multidisciplinary team with the necessary competencies in postural management, and sensory, perceptual and cognitive assessment to decide if the benefits of AAC system justify the resources to administer them. According to NHS Reference Costs 2015 the cost per consultant led attendance with a Speech and Language Therapist is £101 (WF01B, Non-Admitted Face to Face Attendance, First Attendance, Service Code 652).

16.6.4 Quality of evidence

No randomised controlled trials (RCTs) were found which assessed AAC methods in children and young people with cerebral palsy. One RCT (Romski 2010) was identified and excluded due to its mixed population of children with other conditions and evidence for cerebral palsy alone could not be extracted from the published data. The authors were contacted for further information but further details were not received.

Very low quality evidence was available from 2 observational studies (McConachie and Pennington 1997; Udwin and Yule 1990) and included both children and young people with cerebral palsy and familiar communication partners (teachers and assistants).

No evidence was identified regarding the effectiveness of speech generating devices. Consequently a case control study (Hochstein 2003) with just 7 cerebral palsy participants (a smaller sample size than that stipulated in the protocol) was included. The median values and ranges of errors using 2 such devices were calculated and reported. However, the Committee recognised that this evidence should be treated with caution due to its low quality and sample size.

16.6.5 Other considerations

Additional evidence on the impact of AAC was retrieved as part of the evidence review for Speech Intelligibility (see section 15). Evidence was presented to the Committee, mainly from single case or small group studies, on changes in children's ability to label objects and make requests using AAC. Because of the overlap between the evidence reports for Speech Intelligibility and Communication Systems the Committee produced 1 set of recommendations focusing on communication.

The use of AAC is well established in the UK, RCTs comparing intervention and no intervention would be considered unethical. The heterogeneity of children and young people with cerebral palsy, their conversational partners and communication environments means that a broad evaluation of the effectiveness of AAC raises significant challenges. The Committee noted the lack of studies focusing on the effectiveness of interventions addressing particular aspects and stages of speech, language and communication, with an emphasis on facilitating the participation of children and families in real life situations.

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

16.6.6 Key conclusions

A range of AAC interventions is available for children and young people with limited intelligible speech. The evidence presented did not allow comparisons of different systems. Although the Committee recognised that there was very limited good quality evidence to support AAC interventions for children and young people with cerebral palsy, they believed that certain approaches can be effective for particular individuals. For that reason they recommended a specialist assessment when there are concerns with access to interventions, particularly in the areas of speech intelligibility, augmentative and alternative communication, and training for families, carers and professionals in strategies to support all forms of communication. They noted that no evidence had been identified to suggest there were likely harmful effects associated with AAC interventions for these children and young people.

16.7 Recommendations

59. Consider augmentative and alternative communication systems for children and young people with cerebral palsy who need support in the understanding and

producing speech. These may include pictures, objects, symbols and signs, and speech-generating devices.

60. If there are ongoing problems with using augmentative and alternative communication systems, refer the child or young person to a specialist service in order to tailor interventions to their individual needs, taking account of their cognitive, linguistic, motor, hearing and visual abilities.

61. Regularly review children and young people who are using augmentative and alternative communication systems, to monitor their progress and ensure that interventions continue to be appropriate for their needs.

62. Provide individualised training in communication techniques for families, carers, school staff and other people involved in the care of a child or young person with cerebral palsy.

16.8 Research recommendations

5. What is the clinical and cost effectiveness of interventions for managing communication difficulties in children with cerebral palsy?

Table 70: Research recommendation rationale

Research question	What is the clinical and cost effectiveness of interventions for managing communication difficulties in children with cerebral palsy?
Why this is needed	
Importance to 'patients' or the population	Communication is an essential life skill, recognised as a human right. Some children and young people with cerebral palsy find communication difficult because they have little or no clear speech, resulting in social isolation. Alternative and Augmentative Communication (AAC - signing, symbols, communication charts and computer-based speech generating devices) is now an established part of clinical practice but the evidence base to inform good practice is very limited.
Relevance to NICE guidance	High priority: the research is essential to inform future updates of key recommendations in the areas of communication, mental health and information and support in the guidance.
Relevance to the NHS	AAC can be an expensive intervention: speech generating devices can cost up to £6,000. Supporting communication through methods other than speech involves raising awareness of AAC and training carers, and professionals across health, social care the voluntary sector and education. This requires multidisciplinary teams, and has significant cost implications.
National priorities	The need for access to AAC equipment and training is recognised in the following:
Current evidence base	UN Convention on the Rights of Persons with Disabilities Article 21
Equality	Guidance for commissioning AAC services and equipment. NHS England/Specialised Commissioning 2016
Feasibility	Special Educational Needs Code of Practice 2014
Other comments	Research evidence in this area is largely limited to single case studies, with a focus on acquisition of skills (for example recognising symbols, or making requests). This is little evidence available to those who make service provision decisions on how the introduction and development of AAC impacts on health outcomes, patterns of social interaction, and participation.

Table 71: Research recommendation statements

Criterion	Explanation
Population	Children with cerebral palsy who have impaired verbal communication skills.
Intervention	AAC methods and carer training
Comparator	Usual care Intervention A versus intervention B
Outcome	Improved communication (e.g. change in communication production, change in sign/symbol production) Participation Impact on family: stress, coping Parental satisfaction Participation Quality of life
Study design	Multicentre randomised controlled trial
Timeframe	2-5 years

17 Managing saliva control

Review question: In children and young people with cerebral palsy, what interventions are effective in optimising saliva control?

17.1 Introduction

Problems with saliva control are considerable for children and young people with cerebral palsy. They are normally anterior - loss from the front of the mouth, but may be posterior, with pooling of the secretions at the back of the throat, leading to coughing, choking or risk of aspiration. Drooling or dribbling is the unintentional loss of saliva from the mouth. As with any form of continence, normally drooling ceases in early childhood and is abnormal from a neurodevelopmental viewpoint from around the age of 4.

Drooling is common in children with cerebral palsy due to a variety of reasons: abnormalities in swallowing, difficulties moving saliva to the back of the throat, poor mouth closure, jaw instability, tongue thrusting, lack of head control and poor posture, lack of sensation around the mouth, breathing through the mouth, excitement and impaired concentration. Some medicines commonly used in children and young people with cerebral palsy, particularly benzodiazepines, can also increase the amount of saliva production - hypersialia.

The consequences of saliva control problems are significant and have a major impact on the quality of life for both the child or young person and their families and carers. They include the risk of social rejection, damp and soiled clothing, unpleasant odour, irritated chapped skin, mouth infections, interference with speech and eating and drinking, damage to equipment such as communication aids and computers, as well as the clinical risks of dehydration, aspiration, chest infection and disorders of breathing. Successful management of drooling can alleviate the associated hygiene problems, improve appearance, enhance self-esteem and significantly reduce the stress on children or young people with cerebral palsy, their siblings, parents and carers, as well as impacting directly on health problems.

There are a variety of interventions used to try and reduce or eliminate problems with saliva control, including oral-motor therapy, medication and surgery. There is however a lack of clarity in which should be used when in the management of poor saliva control in children and young people with cerebral palsy. The Committee looked at what was the most appropriate management of drooling and pooling of secretions for children and young people with cerebral palsy.

17.2 Description of clinical evidence

Ten randomised controlled trials (Alrefai 2009; Basciani 2011; Camp-Bruno 1989; Lin 2008; Mier 2000; Parr 2016; Reid 2008; Sethy 2011; Wu 2011; Zeller 2012) and 1 historic cohort (Scheffer 2010) were included in the review.

Three studies were conducted in the USA (Camp-Bruno 1989; Mier 2000; Zeller 2012), 1 in the UK (Parr 2016), 1 in Italy (Basciani 2011), 1 in Jordan (Alrefai 2009), 2 in Taiwan (Lin 2008; Wu 2011), 1 in Australia (Reid 2008), 1 in India (Sethy 2011), and 1 in The Netherlands (Scheffer 2010).

With regards to the population considered, 5 studies included children and young people with cerebral palsy (Alrefai 2009; Basciani 2011; Lin 2008; Scheffer 2010; Sethy 2011), 4 studies considered children with cerebral palsy or other neurological diseases (Mier 2000; Parr 2016; Reid 2008; Wu 2011), and the remaining 2 studies considered children and adults with cerebral palsy or other neurological diseases (Camp-Bruno 1989; Zeller 2012). Studies considering mixed populations of participants with cerebral palsy and other non-progressive neurological diseases were reviewed for inclusion. One study included a mixed population of

50 patients, of whom 31 had cerebral palsy and 19 had unspecified neurological diseases (intellectual disability and developmental delay); since data on cerebral palsy participants has been reported separately and provided by a Cochrane review, the study has been included.

With regards to the interventions and comparators studied, 3 studies looked at participants who received botulinum versus those who received a placebo (Alrefai 2009; Lin 2008; Wu 2011); 2 studies compared participants who received botulinum with those who received no treatment (Basciani 2011; Reid 2008); 3 studies compared the use of anticholinergic drugs (either benzotropine or glycopyrrolate) with a placebo (Camp-Bruno 1989; Mier 2000; Zeller 2012); and 1 study looked at the use of behavioural therapy versus usual therapy (Sethy 2011). 1 study indirectly compared botulinum and surgery treatment by analysing improvement in drooling within each intervention group (Scheffer 2010). Finally, 1 study (Parr 2016) compared the use of transdermal hyoscine hydrobromide with glycopyrrolate.

No comparative evidence was retrieved for the following interventions: physical/postural, oro-motor and oro-sensory therapies, intra-oral appliances, and acupuncture.

Of the outcomes listed in the protocol and agreed by the Committee, all studies reported on the reduction of frequency and severity of drooling (Alrefai 2009; Basciani 2011; Camp-Bruno 1989; Lin 2008; Mier 2000; Parr 2016; Reid 2008; Sethy 2011; Wu 2011; Zeller 2012; Scheffer 2010). To assess clinical importance for this outcome, the following minimal important difference thresholds were agreed by the Committee:

- Thomas-Stonell and Greenberg scale: 2-points reduction (1 point for each section of the scale)
- Teacher Drooling scale: 3-points reduction difference
- Drooling Impact score: 10-points reduction

Six studies reported on adverse effects of botulinum or pharmacological treatment (Alrefai 2009; Basciani 2011; Camp-Bruno 1989; Mier 2000; Wu 2011; Zeller 2012).

No results were found for the following 3 outcomes:

- Health-related quality of life
- Psychological wellbeing (for example, depression or anxiety)
- Adverse effects due to surgery: ranula and chest infection

Nine studies were conducted in health-care settings (Alrefai 2009; Basciani 2011; Mier 2000; Parr 2016; Reid 2008; Scheffer 2010; Sethy 2011; Wu 2011; Zeller 2012), 1 in a school setting (Camp-Bruno 1989), and 1 study was conducted in a unspecified setting (Lin 2008).

For full details see review protocol in Appendix E. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

17.2.1 Summary of included studies

A summary of the studies that were included in this review are presented in Table 72.

Table 72: Summary of included studies

Study	Intervention/Comparison	Population	Outcomes	Comments
Alrefai 2009	botulinum/placebo	24 children with cerebral palsy	1.Reduction of frequency and severity of drooling 2.Adverse effects: - Botulinum:	

Study	Intervention/Comparison	Population	Outcomes	Comments
			swallowing problems and breathing problems.	
Basciani 2011	botulinum low or medium or high dose/no treatment	27 children with cerebral palsy	1.Reduction of frequency and severity of drooling 2.Adverse effects: - Botulinum: swallowing problems and breathing problems.	
Camp-Bruno 1989	benztropine/placebo	20 participants (19/20 had cerebral palsy)	1.Reduction of frequency and severity of drooling 2.Adverse effects: - Pharmacological treatment: visual disturbance and constipation.	
Lin 2008	botulinum/placebo	13 children with cerebral palsy	1.Reduction of frequency and severity of drooling	
Mier 2000	glycopyrrolate/placebo	39 children (25/39 had cerebral palsy)	1.Reduction of frequency and severity of drooling 2.Adverse effects: - Pharmacological treatment: visual disturbance and constipation.	
Parr 2016	hyoscine/glycopyrrolate	90 children with cerebral palsy and other non-progressive neurological diseases	1. Reduction of frequency and severity of drooling	
Reid 2008	botulinum/no treatment	50 children with neurological disorders (31/50 had cerebral palsy)	1.Reduction of frequency and severity of drooling	Data on children with cerebral palsy only was provided by authors in Cochrane review 2012.
Scheffer 2010	botulinum and	19 patients with	1. Reduction of	

Study	Intervention/Comparison	Population	Outcomes	Comments
	surgery, pre and post operation comparison	cerebral palsy	frequency and severity of drooling (Drooling quotient)	
Sethy 2011	behaviour therapy/Usual therapy	25 children with cerebral palsy	1.Reduction of frequency and severity of drooling	
Wu 2011	botulinum/placebo	20 children (19/20 had cerebral palsy)	1.Reduction of frequency and severity of drooling 2.Adverse effects: - Botulinum: swallowing problems and breathing problems.	
Zeller 2012	glycopyrrolate/placebo	38 patients (19 had cerebral palsy)	1.Reduction of frequency and severity of drooling 2.Adverse effects: - Pharmacological treatment: visual disturbance and constipation.	20 participants concluded the study, 19 of whom had cerebral palsy.

17.3 Clinical evidence profile

The clinical evidence profiles for this review question (interventions for saliva control) are presented in Table 73, Table 74, Table 75, Table 76, Table 77, Table 78.

Table 73: Botulinum versus placebo

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Placebo	Botulinum toxin		
Reduction of frequency and severity of drooling Total TSG scale at 4 weeks	-	The mean reduction of frequency and severity of drooling in the intervention groups was 1.54 higher (0 to 0 higher)	13 (1 study)	very low[1,2]
Frequency of drooling Frequency section only of TSG scale at 4 weeks	-	The mean frequency of drooling in the intervention groups was 0 higher (0 to 0 higher)	24 (1 study)	low[2,3]
Severity of drooling Severity section of	-	The mean severity of drooling in the intervention	24 (1 study)	low[2,3]

TSG scale at 4 weeks		groups was 0 higher (0 to 0 higher)		
Reduction of frequency and severity of drooling Subjective drooling scale at 4 weeks	-	The mean reduction of frequency and severity of drooling in the intervention groups was 0 higher (0 to 0 higher)	20 (1 study)	low[4]
Reduction of frequency and severity of drooling Salivary flow, mL/min at 4 weeks	-	The mean reduction of frequency and severity of drooling in the intervention groups was 0 higher (0 to 0 higher)	20 (1 study)	low[2,4]
Adverse effects: swallowing problems Reported by parents or carers	Study population		44 (2 studies)	low[4,5]
	-	-		
	Moderate			
	-	-		
Adverse effects: breathing problems - not reported	-		-	
Health-related quality of life - not reported	-	-	-	
Psychological wellbeing - not reported	-	-	-	

MD mean difference; NA not applicable; NC not calculable; NR non reported; P p-value; TSG Thomas-Stonell and Greenberg scale.

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*

1 evidence was downgraded by 2 due to selection bias: authors state 'randomly assigned' but insufficient information to permit judgement; concealment of allocation unclear. Performance bias: states 'double-blind' but the blinding of the person delivering treatment to group is unknown; Unclear if children were blinded to treatment as well. Attrition bias: no information on whether there were withdrawals from treatment, and no adverse effects were reported. Detection bias: unclear from the paper if investigators taking outcome measures are blinded to treatment allocation. It was not possible to calculate imprecision due to lack of information reported in the paper (no 95% CI and SD).

2 imprecision could not be calculated due to lack of information reported in the paper. Study has been downgraded.

3 evidence was downgraded by 1 due to selection bias: 'each patient was given a number and a registered nurse, independent from the investigator assigned the patients to the treatment or placebo group' unclear if the numbers given had a non-random component; unclear allocation concealment because of lack of information. Performance bias: low risk. Attrition bias: data on 16 people only provided although 24 received the first injection. No data provided for outcomes at 4 months. Detection bias: unclear if parents/carers taking outcome measures were blinded to allocation as well. It was not possible to calculate imprecision due to lack of information reported in the paper (no 95% CI and ranges).

4 evidence was downgraded by 1 due to selection bias: unclear as the sequence generation is unspecified as well as concealment of allocation is unspecified. Performance bias: low risk. Attrition bias: low risk. Detection bias: low risk. It was not possible to calculate imprecision due to lack of information reported in the paper (no 95% CI, means and SD).

5 evidence was downgraded by 2 due to selection bias: 'each patient was given a number and a registered nurse, independent from the investigator assigned the patients to the treatment or placebo group' unclear if the numbers given had a non-random component; unclear allocation concealment because of lack of information. Performance bias: person delivering the treatment and patients were blinded to treatment allocation. Attrition bias: data on 16 people only provided although 24 received the first injection. No data provided for outcomes at 4 months. Detection bias: unclear if parents/carers taking outcome measures were blinded to allocation as well.

Table 74: Botulinum versus no treatment

Outcomes	Illustrative comparative risks* (95%	No of	Quality of the

	CI)		Participants (studies)	evidence (GRADE)
	Assumed risk	Corresponding risk		
	No treatment	Botulinum toxin		
Reduction of frequency and severity of drooling Total TSG scale at 4 weeks - medium dose	-	The mean reduction of frequency and severity of drooling in the intervention groups was 5.143 lower (0 to 0 higher)	14 (1 study)	very low[1,2]
Reduction of frequency and severity of drooling Total TSG scale at 4 weeks - high dose	-	The mean reduction of frequency and severity of drooling in the intervention groups was 5.714 lower (0 to 0 higher)	14 (1 study)	very low[1,2]
Reduction of frequency and severity of drooling Drooling impact scale at 4 weeks	-	The mean reduction of frequency and severity of drooling in the intervention groups was 27.38 higher (17.44 to 37.31 higher)	31 (1 study)	moderate[3]
Adverse effects: swallowing problems Diary reports and communication from the parents	Study population		14 (1 study)	very low[1,2]
	-	-		
	Moderate			
	-	-		
Adverse effects: breathing problems - not reported	-	-	-	
Health-related quality of life - not reported	-	-	-	
Psychological wellbeing - not reported	-	-	-	

MD mean difference; NA not applicable; NC not calculable; NR non reported; p-value; TSG Thomas-Stonell and Greenberg scale.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence downgraded by 2 due to selection bias: concealment of allocation not reported; groups haven't been compared at baseline; Performance bias: this is a trial comparing treatment against no treatment and no information is reported on other types of care provided; the study is not blinded; Attrition bias: low dose group had 1 lost at follow-up, medium dose group had 1, control group had 1. No intention to treat analysis reported; Detection bias: the study is not blinded. It was not possible to calculate imprecision due to lack of information reported (No. of participants in each arm not reported).
2 imprecision could not be calculated due to lack of information reported in the paper. Study has been downgraded.
3 evidence was downgraded by 1 due to selection bias: low risk; Performance bias: person delivering treatment was not blinded. Also, children, carers and parents were not blinded to intervention; Attrition bias: outcome measures for baseline and 1 month post baseline for CP group only available to review authors. No outcomes available at 2-6 months and at 1 year for CP group; Detection bias: investigators taken outcomes measures were not blinded to intervention.

Table 75: Anticholinergic drug versus placebo

Outcomes	Illustrative comparative risks*	Relative	No of	Quality of

	(95% CI)		effect (95% CI)	Participants (studies)	the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Placebo	Anticholinergic drug			
Reduction of frequency and severity of drooling Total TSG scale at 8 weeks		The mean reduction of frequency and severity of drooling in the intervention groups was 4.98 lower (0 to 0 higher)	-	- (1 study)	very low[1,2]
Reduction of frequency and severity of drooling Improvement in the mTDS scale at 8 weeks		The mean reduction of frequency and severity of drooling in the intervention groups was 3.23 higher (1.89 to 4.57 higher)	-	36 (1 study)	very low[3]
Reduction of frequency and severity of drooling TDS scale at 2 weeks		The mean reduction of frequency and severity of drooling in the intervention groups was 0 higher (0 to 0 higher)	-	20 (1 study)	very low[2,4]
Health-related quality of life - not reported			-	-	
Adverse effects: constipation	Study population		RR 1.35 (0.45 to 4.03)	38 (1 study)	very low[3,7,8]
	222 per 1000	300 per 1000 (100 to 896)			
	Moderate				
Adverse effects: visual problems - not reported			-	-	
Psychological wellbeing - not reported			-	-	

MD mean difference; NA not applicable; NC not calculable; NR non reported; P p-value; TSG Thomas-Stonell and Greenberg scale; TDS Teacher Drooling scale.

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*

1 evidence was downgraded by 2 due to selection bias: authors do not specify how many participants have been randomised in each group; concealment of allocation not reported; groups haven't been compared at baseline; Performance bias: blinding of person delivering the treatment and patients receiving the treatment. However, parents reported to know when their child was receiving the intervention because of the dramatic improvement in drooling; Attrition bias: data from 12 children who commenced the study (and have been randomised) were not included in the final analysis. No outcome measures reported for those 12 children. Therefore, authors reported outcomes only on the children who completed the study; Detection bias: Not clear whether the person doing the physical examination for side effects was blind to the intervention. It was not possible to calculate imprecision due to lack of information reported (the study doesn't report No. of participants in each arm).

2 imprecision could not be calculated due to lack of information reported in the paper. Study has been downgraded.

3 evidence was downgraded by 2 due to selection bias: unclear as the sequence generation is unspecified as well as concealment of allocation is unspecified; Performance bias: the study is reported to be double-blind but it is also said that 'as patients receiving placebo would be expected to continue drooling chronically, caregivers of this group were encouraged to keep patients in the study until at least the end of 4-week titration period'; Attrition bias: safety and efficacy populations are different (2 participants not included in the efficacy analysis); Detection bias: study reported to be double-blind but lack of information on this.

4 evidence was downgraded by 2 due to selection bias: unclear risk as no information provided on the sequence generation process, nor on the allocation concealment; Performance and Detection bias: unclear risk, as the study is reported to be "double-blind" but unclear if all staff involved in taking outcome measures were blinded to intervention; Attrition bias: high risk as 7 children were eliminated from the study but no details were given regarding the point at which they were excluded. Three patients developed side effects to drug and were excluded on that basis. No data provided for these participants. . It was not possible to calculate imprecision due to lack of information reported (the study doesn't report SD).
5 population considered in the study: children with CP and other neurological disorders (study hasn't been downgraded for Indirectness).
6 study was carried out in a school setting.
7 evidence was downgraded by 1 due to serious imprecision as 95% CI crossed 1 default MID.
8 evidence was downgraded by 2 due to very serious imprecision as 95% CI crossed 2 default MID.

Table 76: Behavioural therapy versus usual care

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Usual care	Behavioural therapy		
Frequency of drooling Each drooling episode over a period of 20 minute was recorded.	-	The mean frequency of drooling in the intervention groups was 0 higher (17.99 to 13.43 lower)	25 (1 study)	Moderate[1]
Health-related quality of life - not reported	-	-	-	
Psychological wellbeing - not reported	-	-	-	-

MD mean difference; NA not applicable; NC not calculable; NR non reported; p-value; SD standard deviation.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 due to selection bias: low risk; Performance bias: patients and carers are not blind to study allocation; Attrition bias: low risk; Detection bias: low risk.

Table 77: Botulinum versus surgery

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Post	Pre		
Drooling quotient after botulinum the percentage of time a person drools and was measured by a speech and language therapist Follow-up: 8 weeks	The mean drooling quotient after botulinum in the control groups was 0	The mean drooling quotient after botulinum in the intervention groups was 11.8 higher (2.6 to 21.0 higher)	19 (1 study)	very low[1]
Drooling quotient after botulinum the percentage of time a person drools and was measured by a speech and language therapist Follow-up: 32 weeks	-	The mean drooling quotient after botulinum in the intervention groups was 7.5 higher (0.1 to 14.8 higher)	19 (1 study)	very low[1,2]
Drooling quotient after surgery	-	The mean drooling quotient after surgery in	19 (1 study)	very low[1,2]

the percentage of time a person drools and was measured by a speech and language therapist Follow-up: 8 weeks		the intervention groups was 18.0 higher (10.5 to 25.6 higher)		
Drooling quotient after surgery the percentage of time a person drools and was measured by a speech and language therapist Follow-up: 32 weeks	-	The mean drooling quotient after surgery in the intervention groups was 23.4 higher (14.2 to 32.6 higher)	19 (1 study)	very low[1,2]

MD mean difference; NA not applicable; NC not calculable; NR non reported; P p-value; SD standard deviation.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 2 due to selection bias: only children who initially underwent botulinum treatment were selected for surgical treatment; attrition bias: n=3, n=2, and n=5 observations lost at follow-up; Confounding was not reported; small sample size. In addition, the authors state that a 6 months 'at least' washout period was observed in order to avoid a carry-over effect, however with 6 months there is an overlap between the 2 interventions of 2 months (therefore a carry-over effect is possible from BoNT-A to surgery).
2 evidence was downgraded by 1 due to serious imprecision as 95% CI crossed 1 default MID.

Table 78: Transdermal hyoscine hydrobromide versus glycopyrronium

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	glycopyrrolate	Hyoscine patches			
Reduction of frequency and severity of drooling (DIS). Scale from: 0 to 100. Follow-up: 4 weeks	The mean reduction of frequency and severity of drooling in the control groups was 25.3	The mean reduction of frequency and severity of drooling in the intervention groups was 6.80 higher (1.05 lower to 14.65 higher)	-	70 (1 study)	low[1,2]
Reduction of frequency and severity of drooling DIS. Scale from: 0 to 100. Follow-up: 12 weeks		The mean reduction of frequency and severity of drooling in the intervention groups was 7.20 higher (1.36 lower to 15.76 higher)	-	71 (1 study)	low[1,2]
reduction of frequency and severity of drooling DSFS Follow-up: 4 weeks		The mean reduction of frequency and severity of drooling in the intervention groups was 0.4 higher (95% CI not calculable)	-	70 (1 study)	low[1,3]
reduction of frequency and		The mean reduction of	-	71 (1 study)	low[1,3]

severity of drooling (Copy) DSFS Follow-up: 12 weeks		frequency and severity of drooling (copy) in the intervention groups was 0 higher (95% CI not calculable)			
adverse effect - constipation	Study population		RR 0.33 (0.1301 to 0.8725)	85 (1 study)	low[1,2]
	316 per 1000	104 per 1000 (41 to 276)			
	Moderate				

MD mean difference; NA not applicable; NC not calculable; NR non reported; P p-value; SD standard deviation; DIS drooling impact scale.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 due to high risk of performance bias (participants, families, and trial clinicians not blind to treatment allocation).
2 evidence was downgraded by 1 due to serious imprecision as the 95% CI crossed 1 MID.
3 imprecision could not be calculated due to lack of information reported. Evidence downgraded by 1.

17.4 Economic evidence

No economic evaluations of interventions relevant to managing saliva control were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

This area was prioritised for de novo economic modelling; consequently, a cost-utility model was developed. The results are presented in terms of the QALY gain necessary to determine the additional (incremental) benefit that would be needed for each of the interventions to be considered as the most cost-effective option, and in terms of incremental cost-effectiveness ratios (ICER), where effectiveness is informed by hypothetical health state utilities on a 9-point drooling score. A series of scenario analyses were undertaken in order to test how sensitive the results are to uncertainty in individual parameters. The methods used to construct the model and their results are reported in Appendix G.

17.5 Evidence statements

17.5.1 Botulinum versus placebo

17.5.1.1 Reduction of frequency and severity of drooling

Low to very low quality evidence from 3 studies with 57 patients showed overall that botulinum injections are more effective than placebo in reducing the frequency and severity of drooling from baseline at 4 weeks follow up.

17.5.1.2 Adverse effects of botulinum: swallowing problems

Low quality evidence from 2 studies with 44 patients showed that 2 participants in the intervention group experienced swallowing problems compared to none in the control group.

17.5.1.3 Adverse effects of botulinum: breathing problems

No evidence was retrieved for this outcome.

17.5.1.4 Health-related quality of life

No evidence was retrieved for this outcome.

17.5.1.5 Psychological wellbeing

No evidence was retrieved for this outcome.

17.5.2 Botulinum versus no treatment

17.5.2.1 Reduction of frequency and severity of drooling

Moderate to very low quality evidence from 2 studies with 58 patients showed that botulinum injections are more effective than no treatment in reducing the frequency and severity of drooling from baseline at 4 weeks follow up.

17.5.2.2 Adverse effects of botulinum: swallowing problems

Low quality evidence from 1 study with 27 patients showed that 2 participants in the high dosage group experienced swallowing problems compared to none in the control group.

17.5.2.3 Adverse effects of botulinum: breathing problems

No evidence was retrieved for this outcome.

17.5.2.4 Health-related quality of life

No evidence was retrieved for this outcome.

17.5.2.5 Psychological wellbeing

No evidence was retrieved for this outcome.

17.5.3 Anticholinergic drug (glycopyrrolate or benztropine) versus placebo

17.5.3.1 Reduction of frequency and severity of drooling

Low to very low quality evidence from 3 studies with 78 patients showed that anticholinergic drugs are more effective than placebo in reducing the frequency and severity of drooling from baseline at 8 weeks follow up.

17.5.3.2 Adverse effects of medication: constipation

Very low quality evidence from 1 study with 38 patients showed no difference between patients who received glycopyrrolate and those who received placebo with regards to the risk of constipation.

17.5.3.3 Adverse effects of medication: visual problems

No evidence was retrieved for this outcome.

17.5.3.4 Health-related quality of life

No evidence was retrieved for this outcome.

17.5.3.5 Psychological wellbeing

No evidence was retrieved for this outcome.

17.5.4 Behavioural therapy versus usual care

17.5.4.1 Reduction of frequency and severity of drooling

Moderate evidence from 1 study with 25 patients showed no difference between patients who received behaviour therapy and those who received usual care with regards to drooling frequency and severity.

17.5.4.2 Health-related quality of life

No evidence was retrieved for this outcome.

17.5.4.3 Psychological wellbeing

No evidence was retrieved for this outcome.

17.5.5 Botulinum and Surgery (SMDR): pre- and post-comparison

17.5.5.1 Botulinum: Drooling quotient

Very low quality evidence from 1 study with 19 patients suggested an association in the reduction in drooling frequency after Botulinum injections at 8 weeks and at 32 weeks.

17.5.5.2 Surgery: Drooling quotient

Very low quality evidence from 1 study with 19 patients suggested an association in the reduction in drooling frequency after surgical treatment at 8 weeks and at 32 weeks.

17.5.5.3 Adverse effects of medication: visual problems

No evidence was retrieved for this outcome.

17.5.5.4 Health-related quality of life

No evidence was retrieved for this outcome.

17.5.5.5 Psychological wellbeing

No evidence was retrieved for this outcome.

17.5.6 Transdermal hyoscine hydrobromide versus glycopyrrolate

Low quality evidence from 1 study with 90 participants found that there is no clinically significant difference between transdermal hyoscine hydrobromide and glycopyrrolate in reducing the severity and frequency of drooling at either 4 weeks or 12 weeks follow up.

Low quality evidence from 1 study with 90 participants found that there is a clinically beneficial effect of transdermal hyoscine hydrobromide compared to glycopyrrolate for constipation (adverse effect).

17.5.6.1 Adverse effects of medication: visual problems

No evidence was retrieved for this outcome.

17.5.6.21 Health-related quality of life

No evidence was retrieved for this outcome.

17.5.6.33 Psychological wellbeing

No evidence was retrieved for this outcome.

17.65 Evidence to recommendations

17.6.16 Relative value placed on the outcomes considered

The aim of this review was to assess the clinical and cost effectiveness of treatments for optimising saliva control in children and young people with cerebral palsy. The Committee indicated the following to be the critical outcomes of this review: drooling severity and frequency, heath-related quality of life and adverse effects. In addition, psychological wellbeing (for example, depression or anxiety) was considered to an important outcome.

17.6.22 Consideration of clinical benefits and harms

The Committee was aware that despite the fact that several interventions were available for children and young people who drool, good quality evidence was limited. In addition, good quality evidence was not retrieved for the following interventions listed in the review protocol: physical/postural, oro-motor and oro-sensory therapies, intra-oral appliances, and acupuncture.

Based on the Committee's experience and by consensus, they agreed that initially conservative options should be part of saliva control management. These include optimising head position and posture to minimise pre-oral saliva loss, dabbing of the mouth rather than wiping in order to reduce stimulus and the use of non-foaming toothpaste before initiating pharmacological treatment.

The Committee noted the comparative lack of evidence on the use of transdermal hyoscine hydrobromide even though this is 1 of the most common interventions for drooling in clinical practice. During the re-run of the searches, 1 additional trial was identified which reported that transdermal hyoscine hydrobromide was of equal benefit to oral anticholinergic treatment. As they are substantially cheaper transdermal hyoscine hydrobromide was recommended by the Committee as a first line treatment. However the duration of the study was only 3 months and in practice the Committee were concerned about the proven tolerability and potential increased side effect profile of transdermal hyoscine hydrobromide over time, such as skin irritation and deterioration of seizure control. They also considered it important to highlight the importance of not cutting transdermal hyoscine hydrobromide patches as the active ingredient is maintained in a matrix between 2 membranes, and if the integrity of the patch is altered so will its effectiveness.

The evidence regarding the clinical effectiveness of anticholinergic drugs versus placebo for saliva control was discussed, and the Committee agreed that the 2 trials on glycopyrrolate were showing a meaningful clinical effect. The Committee agreed that a reduction in frequency and severity of drooling by 2 points in the Thomas-Stonell and Greenberg scale (1 point for each section of the scale) and by 3 points in the Teacher Drooling scale was considered to be a minimal important difference. The Committee also discussed how they considered that the evidence reviewed was not comprehensive in terms of the side effects profile as in their clinical experience they were aware that beyond constipation glycopyrrolate was commonly associated with visual disturbances and urinary retention. Therefore, in light of the side effects profile and because of the low quality data, the Committee agreed that glycopyrrolate should be considered if transdermal hyoscine hydrobromide is contra-indicated, not tolerated or not effective. The Committee noted 1 study using benztropine and

they decided not to mention this specifically in the recommendations as it is not used in drooling children.

The Committee noted that consideration of other interventions in saliva control should take place in a tertiary setting for specialist assessment and review.

The Committee then considered the evidence presented regarding the clinical effectiveness of Botulinum toxin and agreed that a 2-points reduction in frequency and severity of drooling in the Thomas-Stonell and Greenberg scale (1 point for each section of the scale) and a 10 points reduction in the Drooling Impact score was considered to be a minimal important difference. As the evidence showed an overall meaningful clinical effect, the Committee decided to recommend this as a second line treatment for drooling when anticholinergic drug treatment shows no effect or poor tolerance. The Committee acknowledged that the studies varied in terms of the preparations used (i.e. Botulinum toxin type A or type B) and in terms of the location of the injection. They also pointed out that there was uncertainty in terms of the duration of the effect. In line with international consensus and recommendations, a specification was added to the recommendation to ensure that health care professionals use ultrasound to guide the injection, which was also reflected in the evidence reviewed.

The Committee expressed their concern that the included evidence did not report the side effects they were aware of with the use of anticholinergic medication and botulinum toxin injections. They considered that this was because of the small sample sizes and short follow-up periods of the included RCTs. They agreed that health care professionals should regularly review any potential side effects and that dose ranges of botulinum toxin used should initially be cautious, in order to minimise theoretical risk to swallowing.

No RCTs were found on surgical treatment and comparative observational evidence on surgical treatment for saliva control was very limited and the Committee decided that there was insufficient evidence to support recommending the routine use of surgery as part of the management of drooling. However, they did discuss the role of surgery in the event of failure of efficacy or intolerance of pharmacological management or botulinum toxin injections.

The Committee acknowledged the evidence retrieved regarding behavioural therapy and agreed that it was not part of common practice in the management of drooling.

No evidence was found for the following outcomes: health-related quality of life, although it was noted that the Drooling Impact Scale, used in studies, does contain items on quality of life that contribute to the overall score), psychological wellbeing (for example, depression or anxiety), and adverse effects due to surgery.

17.6.3.4 Consideration of economic benefits and harms

It was noted during the Committee's discussion that ipratropium bromide inhalation was being increasingly used off-license for this indication as a first line treatment. The Committee also stated that this treatment was relatively cheap (BNF 71: 20micrograms/dose inhaler CFC free, 200 doses, £5.56; 500micrograms/2ml nebuliser liquid unit dose vials, 20 units, £2.88; 250micrograms/1ml nebuliser liquid unit dose vials, 20 units, £4.39) potentially dominating (less expensive and more effective) the alternatives under consideration. However, the Committee were unable to make recommendations on this treatment as it was not considered as a relevant treatment when the protocol was developed. The Committee were also unaware of any published studies for this indication in a population with children and young people with cerebral palsy, advising that the literature should be searched again for this treatment when the guideline is reviewed for an update in 4 years.

The Committee agreed that if transdermal hyoscine hydrobromide and glycopyrrolate bromide were equally effective at reducing drooling in children and young people with cerebral palsy, transdermal hyoscine hydrobromide should be recommended as a first line treatment as it is substantially cheaper. However, the Committee noted that the trials

included in the clinical evidence review were too short to demonstrate the risk of adverse events sometimes seen in clinical practice, particularly for transdermal hyoscine hydrobromide. Consequently, the Committee made a recommendation to consider glycopyrrolate bromide if transdermal hyoscine hydrobromide was not tolerated. A recommendation was also prioritised to ensure monitoring for tolerance and side effects was in place for all treatments, especially when used in children with severe communication difficulties who could not easily report adverse effects.

The Committee believed that transdermal hyoscine hydrobromide becomes less effective than glycopyrrolate bromide over time, referring to the finding by Parr 2016 that by week-12 of the study 26/47 (55%) children that started treatment continued transdermal hyoscine hydrobromide in compared with 31/38 (82%) who started on glycopyrrolate bromide. In light of this, a sensitivity analysis was conducted where the effectiveness of transdermal hyoscine hydrobromide, on a 9-point scale, was reduced from a 3 point improvement to a 2 point improvement, over a 6 month time horizon. In this scenario transdermal hyoscine hydrobromide would still be considered cost-effective with an incremental cost-effectiveness ratio (ICER) of £6,020, whilst glycopyrrolate bromide is dominated by botulinum toxin type A as it is more expensive and less effective.

Glycopyrrolate bromide was also dominated by botulinum toxin type A in the base case and all other scenarios that were explored, except for a lifetime horizon (40 years) where surgery dominated the alternatives as it was the cheapest and most effective treatment.

In view of this, the Committee considered if botulinum toxin type A could be recommended as a second line treatment, instead of glycopyrrolate bromide, if transdermal hyoscine hydrobromide were not tolerated or ineffective. The Committee agreed that glycopyrrolate bromide was an expensive ongoing pharmacological treatment, but noted that a recommendation in favour of botulinum toxin type A over glycopyrrolate bromide would lead to a large change in clinical practice. It was reiterated by the Committee that it would be unrealistic to expect the limited number of current specialists to inject botulinum toxin type A in a much larger population.

The Committee were advised that over the longer term, the investment to increase the supply of specialists to administer botulinum toxin type A could be considered cost-effective. However, the Committee strongly advised that if there were to be an investment of resources in this area, it would be extremely difficult to recruit specialists willing to undertake the procedure because of the potential detrimental effects on the nervous system if the wrong site is injected. As a result, the Committee concluded that it would be unrealistic to increase the supply of specialists to cope with the increase in demand as those specialists would conclude that the benefits would only outweigh the risks in severe drooling cases i.e. those cases when botulinum toxin type A currently displaces glycopyrrolate. The Committee also stated that the evidence on those risks was not provided by the literature, but has been seen during their clinical experience.

The Committee also highlighted that the cost of glycopyrrolate is expected to fall substantially by the end of the year due to the anticipated licensing in Europe. As a result, the cost-effectiveness of glycopyrrolate relative to hyoscine hydrobromide may increase in the near future, potentially reducing the cost-saving opportunities to recommend botulinum toxin type A ahead of glycopyrrolate the model has inferred.

The Committee agreed that the cost of surgery is soon overtaken by pharmacological treatments that require ongoing administration. As a result, the Committee made a recommendation to consider surgery if lifetime pharmacological treatment is anticipated, given that if surgery is less expensive and more effective, surgery will dominate the alternatives. However, the Committee advised that surgery should not be performed in children under the age of 14 as this increases the chance of a repeat procedure. The Committee also noted that surgery is contraindicated in many children and young people in cerebral palsy who require lifetime treatment, but agreed a recommendation should be

prioritised as this could lead to a substantial cost saving if health care professionals are reluctant to consider surgery when ongoing pharmacological treatment is effective.

The Committee was unable to say if the disutility value applied in the model to increasing scores was reasonable and agreed that a research recommendation should be considered to reduce this uncertainty. However, the Committee agreed that the ordering of treatments would not change, but their cost-effectiveness relative to the NICE threshold may. Given that the Committee were able to apply their clinical experience to infer if the "QALY gain necessary" was achievable, the Committee agreed not to prioritise this as a research recommendation, as this data would be unlikely to change their recommendations.

17.6.4 Quality of evidence

Nine randomised controlled trials and 1 historic cohort were included in the review. The quality of the evidence for this review ranged from very low to moderate. Main reasons of bias were: lack of information on the randomisation method used, concealment of allocation unreported or unclear, lack of blinding of investigators, difficulty assessing the imprecision of the estimates due to lack of information reported (95% CI, standard deviations, exact p-values) and the limited follow-up periods.

17.6.5 Other considerations

The Committee pointed out that many young people with cerebral palsy felt that the problems with drooling also translated into social isolation during adult life. This is 1 area which the Committee considered was particularly neglected in adult care provision.

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

17.6.6 Key conclusions

The Committee concluded other factors like routine assessment of posture and head positioning need to be considered before initiating pharmacological treatment to drooling.

17.7 Recommendations

63. Assess factors that may affect drooling in children and young people with cerebral palsy, such as positioning, medication history, reflux and dental issues, before starting drug therapy.

64. To reduce the severity and frequency of drooling in children and young people with cerebral palsy, consider transdermal hyoscine hydrobromide. [i]

65. If transdermal hyoscine hydrobromide is contraindicated, not tolerated or not effective, consider:

- glycopyrrolate[j] (oral or by enteral tube) **or**

[i] At the time of consultation (August 2016), transdermal hyoscine hydrobromide (scopolamine hydrobromide) did not have a UK marketing authorisation for use in children and young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[j] At the time of consultation (August 2016), glycopyrrolate did not have a UK marketing authorisation for use in children and young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

- other anticholinergic drugs, such as trihexyphenidyl hydrochloride[k] for children with dyskinetic cerebral palsy, but only with input from specialist services.

66. Regularly review the effectiveness, tolerability and side effects of all drug treatments used for saliva control.

67. Refer the child or young person to a specialist service if the anticholinergic drug treatments outlined in recommendations 65 and 66 are contraindicated, not tolerated or not effective, to consider other treatments for saliva control.

68. Consider specialist assessment and use of botulinum toxin A injections[l] to the salivary glands with ultrasound guidance to reduce the severity and frequency of drooling if anticholinergic drugs provide insufficient benefit or are not tolerated.

69. Advise children and young people and their parents or carers that high-dose botulinum toxin A injection[l] to the salivary glands can rarely cause swallowing difficulties, and so they should return to hospital immediately if breathing or swallowing difficulties occur.

70. Consider referring young people for a surgical opinion, after an assessment confirming clinically safe swallow, if there is:

- a potential need for lifelong drug treatment or
- insufficient benefit or non-tolerance of anticholinergic drugs and botulinum toxin A injections[l].

17.8 Research recommendations

None identified for this topic.

[k] At the time of consultation (August 2016), trihexyphenidyl hydrochloride did not have a UK marketing authorisation for use in children and young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[l] At the time of consultation (August 2016), some botulinum toxin A products had a UK marketing authorisation for use in the treatment of focal spasticity in children, young people and adults, including the treatment of dynamic equinus foot deformity due to spasticity in ambulant paediatric cerebral palsy patients, 2 years of age or older. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

18 Risk factors for low bone mineral density

Review question: In children and young people with cerebral palsy, what are the risk factors for reduced bone mineral density and low-impact fractures?

18.1 Introduction

It is well recognised that children and young people with cerebral palsy have a variety of potential risk factors for compromised bone health, including suboptimal dietary intake, reduced sun exposure, lower levels of exercise, prolonged use of anticonvulsants and, at higher levels of disability, reduced weight bearing.

They are also known to have an associated risk of low impact fractures, particularly of the lower limbs, which in turn has a significant impact on quality of life for the young person and their families and carers.

The Committee considered it was important to identify which cerebral palsy subgroups were at greatest risk with a view to inform the need for more frequent assessment and early intervention.

The Committee prioritised the following risk factors:

- Gross motor function classification system (GMFCS) group
- Type of cerebral palsy (spasticity/dyskinetic)
- Anticonvulsant therapy
- Nutritional inadequacy
  - Low Vitamin D status
  - Low weight for age, low weight/height or low body mass index (BMI) SD scores
- History of metabolic bone disease of pre-mature birth

The aim of this evidence review is to identify who is at most risk of reduced bone mineral density and low-impact fractures in children and young people with cerebral palsy with a view to inform the need for more frequent assessment and early intervention.

18.2 Description of clinical evidence

Seven observational studies have been identified for this review (Coppola 2012; Chen 2010; Esen 2011; Finbraten 2015; Henderson 1995; Henderson 2004; Kilpinen-Loisa 2009).

Sample sizes ranged from 51 to 113 participants with cerebral palsy, with 1 study considering a mixed population of 59 children and young people with severe cerebral palsy, myelomeningocele, muscular dystrophy, or various syndromes causing motor disability (Kilpinen-Loisa 2009).

With regards to the features studied as possible risk factors for reduced bone mineral density (BMD) and/or low-impact fractures, functional disability reported as GMFCS levels was the most studied (Chen 2010; Esen 2011; Finbraten 2015; Henderson 2004; Kilpinen-Loisa 2009), followed by use of anticonvulsants (Coppola 2012; Esen 2011; Henderson 2004); vitamin D status was reported by 1 study (Esen 2011) while another study reported on previous fractures and feeding difficulty (Henderson 2004). No evidence was retrieved for the following risk factors: type of cerebral palsy, and history of metabolic bone disease of pre-mature birth.

Only 1 study was retrieved that reported on factors associated with low impact fractures in children and young people with cerebral palsy (Kilpinen-Loisa 2009).

The studies used different statistical methods (stepwise linear regression, multivariate analysis), and results were reported as adjusted BMD z-scores.

Outcomes are reported as described in the original papers, so reflect the variation in reporting. Only studies presenting adjusted analyses have been considered for this review.

Studies were heterogeneous with regards to population and subgroups considered, risk factors studied, covariates included in the multivariate models, and statistical methods used. For these reasons, it was decided not to pool the data.

For this evidence review, the quality appraisal of the evidence has been conducted using the NICE manual methodology checklist for prognostic studies. Quality appraisal has been conducted by study, and not by outcome. For full details see 'quality of evidence' section.

Full review protocol is in Appendix E. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

18.2.13 Summary of included studies

A summary of the studies that were included in this review are presented in Table 79.

Table 79: Summary of included studies

Study	Sample and population studied	Risk factor studied	Result	Adjustment	Quality of the study
Coppola 2012	113 patients (63 males and 50 females), mixed: cerebral palsy, mental retardation, epilepsy.	BMI Epilepsy	BMD z-scores, estimate (SE): **BMI** = 0.06 (0.02), p 0.002	Sex, age, puberty, walking, mental retardation, cerebral palsy Adjusted R^2 = 0.4068	Moderate
			BMD z-scores, estimate (SE): **Epilepsy** = -0.39 (0.20), p 0.052		
Chen 2010	56 children with spastic CP aged 4 to 12 years.	GMFCS levels	BMAD (g/cm2), coefficient, adjusted r^2 and p-value: **Femur** = 0.01, r2 = 0.56, p<0.001	Body weight (kg)	Moderate
Esen 2011	102 children with CP aged 3.2 to 17.8 years.	GMFCS levels Anticonvulsants (yes/no) Vitamin D status (deficient or insufficient/normal)	BMAD z-scores, mean ±SD: Vitamin D status deficient or insufficient (25-OH-D <20ng/ml) = -1.79 ±1.59, p<0.01 - Normal (25-OH-D >20ng/ml)= -0.85 ±1.00, p<0.01	Height-for-age	Moderate
			BMAD z-scores, mean ±SD: **Anticonvulsants** Yes = -1.57 ±1.51, p>0.05 No = -1.77 ±1.60, p>0.05		

Study	Sample and population studied	Risk factor studied	Result	Adjustment	Quality of the study
			BMAD z-scores, mean ±SD: **Vitamin D status** - Deficient or insufficient = -1.79 ±1.59, p<0.01 - Normal = -0.85 ±1.00, p<0.01		
Finbraten 2015	51 children with CP, aged 8-18 years.	GMFCS level: walkers (level I-III) versus non-walkers (level IV-V)	OR (95% CI) for low BMD for age = 5.7 (1.5 to 22.1) in children unable to walk, using walkers as reference.	Age	Moderate
Henderson 1995	139 children with spastic CP of age ranging 3 to 15 years.	Mobility level (normal ambulators, community ambulators, household ambulators, non-ambulators)	BMD z-scores, p value and cumulative r^2: Mobility level - Proximal parts of femora = 0.0001, r^2 0.43 - Lumbar spine = 0.0001, r^2 0.30	Age, nutritional score, involvement, calcium intake	Low
Henderson 2004	107 participants with moderate to severe spastic CP, of age ranging 2 years 1 month to 21 years 1 month.	GMFCS level Feeding difficulty Previous fracture Use of anticonvulsants *All of the above analysed separately and together in the same model.* *Caregivers reported difficulty feeding children due to oromotor dysfunction, on a categorical scale developed for this population (Fung et al. 2002). The scale is based on the following categories: the child has no*	BMD z-scores **GMFCS** Lev III = ref Lev IV = -0.91 Lev V = -1.62 P<0.0001 and r2 = 0.46 **Feeding difficulty** None = ref Moderate or severe = -1.20 P<0.0001, r2 = 0.48 **Previous fracture** None = ref Yes = -0.70 P<0.0001, r2 = 0.36 **Anticonvulsants** None = ref Yes = -0.79 P<0.0001, r2 = 0.39 **All 4 risk factors, ordered by best predictors:** GMFCS levels = -0.86 (lev V) to -0.71 (lev IV)	Age and weight	High

Study	Sample and population studied	Risk factor studied	Result	Adjustment	Quality of the study
		problem with a regular diet (none); the child has slight difficulty swallowing or feeding and requires some modification of foods (mild); the child has moderate feeding difficulties, some difficulty swallowing liquids, and requires moistened, mashed, or chopped foods (moderate); or the child has a diet limited to well-moistened solid foods, thickened fluids, and/or is tube fed (severe).	Feeding difficulty = -0.81 Previous fracture = -0.53 Anticonvulsants = -0.31		
Kilpinen-Loisa 2009	Mixed population of 59 children aged from 5 to 16 years.	BMAD GMFCS IV-V	Fractures, OR (95% CI) and p value **BMAD < -1.5** = 9.82 (0.82-7.58x10^{52}), p 0.026 **GMFCS IV-V** = 0.85 (2.87x10^{-25} – 4.09x10^{16}), p 0.86	Age, gender, calcium intake, hypercalciuria	Low

CP cerebral palsy, BMD bone mineral density, BMAD bone mineral apparent density, GMFCS gross motor function classification system, OR odds ratio, BMI body mass index.

18.3 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

18.4 Evidence statements

18.4.1 GMFCS group

High to moderate quality evidence from 3 studies with 163 participants showed that GMFCS levels acted as predictors included in the model and explained 55%-56% of the variability in BMD in children and young people with cerebral palsy, with the most affected groups (levels IV-V) being 5.7 times more likely to have lower BMD compared to less affected children (levels I-III).

One low quality study with 139 children and young people with cerebral palsy showed that mobility level (defined as normal ambulators, community ambulators, household ambulators, and non-ambulators) explained 30% to 43% of the variability in BMD z-scores, with non-ambulators children being the most affected.

One moderate quality study with 102 children and young people with cerebral palsy showed a significant association between GMFCS levels and BMD z-scores. However, 1 low quality study with a mixed population of 59 children found no significant association between GMFCS levels IV-V and fractures.

18.4.2 Type of cerebral palsy (spasticity/dyskinetic)

No evidence was retrieved for this risk factor.

18.4.3 Anticonvulsant therapy

High to moderate quality evidence from 2 studies with 220 participants showed that epilepsy and the use of anticonvulsants is significantly associated with lower BMD z-scores.

18.4.4 Nutritional inadequacy

Moderate to high quality evidence from 2 studies with 209 children and young people with cerebral palsy showed that deficient vitamin D status, and feeding difficulty are significantly associated with reduced BMD z-scores, and that feeding difficulty as a predictor included in the model explained up to 48% of the variability in BMD.

18.4.5 History of metabolic bone disease of pre-mature birth

No evidence was retrieved for this risk factor.

18.5 Evidence to recommendations

18.5.1 Relative value placed on the outcomes considered

The aim of this review was to identify who is at most risk of reduced bone mineral density and low-impact fractures in children and young people with cerebral palsy with a view to inform the need for more frequent assessment and early intervention.

The Committee prioritised the following risk factors that were most commonly seen in clinical practice: GMFCS group; type of cerebral palsy (spastic/dyskinetic); anticonvulsant therapy; Nutritional inadequacy (deficient Vitamin D status , presence of feeding difficulties, low weight for age, low weight/height or low BMI SD scores) and history of metabolic bone disease of pre-mature birth.

18.5.21 Consideration of clinical benefits and harms

The Committee agreed that children and young people with cerebral palsy are potentially more likely to have low bone mineral density than children and young people without cerebral palsy and that this should be recognised by health care professionals in the first place.

The Committee recognised that there was some evidence for an association between a reduction in bone mineral density and:

- GMFCS level IV or V, (i.e. non ambulant) children and young people with cerebral palsy
- Vitamin D deficiency Presence of eating, drinking, swallowing diffculties and nutritional difficulties
- History of previous low impact fracture
- Use of concomitant anticonvulsant medication
- Low weight for age (below 2nd centile)

The Committee noted that the correlation coefficients were progressively smaller for GMFCS levels; eating, drinking, swallowing and nutritional difficulties; history of previous fracture; and use of anti-convulsant medication in 1 study. Nevertheless all of these were all independent risk factors.

The Committee noted that there was less evidence specifically regarding risk factors for low-impact fractures in children and young people with cerebral palsy, but they agreed that this might be explained by the lower incidence of fractures compared with the incidence of reduced BMD. There was low quality evidence however indicating that in children and young people with cerebral palsy, an association exists between reduced BMD and the risk of low impact fractures, and the Committee made a recommendation to this effect.

No evidence was identified regarding the association between age and fracture risk, but the Committee was well aware that children are most at risk as they become increasingly mobile, as would be expected.

The Committee also agreed by consensus that the child or young person with cerebral palsy and the team around the person (including parents and carers) need to be informed of the risk factors associated with low bone mineral density. In particular, it was discussed how the team around the patient not only has to be aware of the risk factors, but has to know what the implications are for their on-going management.

The Committee agreed by consensus and based on their clinical knowledge to reinforce the importance of monitoring children and young people with cerebral palsy for risk factors, on a regular basis, at the time of routine re-assessments (reconsidering/re-assess risk factors or measuring bone mineral density).

18.5.36 Consideration of economic benefits and harms

Knowing the risk factors of reduced BMD and low-impact fractures may lead to better prediction, identification (and thus more timely management) and possibly prevention of fractures in this population and has therefore, indirectly, potentially important resource implications. However, this is an epidemiological review question and economic analysis is not applicable.

Even so, the Committee discussed monitoring strategies based on the risk factors identified; hence there are considerations for the resources and costs these strategies may entail. To assess the risk of reduced BMD in children and young people with cerebral palsy, patients would undergo regular DEXA scans. According to NHS Reference Costs 2015 the national average unit cost of a DEXA scan is £59 (IMAGDA, RD50Z, Outpatient). Based on the risk factors identified, monitoring for low BMD should be higher for GMFCS levels 4 and 5 than

levels 1 to 3. However the Committee iterated that levels 1 to 3 should also undergo regular monitoring because they have a higher risk of low BMD compared to the general population.

The Committee also advised that vitamin D levels should be monitored if this is another risk factor for low BMD. However it was noted that this would be unnecessary if children and young people with cerebral palsy were receiving vitamin D supplementation.

The Committee acknowledged that monitoring for low BMD using a DEXA scan would not be considered cost-effective if the patient's management is not changed by the results of the procedure; however, the Committee advised that it would be difficult to accurately judge a patient's BMD prior to a DEXA scan. Following this, the Committee considered when DEXA scans should be performed and how the patient's management would change, but a recommendation was not prioritised.

18.5.4 Quality of evidence

The quality of each study was assessed using the NICE manual methodology checklists. Overall quality ranged between high and low, with main reasons for downgrading being: no appropriate statistical analysis presented, confounders accounted for, and loss to follow up. Only studies presenting adjusted analyses were included in the review, and the following covariates were indicated as the most relevant: age, gender.

18.5.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

18.5.6 Key conclusions

The Committee concluded that functional disability measured by GMFSC levels better explained the variability in BMD in children and young people with cerebral palsy, with the most affected groups being more likely to have lower BMD compared to less affected children. Other associated factors are low weight for age, the use of anticonvulsants and deficient vitamin D levels.

18.6 Recommendations

71. Recognise that in children and young people with cerebral palsy the following are independent risk factors for low bone mineral density:

- non-ambulant (GMFCS level IV or V)
- vitamin D deficiency
- presence of eating, drinking and swallowing difficulties or concerns about nutritional status
- low weight for age (below the 2nd centile).
- history of low-impact fracture
- use of anticonvulsant medication

72. Recognise that there is an increased risk of low-impact fractures in children and young people with cerebral palsy who are non-ambulant or have low bone mineral density.

73. Inform children and young people with cerebral palsy and their parents or carers if they are at an increased risk of low-impact fractures.

18.7 Research recommendations

None identified for this topic.

19 Prevention of reduced bone mineral density

Review question: In children and young people with cerebral palsy, what interventions are effective in preventing reduced bone mineral density and low-impact fractures?

19.1 Introduction

A diverse range of disorders, such as inflammatory bowel disease and muscular dystrophy are known to be associated with a risk of reduced bone mineral density (BMD). This is also true of cerebral palsy. Reduced bone mineral density can predispose to a risk of fracture, and particularly to the occurrence of low-impact fractures.

Children with cerebral palsy have reduced bone mineralization for a variety of reasons. This reduction in comparison to age related populations increases with age. After about 20 years of age increase in BMD is unusual and those who enter adult life with a low BMD may suffer further reduction later in life as a normal process of aging. In addition to the increased risk of fractures in children and young people therefore there may be an even greater risk in later life.

Strategies to enhance bone development and avoid loss of BMD in early life are therefore vital as well as those aimed at improving BMD in children and young people with proven Osteopaenia or Osteoporosis. The treatment of those with markedly reduced BMD associated with fractures is an area requiring specialist expertise.

This guideline aimed to consider the evidence on preventing reduced BMD and in particular make recommendations on identifying those children and young people with cerebral palsy who may be at especially high risk of reduced BMD. It also covers strategies that may be effective in preventing reduced BMD and low impact fractures and on the indications for referral for specialist advice.

The Committee was aware of significant variation in clinical practice in the UK. A variety of interventions were sometimes offered, including calcium and vitamin D supplementation, encouragement of active exercise, the use of vibration therapy and promoting assisted standing with special equipment. Those with proven osteoporosis might be offered bisphosphonate treatment (drugs such as enteral risedronate or intravenous pamidronate) to treat the disorder.

The aim of this review was to assess the clinical and cost effectiveness of any such intervention used to prevent reduced bone mineral density and low-impact fractures in children and young people with cerebral palsy.

19.2 Description of clinical evidence

Six randomised controlled trials (Caulton 2004; Ruck 2010; Chen 2013; Chad 1999; Iwasaki 2008; Henderson 2002) and 2 prospective cohorts (Jekovec 2000; Arrowsmith 2010) were included in the review.

Two studies were conducted in Canada (Ruck 2010; Chad 1999), 1 in Australia (Arrowsmith 2010), 1 in the UK (Caulton 2004), 1 in Taiwan (Chen 2013), 1 in the US (Henderson 2002), 1 in Japan (Iwasaki 2008), and 1 in Slovenia (Jekovec 2000).

With regards to the population considered, 2 studies (Arrowsmith 2010; Henderson 2002) included children with quadriplegic cerebral palsy, 1 study included non-ambulant children with cerebral palsy (Caulton 2004), 2 studies included children with spastic cerebral palsy

(Chad 1999; Chen 2013), 1 study included children with secondary osteoporosis and cerebral palsy (Iwasaki 2008), 1 study included children with quadriplegic cerebral palsy (Jekovec 2000), and 1 study included children with cerebral palsy and GMFCS levels III-V (Ruck 2010). The overall sample size ranged between 14 and 27 participants. Studies considering mixed populations of participants with cerebral palsy and other non-progressive neurological diseases were reviewed for inclusion but none ended up being included.

With regards to the interventions and comparators studied:

- 1 RCT investigated the use of standing frame compared to no increase in the regular standing duration (Caulton 2004).
- 1 RCT investigated the use of vibration therapy in addition to the usual physiotherapy program, compared to physiotherapy alone (Ruck 2010)
- 2 RCTs investigated the use of cycling training and weight bearing (active exercise programmes) compared to maintaining general physical activity at home and usual life style habits respectively (Chen 2013; Chad 1999).
- 1 RCT investigated the supplementation of vitamin D versus the use of vitamin D + bisphosphonates (Iwasaki 2008).
- 1 RCT investigated the use of pamidronate (daily dose was 1 mg pamidronate/kg body weight) compared to placebo (Henderson 2002).
- 1 prospective cohort study investigated the use of calcium + vitamin D pre and post intervention (Jekovec 2000).
- 1 prospective cohort study investigated the use of gastrostomy tube feeding pre and post intervention (Arrowsmith 2010).

No comparative evidence was retrieved for calcium supplementation.

Of the outcomes listed in the protocol and agreed by the Committee, all studies reported on the changes in bone mineral density (BMD) and bone mineral composition (BMC) measured with DEXA scans. None of the included studies reported on the other outcomes listed in the review protocol: change in frequency of minimally traumatic fractures, patients' satisfaction/acceptability, QoL score, pain, adverse effects (bone fragility and/or gastric/oesophageal irritation/ulceration).

For full details see review protocol in Appendix E. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

19.3 Clinical evidence profile

The clinical evidence profiles for this review question (interventions to prevent reduced bone mineral density) are presented in Table 50: Table 81, Table 82, Table 83, Table 84, Table 85, Table 86, Table 87:

Table 80: Summary clinical evidence profile [standing frame compared to no increase in the regular standing duration]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Usual time on standing frame	Increased time spent on standing frame		
Change in the vertebral BMD DEXA scan (mg/cm3) Follow-up: 9	-	The mean change in the vertebral BMD in the intervention groups was 8.91 higher (2.4 to 15.41 higher)	26 (1 study)	low[1,2]

months				
Change in the proximal tibial BMD DEXA scan (mg/cm3) Follow-up: 9 months	-	The mean change in the proximal tibial BMD in the intervention groups was 0.85 lower (16.83 lower to 15.13 higher)	26 (1 study)	moderate[1]

BMD bone mineral density, DEXA dual energy X-ray absorptiometry.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 due to lack of blinding.
2 evidence was downgraded by 1 due to serious imprecision as 95%CI crossed 1 default MID

Table 81: Summary clinical evidence profile [whole-body vibration versus usual physiotherapy]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Usual physiotherapy	Whole-body vibration + usual physiotherapy		
Lumbar spine areal BMD (mg/cm3) DEXA scan Follow-up: 6 months	-	P value = 0.89	17 (1 study)	low[1,2]
Distal femur region 1 areal BMD (mg/cm3) DEXA scan Follow-up: 6 months	-	P value = 0.11	17 (1 study)	low[1,2]
Distal femur region 2 (mg/cm3) DEXA scan Follow-up: 6 months	-	P value = 0.41	17 (1 study)	low[1,2]
Distal femur region 3 areal BMD (mg/cm3) DEXA scan Follow-up: 6 months	-	P value = 0.03	17 (1 study)	low[1,2]

BMD bone mineral density, DEXA dual energy X-ray absorptiometry.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 due to high performance bias.
2 imprecision could not be calculated due to lack of information reported in the paper. Study has been downgraded by 1.

Table 82: Summary clinical evidence profile [home-based virtual cycling versus usual physical activity]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		

	Usual and general physical activity at home	Home-based virtual cycling training		
Lumbar areal BMD (g/cm3) DEXA scan Follow-up: 12 weeks	-	P value = 0.357	27 (1 study)	very low[1,2]
Femur areal BMD (g/cm3) DEXA scan Follow-up: 12 weeks	-	P value = 0.022	27 (1 study)	very low[1,2]

BMD bone mineral density, DEXA dual energy X-ray absorptiometry.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 2 due to high selection bias and high performance bias.
2 imprecision could not be calculated due to lack of information reported in the paper. Study has been downgraded.

Table 83: Summary clinical evidence profile: [physical activity program versus usual life style habits]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Usual life style habits	Physical activity program (weight bearing)		
% change in proximal femur BMC (g) DEXA scan Follow-up: 8 months	-	P value = 0.08	18 (1 study)	very low[1,2]
% change in femural neck BMC (g) DEXA scan Follow-up: 8 months	-	P value = 0.03	18 (1 study)	very low[1,2]
% change in femoral neck vBMD (g/cm3) DEXA scan Follow-up: 8 months	-	P value = 0.02	18 (1 study)	very low[1,2]

BMD bone mineral density, DEXA dual energy X-ray absorptiometry.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 2 due to high selection bias and high performance bias.
2 imprecision could not be calculated due to lack of information reported in the paper. Study has been downgraded.

Table 84: Summary clinical evidence profile: [vitamin D only versus vitamin D + bisphosphonates]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence
	Assumed risk	Corresponding risk		

				(GRADE)
	Vitamin D + bisphosphonates	Vitamin D		
BMD pre versus post treatment in Monotherapy group DEXA scans Follow-up: 6 months	-	P value = 0.03	20 (1 study)	very low[1,2]
BMD pre versus post treatment in Polytherapy group DEXA scans Follow-up: 6 months	-	P value = 0.035	20 (1 study)	very low[1,2]

BMD bone mineral density, DEXA dual energy X-ray absorptiometry.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 2 due to high selection bias and high detection bias.
2 imprecision could not be calculated due to lack of information reported in the paper. Study has been downgraded by 1.

Table 85: Summary clinical evidence profile: [calcium + vitamin D versus observation only]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Observation only	Calcium and vitamin D		
BMD in intervention group DEXA scan Follow-up: 9 months	-	P<0.001	23 (1 study)	very low[1,2]
BMD in control group DEXA scan Follow-up: 9 months	-	P value = 0.013	23 (1 study)	very low[1,2]

BMD bone mineral density, DEXA dual energy X-ray absorptiometry.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 2 due to moderate selection bias, weak study design, confounders not included in analysis, no blinding.
2 imprecision could not be calculated due to lack of information reported in the paper. Study has been downgraded by 1.

Table 86: Summary clinical evidence profile: [pamidronate versus placebo]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Placebo	Bisphosphonates		
% change in distal femur	-	The mean % change in distal femur region 1 in the	14 (1 study)	low[1,2]

region 1 DEXA scan Follow-up: 1 years		intervention groups was 80.0 higher (37.19 to 122.28 higher)		
% change in distal femur region 2 DEXA scan Follow-up: 1 years	-	The mean % change in distal femur region 2 in the intervention groups was 27.0 higher (8.93 to 45.07 higher)	14 (1 study)	low[1,2]
% change in distal femur region 3 DEXA scan Follow-up: 1 years	-	The mean % change in distal femur region 3 in the intervention groups was 12.0 higher (1.85 lower to 25.85 higher)	13 (1 study)	low[1,2]
% change in lumbar spine DEXA scan Follow-up: 1 years	-	The mean % change in lumbar spine in the intervention groups was 18.0 higher (6.57 to 29.42 higher)	14 (1 study)	low[1,2]

BMD bone mineral density, DEXA dual energy X-ray absorptiometry.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 due to high selection bias.
2 evidence was downgraded by 1 due to serious imprecision as 95%CI crossed 1 default MID

Table 87: Summary clinical evidence profile: [gastrostomy pre- and after intervention]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Control	Gastrostomy tube feeding		
BMD, DEXA scan	-	P<0.05	21 (1 study)	very low[1,2]
BMD for age, SDS DEXA scan	-	P ns	21 (1 study)	very low[1,2]
BMD for height SDS DEXA scan	-	P ns	21 (1 study)	very low[1,2]

BMD bone mineral density, DEXA dual energy X-ray absorptiometry, SDS standard deviations,
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 2 due to weak selection bias, weak study design, confounders not fully assessed in analysis, no blinding.
2 imprecision could not be calculated due to lack of information reported in the paper. Study has been downgraded by 1.

19.46 Economic evidence

No economic evaluations of interventions relevant to preventing reduced bone mineral density or low impact fractures were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

This area was prioritised for de novo economic modelling; consequently, a cost-utility model was developed that converted BMD Z-scores into a probability of fracture, where the fracture was associated with a disutility and treatment cost. A series of scenario analyses were undertaken in order to test how sensitive the results were to uncertainty in individual parameters. The methods used to construct the model and their results are reported in Appendix G.

19.5 Evidence statements

19.5.1 Standing frame

One low quality randomised controlled trial with a total of 26 participants showed that there is a clinically beneficial effect of increased time spent on the standing frame compared to no increase in the regular standing duration for vertebral bone mineral density.

One moderate quality randomised controlled trial with a total of 26 participants showed that there is no clinically significant difference between increased time spent on the standing frame compared to no increase in the regular standing duration for proximal tibial bone mineral density.

19.5.2 Vibration

One low quality randomised controlled trial with a total of 20 participants showed that there is no significant difference between whole-body vibration and usual physiotherapy for bone mineral density of the lumbar spine and distal femur.

19.5.3 Cycling program

One very low quality randomised controlled trial with a total of 27 participants showed that there is no significant difference between home-based cycling program and usual physical activity for bone mineral density of the lumbar spine; however the same study found a significant difference between the 2 groups for bone mineral density of the femur.

19.5.4 Active exercise program (weight-bearing)

One very low quality randomised controlled trial with a total of 17 participants showed that there is no significant difference between weight-bearing exercises program and usual life style for bone mineral content of the proximal femur; the same study found a significant difference between the 2 interventions for bone mineral content and bone mineral density of femoral neck.

19.5.5 Vitamin D supplementation alone and with risedronate

One very low quality randomised controlled trial with a total of 20 participants showed a significant difference in bone mineral density between pre- and post-intervention in those children who received vitamin D supplementation only; the same study found a significant difference in bone mineral density between pre- and post-intervention in those children who received vitamin D supplementation together with risedronate.

19.5.6 Calcium supplementation

No evidence was retrieved for this intervention.

19.5.7 Calcium and vitamin D supplementation

One very low quality prospective cohort with a total of 23 participants showed a significant difference in bone mineral density between pre- and post-intervention in those children who received vitamin D with calcium supplementation; the same study found a significant difference in bone mineral density between pre- and post-intervention in those children who received no supplementation (observation only).

19.5.8 Bisphosphonates

One low quality randomised controlled trial with a total of 14 participants showed that there is a clinically beneficial effect of pamidronate compared to placebo for bone mineral density in distal femur region 1, 2 and in the lumbar spine, but no clinically significant difference for bone mineral density in distal femur region 3.

19.5.9 Nutritional support

One very low quality prospective cohort study with a total of 21 participants showed a significant difference in bone mineral content between pre- and post-intervention in those children who received gastrostomy tube feeding; no significant change was found between pre- and post-intervention for age or height.

19.6 Evidence to recommendations

19.6.1 Relative value placed on the outcomes considered

The aim of this review was to assess the clinical and cost effectiveness of interventions to prevent (both primary and secondary prevention) reduced bone mineral density and low-impact fractures in cerebral palsy. The Committee indicated the following to be the critical outcomes of this evidence review:

- alteration on DEXA score (as a standard of levels of bone mineral density),
- change in frequency of minimally traumatic fractures, and
- patients' satisfaction/acceptability.

Other important outcomes listed in the review protocol were: QoL score, pain, adverse effects (for example bone fragility and gastric/oesophageal irritation/ulceration).

19.6.2 Consideration of clinical benefits and harms

The Committee considered that timely recognition of reduced bone mineral density was important if further deterioration was to be prevented and therefore the recommendations made in relation to the risk factors for low bone mineral density and low-impact fractures were closely linked. For further information on the evidence reviewed for risk factors for low bone mineral density see section 18.

The Committee noted that the most frequently reported outcome was change of DEXA scan score, and that no data was reported on pain, adverse effects, patient satisfaction, or quality of life score.

With regard to calcium and vitamin D supplementation the Committee noted that the evidence for this intervention was limited, being based on 1 small very low quality prospective cohort study. However, they noted the identification of vitamin D deficiency as an independent risk factor for reduced bone mineral density. They therefore recommended a dietary assessment to ensure that the intake of calcium and vitamin D is appropriate linked with a laboratory assessment of calcium and vitamin D status. Children and young people should then be given supplementation if appropriate. The also agreed that for children and

young people with 1 or more of the risk factors for low bone mineral density that an individualised plan should be created.

The Committee outlined some possible therapy interventions to reduce the risk of reduced bone mineral density. With regard to active exercise the Committee noted that 1 small low quality randomised controlled trial of an active exercise programme based on cycling reported improved bone mineral density in the femur, though not in the lumbar spine. Another small very low quality randomised controlled trial reported that an active weight bearing exercise programme was associated with improved bone mineral density in the femoral neck but not in the proximal femur. Despite the lack of supportive evidence based on these reported findings, and on the potential wider benefits of active exercise and the lack of adverse effects for most children and young people the Committee agreed that active movement and active weight bearing programmes be considered for those at risk of reduced bone mineral density.

Another small very low quality prospective cohort study showed evidence of improved bone mineral content associated with gastrostomy tube feeding, and the Committee recommended that where appropriate dietetic interventions be considered in those at risk of reduced bone mineral density. The Committee also advised that the risk of fracture associated with movement and handling, and adequate nutrition and weight should be considered as first line interventions when creating a tailored plan for children and young people at high-risk of reduced bone mineral density. In those at risk the Committee recommended minimising the risk of low-impact fractures associated with movement and handling.

Based on their experience, and international consensus and recommendations, the Committee agreed that the bone mineral density should be assessed using DEXA scanning under specialist advice in children and young people with cerebral palsy who have had a low-impact fracture.

The Committee noted that there was evidence of improved bone mineral density with bisphosphonate therapy but the use of these potentially toxic therapies required expertise. They recommended that children and young people with cerebral palsy with reduced bone mineral density and a history of low-impact fracture should be referred to a specialist centre for consideration of bisphosphonate therapy.

Based on the lack of good quality evidence and cost-effectiveness, the Committee recommended that vibration therapy and the use of standing frames should not be offered solely to prevent reduction in bone mineral density.

19.6.3 Consideration of economic benefits and harms

In the de novo economic model, described in Appendix G, neither vibration therapy nor standing frames would be considered cost-effective to limit reductions in BMD as their incremental cost-effectiveness ratios (ICERs) relative to “no treatment” were substantially above NICE’s advisory cost-effective threshold. This also holds when the cost of equipment is reduced by 50%. Based on these findings and their own clinical experience the Committee did not want to recommend standing frames or vibration therapy solely to limit reductions in BMD in children and young people with cerebral palsy. However they wanted to highlight that those interventions could be considered cost-effective for other purposes that are beyond the scope of this review question.

For children and young people with cerebral palsy with proven osteoporosis, pamidronate disodium would not be considered cost-effective relative to risedronate plus vitamin D. Depending on the site of BMD (lumbar spine or distal femur) chosen in the model (described in Appendix G), pamidronate disodium is either dominated by risedronate plus vitamin D (more expensive and less effective) or provides a little more benefit at a much greater cost resulting in an ICER substantially above NICE’s advisory threshold for cost-effectiveness. In light of this, the Committee agreed pamidronate disodium should not be recommended for

this indication, adding that the 2 day inpatient IV administration is painful and burdensome. However, the Committee did not specify the type of bisphosphonate specialist centres should administer in their recommendations as specialists should use their expertise to infer if the benefit of therapy outweigh the costs.

In the de novo economic model, described in Appendix G, Vitamin D and Vitamin D plus calcium were found to be cost-effective interventions compared to “no treatment” in a population at increased risk of reduced BMD. However, the risk of fracture post-treatment for vitamin D plus calcium may be overestimated in the model, as clinical effectiveness data informed by Jekovec 2000 included participants with proven osteoporosis who have the potential for greater improvements in BMD than participants without osteoporosis. Despite this potential uncertainty, the Committee agreed that children and young people with cerebral palsy at high risk of reduced BMD should be offered calcium and vitamin D supplementation if their levels are found to be inadequate.

The Committee also agreed that the cost-effectiveness of cycling in a population at increased risk of reduced BMD was highly uncertain in the model as it provided different conclusions (more expensive, and more or less effective) according to the site of BMD used to inform clinical effectiveness. However, the Committee added that active exercise, such as cycling, or active weight bearing activities may have beneficial effects beyond BMD by improving cardiovascular fitness and muscle tone which may increase mobility and the ability to perform usual activities. The Committee also added that exercise can be undertaken without supervision and if it is something children and young people with cerebral palsy choose to do and enjoy, it should be encouraged. Overall, the Committee concluded that the clinical and economic evidence combined with their clinical expertise was sufficient to provide cost-effective recommendations in favour of active exercise programmes, such as cycling, and weight bearing activities, to prevent reductions in BMD.

19.6.4 Quality of evidence

Six randomised controlled trials and 2 prospective cohorts were included in the review. The quality of the evidence for this review ranged from moderate to very low. The main sources of potential bias were: lack of information on the randomisation method used; concealment of allocation unreported or unclear; lack of blinding of investigators; and difficulty assessing the imprecision of the estimates due to lack of information reported (95% CI, standard deviations, exact p-values).

19.6.5 Other considerations

The Committee agreed that recognising signs of reduced bone mineral density is the first step for effective prevention and therefore the recommendations for the review on risk factors for low bone mineral density and low impact fractures are closely linked. The Committee were also aware of related NICE guidance in this area including Vitamin D: increasing supplement use in at-risk groups, Sunlight exposure: risks and benefits and Osteoporosis in adults. The recommendations related to this evidence review were based on the evidence and the Committee’s clinical experience.

19.6.6 Key conclusions

The Committee concluded that several interventions are reported in the literature that are used to improve reduced bone mineral density in cerebral palsy. Some low quality evidence has been found that demonstrate a clinically significant beneficial effect of bisphosphonates for bone mineral density compared to placebo.

19.7 Recommendations

74. If a child and young person with cerebral palsy has 1 or more risk factors for low bone mineral density (see recommendation 71):

- assess their dietary intake of calcium and vitamin D **and**
- consider the following laboratory investigations of calcium and vitamin D status:
  - serum calcium, phosphate and alkaline phosphatase
  - serum vitamin D
  - urinary calcium/creatinine ratio.

75. Create an individualised care plan for children and young people with cerebral palsy who have one or more risk factors for low bone mineral density (see recommendation 71).

76. Consider the following as possible interventions to reduce the risk of reduced bone mineral density and low-impact fractures:

- an active movement programme
- active weight bearing
- dietetic interventions as appropriate, including nutritional support and calcium and vitamin D supplementation
- minimising risks associated with movement and handling.

77. Consider a DEXA scan under specialist guidance for children and young people with cerebral palsy who have had low-impact fracture.

78. Refer children and young people with cerebral palsy with reduced bone density and a history of low-impact fracture to a specialist centre for consideration of bisphosphonate therapy.

79. Do not offer standing frames solely to prevent low bone mineral density in children and young people with cerebral palsy.

80. Do not offer vibration therapy solely to prevent low bone mineral density in children and young people with cerebral palsy.

19.8 Research recommendations

None identified for this topic.

20 Causes of pain, discomfort, distress, and sleep disturbance

Review question: In children and young people with cerebral palsy, what are the common causes of pain, discomfort, distress and sleep disturbance?

20.1 Introduction

It is increasingly recognised that pain and distress may be under recognised and under reported in children and young people with cerebral palsy and this could result in suboptimal management. Rates of both acute and chronic discomfort are higher than those reported in a wider peer population, especially in those with more severe involvement this has a considerable impact on quality of life and participation, both for the child and young person and their families. It can be, however, challenging to elicit underlying causes not least because of primary anatomical, behavioural and physiological problems but also because of the variety of comorbidities observed, which can cause pain directly and indirectly. A better understanding of how these factors interact is needed to inform management.

In particular, in a child or young person with challenges in communication and cognition it can be difficult to distinguish between the sensory element of pain or discomfort due to physical causes and the emotional aspect of distress. This complex interaction of the sensory and emotional aspects of pain can lead to hypersensitivity and hyperalgesia. Whilst children and young people with cerebral palsy can experience the same dental pain, dysmenorrhea, and headaches as their non-disabled peers, they also experience pain due to the condition itself, the comorbidities or from therapy or other interventions.

A range of sleep disorders have been reported including difficulty settling to sleep or staying asleep, excessive day time sleepiness, sleep breathing disorders, sleep/wake transition disorders, night sweats, sleep apnoea. Causes of sleep disturbances may be complex and may include factors related to health or the disability such as pain, epilepsy, poor nutrition, medications, or disturbed sleep-wake cycles. The child or young person may be subject to the same environmental and sleep hygiene factors as their non-disabled peers.

The aim of this review is to identify the most common underlying causes of discomfort, pain, and distress and sleep disturbance in children and young people with cerebral palsy. The review will consider sources directly arising from the condition itself (for example spasticity) as well as those caused by secondary issues.

20.2 Description of clinical evidence

Five studies were included for causes of pain, discomfort and distress (Alriksson- Schmidt 2016, Doralp and Bartlett 2010, Houlihan 2008, Parkinson 2013 and Penner 2013). These studies were from European and Canadian populations. Of these studies, 1 (Parkinson 2013) reported on the correlation between pain and emotional difficulties score (EDS). Additionally, 1 study (Houlihan 2008) was below the sample size limit of 250 participants, yet was included as relevant evidence for dental pain. No evidence was found for dysmenorrhea. Four studies were included for causes of sleep disturbance (Adiga 2014, Elsayed 2013, Newman 2006 and Romeo 2014). Of these studies, 3 (Adiga 2014, Newman 2006 and Romeo 2014) used the Sleep Disturbance Scale for Children (SDSC). Epilepsy was not reported as cause of sleep disturbance, yet 1 study (Newman 2006) reported the association between pathological sleep and epilepsy. Behavioural disorders including attention deficit hyperactivity disorder (ADHD) were not reported as a cause of sleep disturbance.

As prevalence data can be sourced from various study designs, studies have been assigned high quality and downgraded based on the limitations identified. The methodological tool validated by Munn et al. assesses critical issues of internal and external validity that must be considered when addressing validity of prevalence data. The criteria address the following issues:

- Ensuring a representative sample
- Ensuring appropriate recruitment
- Ensuring an adequate sample size
- Ensuring appropriate description and reporting of study subjects and setting
- Ensuring data coverage of the identified sample is adequate
- Ensuring the condition was measured reliably and objectively
- Ensuring appropriate statistical analysis
- Ensuring confounding factors/subgroups/differences are identified and counted for.

For full details see review protocol in Appendix E. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

20.2.16 Summary of included studies for pain, discomfort, distress and sleep disturbance

The summary of the included studies are presented in Table 88 and Table 89.

Table 88: Summary of included studies for causes of pain, discomfort and distress

Study	Country	Assessment	Population	Outcomes
Alriksson-Schmidt 2016	Sweden	General survey completed by the physiotherapist that asks whether the child has experienced pain and the location of the pain.	2777 children and young people (57% boys) with a mean age of 7 years (SD=3.6 years old)	Pain frequency by GMFCS level
Doralp and Bartlett 2010	Canada	Self-developed questionnaire.	230 children above 11 years with CP (from 343 contacted), with mean age 14.7 and 14.8 years for females (N = 104) and males (N = 126) respectively.	Overall pain prevalence and pain prevalence by GMFCS level
Houlihan 2008	United States of America	Adapted version of Pediatric Pain Questionnaire (Varni-Thompson) – parent reported using non-verbal and verbal cues.	N = 38 (of 157 recruited), 4 – 18 years	Toothache (discomforting)
Parkinson 2013	SPARCLE study: 6 European countries with 8 regional CP registers and an	Bodily Pain and Discomfort items of the Child Health Questionnaire.	N = 667. 429 (64%) reported own pain. Parent reported pain was available for 657 (99%) of children.	Total self-reported pain and parent-reported pain. Site of pain in previous week and pain due to

Study	Country	Assessment	Population	Outcomes
	additional region from Northwest Germany.		Age range: 13 – 17 years.	physiotherapy in the past year.
Penner 2013	Holland	Health Utilities Index 3 (HUI3) completed by carer. If able, children completed Wong-Baker Faces Pain Scale. A physician reported if participant experienced pain and to designate main cause of pain.	252 children, mean age 9.5 ± 4.2 years. Majority of children GMFCS level III, IV and V.	Physician reported cause of pain.

1 **Table 89: Summary of included studies for causes of sleep disturbance**

Study	Country	Assessment	Population	Outcomes
Adiga 2014	India	Sleep disturbance scale for children (SDSC) over 6 months, January – June 2013. T-score of < 70 was considered normal and o> 70 considered pathological (abnormal).	50 children, age range: 6.5 – 15 years. 84% spastic CP, 10% mixed CP, 6% dyskinetic CP.	Disorders of initiating and maintaining sleep. Sleep breathing disorders Disorders of arousal Sleep wake transition disorders Disorders of excessive somnolence Sleep hyperhydrosis
Elsayed 2013	Egypt	Paediatric day time sleepiness scale (PDSS), paediatric sleep evaluation questionnaire (PSEQ), paediatric sleep questionnaire (PSQ). Unclear which questions where obtained from which questionnaires.	100 children with CP. Pre-school group: mean age 2.4 years. 26% diplegic, 25% hypotonic, 24% hemiplegic. School group: mean age 10.2 years. 25% hemiplegic, 25% diplegic, 16.7% hypotonic, 15% quadriplegic.	Early insomnia Interrupted sleep Difficult morning awakening Sleep disordered breathing Periodic limb movement disorder/restless leg syndrome. Excessive daytime sleepiness
Newman 2006	Ireland	SDSC	173 children with CP, mean age 8 years 10 months.	Total with pathological sleep. Difficulty initiating and maintaining sleep Sleep-wake transition disorders Sleep related breathing disorders Excessive somnolence Disorders of arousal Sleep hyperhydrosis.

Study	Country	Assessment	Population	Outcomes
				Percentage with 1 or more sleep disorder.
Romeo 2014	Italy	SDSC	165 children with CP, mean age 11 years	Total with pathological sleep Disorders of initiating and maintaining sleep Sleep breathing disorders Disorders of arousal Sleep-wake transition disorders Disorders of excessive somnolence Sleep hyperhydrosis

20.2.21 Clinical evidence profile

2 The results are presented in Table 90 and Table 91.

3 **Table 90: Results of included studies for causes of pain, discomfort and distress**

Study	N	Outcomes	Notes	Study quality
Alriksson-Schmidt 2016	2777	Overall pain prevalence = 32.4% Pain prevalence by GMFCS level: • GMFCS I = 5.8% • GMFCS II: 6.3% • GMFCS III: 9.3% • GMFCS IV: 6.3% • GMFCS V: 5.9%	Pain was reported in lower extremities and in abdomen Data on the site of pain was available for n=829/900 (92.1%)	Moderate - Site of pain was not measured reliably. - 95% CI not reported for pain site.
Doralp and Bartlett 2010	230	Overall pain prevalence = 63% in females and 49% in males. Pain prevalence by GMFCS level: GMFCS I = 40.7% females, 50% males GMFCS II: 66.7% females, 58.8% males GMFCS III: 75% females, 47.1% males GMFCS IV: 66.7% females, 51.5% males GMFCS V: 82.4% females, 45.8% males	Location of pain (ankle and foot, calf, knee, lower back) was reported in figures.	Very low - 95% confidence intervals not provided -Musculoskeletal pain prevalence (for example, lower back pain) was not reported as percentage. - Condition not measured reliably: self-developed questionnaire.
Houlihan2008	38	Discomforting toothache = 28.2%	Parent reported using non-verbal and verbal cues.	Very low - 95% confidence intervals not provided - Sample below 250 participants - Incomplete data (other severities of

Study	N	Outcomes	Notes	Study quality
				toothache including mild, horrible and excruciating not report).
Parkinson 2013	667 (429 self-reported, 657 parent reported)	Total prevalence of self-reported pain = 74% (95% CI: 69% - 79%) Total prevalence parent-reported pain = 77% (95% CI: 73% - 81%) Site of pain in previous week, self-reported: Headache = 34% (associated with increased GMFCS level) Stomach = 26% Back = 27% Hips = 14% Operation sites = 10% (associated with increased GMFCS level). Pain due to therapy in the past year, self-reported: During physiotherapy = 45% During other therapy = 9% During botulinum injections = 26% Only pain during to physiotherapy associated with increased GMFCS levels. Site of pain in previous week, parent reported: Headache = 30% Stomach = 32% Back = 25% Hips = 21% Operation sites = 14% All were associated with increased GMFCS levels. Pain due to therapy in the past year, parent reported: During physiotherapy = 50% During other therapy = 18% During botulinum injections = 29% Pain during physiotherapy and other therapies associated with increased GMFCS levels.	In multivariable model, only walking ability and emotional difficulties score from Strength and Difficulties Questionnaire (SDQ) were associated with pain. Parent and self-reported pain were significantly correlated, but parents tended to overestimate their child's pain if self-reported pain was infrequent or mild and underestimate it if self-reported pain was frequent or severe.	Moderate - 95% confidence intervals not reported for site of pain and pain due to physiotherapy.
Penner 2013	252	Caregivers identified pain in 54% of children. Physicians reported pain in	- MSK deformity excludes hip dislocation/sublux	Moderate - 95% confidence intervals not

Study	N	Outcomes	Notes	Study quality
		38.7% of participants. Primary causes of pain identified by physician: Hip dislocation/subluxation = 16% Dystonia = 12% Musculoskeletal (MSK) deformity = 11% Constipation = 9% Focal muscle spasm = 9% Muscle weakness/overuse/fatigue = 9% Spasticity = 9% Abnormal gait pattern = 6% Muscle contractures = 6% Other = 6% Postoperative MSK pain from orthopaedic surgery = 4% Gastro-oesophageal reflux (GOR) = 3% Pain due to falls = 1% Physician identified pain in children experiencing severe pain (HUI levels 3 and 4) (N= 25). Hip dislocation/subluxation = 24% Dystonia = 16% MSK deformity = 12% GOR = 8% Postoperative MSK pain from orthopaedic surgery = 8% Constipation = 8% Muscle contractures = 8% Other = 8% Abnormal gait pattern = 4% Focal muscle spasms = 4%	ation and muscle contractures and include foot and hand deformity, scoliosis and lumbar lordosis. - Focal muscle spasm was identified by physician if the child reported a focal area of tenderness in 1 or 2 muscles. - 'Other' causes of pain include muscle soreness after massage therapy, seizures, headaches, knee bursitis and osteomyelitis. 28 children were identified as having severe pain (HUI level 4 and 5). Physician diagnosed pain in 25 cases and 3 were not identified as having pain. There was significant interrater agreement between physician report of pain and caregiver-reported pain. There was significant correlation between HUI3 score and GMFCS level.	reported.

1 **Table 91: Results of included studies for causes of sleep disturbance**

Study	Country	N	Outcomes	Notes	Study quality
Adiga 2014	India	50	Prevalence of children with pathological (abnormal) score in SDSC. Disorders of initiating and maintaining sleep = 50% Sleep breathing disorders = 12% Disorders of arousal = 8%	Pittsburgh sleep quality index was used sleep disorders in carers of these children with CP. These results were not extracted.	Moderate 95% confidence intervals not reported

Study	Country	N	Outcomes	Notes	Study quality
			Sleep wake transition disorders = 26% Disorders of excessive somnolence = 10% Sleep hyperhydrosis = 6%		
Elsayed 2013	Egypt	100	Early insomnia: preschool group = 46.%, school group = 25% Interrupted sleep: preschool group = 34.6%, school group = 37.5% Difficult morning awakening: preschool group = 11.5%, school group = 25% Sleep disordered breathing: preschool group = 38.6%, school group = 50% Periodic limb movement disorder/restless leg syndrome: preschool group = 42.3%, school group = 50% Excessive daytime sleepiness: preschool group = 50%, school group = 62.5%	Combination of 3 questionnaires were used and unclear which domains or questions are from which questionnaires.	Low 95% confidence intervals not reported Unclear if condition was measured reliably
Newman 2006	Ireland	173	Total with pathological sleep = 22.5% Difficulty initiating and maintaining sleep = 24.3% Sleep-wake transition disorders = 17.9% Sleep related breathing disorders = 14.5% Excessive somnolence = 11% Disorders of arousal = 8.1% Sleep hyperhydrosis = 5.8% Percentage with 1 or more sleep disorder: 1 disorder = 20.8% 2 disorders = 13.9% 3 disorders = 6.4% Between 4 and 6 disorders = 2.9%	Pathological sleep was significantly associated with presence of active epilepsy, being the child of a single parent and sleeping with parents. - Difficulty initiating and maintaining sleep was significantly associated with spastic quadriplegia, dyskinetic CP and severe visual impairment and bed sharing. - Sleep-wake transition disorders were less frequent in females and more frequent with bed sharing. - Disorders of excessive somnolence were associated with active epilepsy. - Disorders of arousal occurred	Moderate 95% confidence intervals not reported.

Study	Country	N	Outcomes	Notes	Study quality
				less in females and more in children with single parents.	
Romeo 2014	Italy	165	Total with pathological sleep = 19% Disorders of initiating and maintaining sleep = 22% Sleep breathing disorders = 14% Disorders of arousal = 10% Sleep-wake transition disorders = 15% Disorders of excessive somnolence = 13% Sleep hyperhydrosis = 7%	Sleep wake transition disorders more associated with dyskinetic CP ($p < 0.05$) and sleep hyperhidrosis ($p < 0.01$) than hemiplegia, quadriplegia or diplegia. Multivariate analysis (adjusting for IQ, active epilepsy, abnormal child behaviour checklist (CBCL) scores and GMFCS level 5. Abnormal SDCS score associated only CBCL scores, both internalising and externalising ($p < 0.01$).	Moderate 95% confidence intervals not reported.

20.3 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations on the common causes of pain, discomfort, distress or sleep were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

20.4 Evidence statements

20.4.1 Pain, discomfort and distress

20.4.1.1 Overall

One very low quality study with 230 children found that overall pain prevalence was 63% in females and 49% in males. This study also reported pain per GMFCS levels and gender, and ranged from 40.7% in females with GMFCS level I to 82.4% in females with GMFCS level V.

One moderate quality study with 429 children found that self-reported pain was 74% (95% CI: 69% - 79%). Additionally, this study found that parent reported pain from 657 parents and carers was 77% (95% CI: 73% - 81%).

One moderate quality study with 252 children reported that caregivers identified pain in 54% of children. Additionally, physicians reported pain in 38.7% of children.

20.4.1.2 Musculoskeletal

One moderate quality study with 429 children found that self-reported back pain in previous week was 27% and self-reported hip pain in previous week was 14%. Additionally, parent reported back and hip pain from 657 parents and carers in the previous week was 25% and 21% respectively. Parent reported pain was associated with increased GMFCS levels.

One moderate quality study with 252 children found that the primary cause of pain identified by a physician was hip dislocation/subluxation in 16%, dystonia in 12%, musculoskeletal deformity in 11%, focal muscle spasm in 9%, muscle weakness/overuse/fatigue in 9%, spasticity in 9%, abnormal gait pattern in 6%, muscle contractures in 6%, other muscle pain in 6% and pain due to falls in 1%. Similar findings were found for 25 children with severe pain (HUI levels 3 and 4).

One moderate quality study with 2777 participants found that parent-reported or self-reported pain was found in an overall rate of 32.4% (n=900) participants. Pain in feet was reported in 36.1% (n=325) of the participants, 21.4% (n=193) reported knee pain, 29.9% (n=263) reported pain in hips, 10.8% (n=97) reported pain in abdomen, 9.3% (n=84) reported back pain, 9% (n=81) reported pain in arms/hands and 9.2% (n=83) reported pain in head/neck. The proportion of children with pain increased with age, from 17% of children of 2 years of age to 50% of children of 14 years of age. After adjusting for age and gender, children at GMFCS levels III and V were significantly more likely to report pain than those at GMFCS level I.

20.4.1.3 Gastrointestinal

One moderate quality study with 429 children found that self-reported stomach pain was 26% and parent reported stomach pain from 657 parents and carers was 32% (associated with increased GMFCS levels).

One moderate quality study with 252 children found that the primary cause of pain identified by a physician was gastro-oesophageal reflux in 3%. 25 children had severe pain and 8% of them were identified to have constipation.

20.4.1.4 Surgical pain/discomfort

One moderate quality study with 429 children found that self-reported pain from operation sites was 10% and associated with increased GMFCS levels. Additionally, parent reported stomach pain from 657 parents and carers was 32% and associated with increased GMFCS levels.

One moderate quality study with 252 children found that the primary cause of pain identified by a physician was postoperative musculoskeletal pain from orthopaedic surgery in 4%.

20.4.1.5 Physical therapy causing pain/discomfort

One moderate quality study with 429 children found that self-reported pain in the past year during physiotherapy was 45% and was associated with increased GMFCS levels. Self-reported pain during other therapy and botulinum injections was 9% and 26% respectively. Additionally, this study found that parent reported pain in the past year from 657 parents and carers was 50% during physiotherapy, 18% during other therapy and 29% during botulinum injections. Pain during physiotherapy and other therapies were associated with increased GMFCS levels.

20.4.1.6 Dysmenorrhea

No studies were found which reported dysmenorrhea as a cause of pain, discomfort or distress.

20.4.1.7 Dental

One very low quality study with 38 children found that parent reported toothache was 28.2%.

20.4.1.8 Headache

One moderate quality study with 429 children found that self-reported pain due to headaches was 34% and associated with increased GMFCS levels. Additionally, parent reported headaches from 657 parents and carers was 30% and associated with increased GMFCS levels.

20.4.2 Sleep disturbance

20.4.2.1 Sleep disordered breathing

One moderate quality study with 50 children reported that sleep breathing disorders occurred in 12% of children.

One low quality study with 100 children reported that sleep breathing disorders occurred in 38.6% of preschool children and 50% of school children.

One moderate quality study with 173 children reported that sleep related breathing disorders occurred in 14.5% of children.

One moderate quality study with 165 children reported that sleep breathing disorders occurred in 14% of children.

20.4.2.2 Seizures

No studies included reported seizures as a cause of sleep disturbance. However, 1 moderate quality study with 173 children found that disorders of excessive somnolence were associated with active epilepsy.

20.4.2.3 Behavioural difficulties (including ADHD)

No studies included reported behavioural difficulties as a cause of sleep disturbance. However, 1 moderate quality study with 165 children found that abnormal sleep disturbance checklist score (SDCS) was associated with only with child behavioural checklist (CBCL) score.

20.4.2.4 Pain

No studies included reported pain as a cause of sleep disturbance.

20.4.2.5 Other

20.4.2.5.1 Disorders of initiating and maintaining sleep

One moderate quality study with 50 children found that disorders of initiating and maintaining sleep was 50%.

One moderate quality study with 165 children found that disorders of initiating and maintaining sleep was 22%.

One moderate quality study with 173 children found that difficulty initiating and maintaining sleep occurred in 24.3% of children.

20.4.2.5.2 Disorders of arousal

One moderate quality study with 50 children found that disorders of arousal was 8%.

One moderate quality study with 173 children found that disorders of arousal was 8.1%.

One moderate quality study with 165 children found that disorders of arousal was 10%.

20.4.2.5.3 Sleep-wake transition disorders

One moderate quality study with 50 children found that sleep-wake transition disorders occurred in 26% of children.

One moderate quality study with 173 children found that sleep-wake transition disorders occurred in 17.9% of children.

One moderate quality study with 165 children found that sleep-wake transition disorders occurred in 15% of children.

20.4.2.5.4 Disorders of excessive somnolence

One moderate quality study with 50 children found that disorders of excessive somnolence occurred in 10% of children.

One moderate quality study with 165 children found that disorders of excessive somnolence occurred in 13% of children.

20.4.2.5.5 Sleep hyperhydrosis

One moderate quality study with 50 children found that sleep hyperhydrosis occurred in 6% of children.

One moderate quality study with 173 children found that sleep hyperhydrosis occurred in 5.8% of children.

One moderate quality study with 165 children found that sleep hyperhydrosis occurred in 7% of children.

20.4.2.5.6 Excessive daytime sleepiness

One low quality study with 100 children found that excessive daytime sleepiness occurred in 50% of preschool children and 62.5% of school group children.

20.4.2.5.7 Difficult morning awakening

One low quality study with 100 children found that difficult morning awakening occurred in 11.5% of preschool children and 25% of school group children.

20.4.2.5.8 Early insomnia

One low quality study with 100 children found that early insomnia occurred in 46% of preschool children and 25% of school group children.

20.4.2.5.9 Interrupted sleep

One low quality study with 100 children found that interrupted sleep occurred in 34.6% of preschool children and 37.5% of school group children.

20.4.2.5.10 *Periodic limb movement/restless leg syndrome*

One low quality study with 100 children found that periodic limb movement/restless leg syndrome occurred in 42.3% of preschool children and 50% of school group children.

20.5 Evidence to recommendations

20.5.1 Relative value placed on the outcomes considered

The Committee prioritised the prevalence of pain, discomfort, distress and sleep disturbance for this evidence review.

20.5.2 Consideration of clinical benefits and harms

This evidence review covered the main causes of pain, distress and sleep disturbance. Although there is a complex interaction, particularly between pain and sleep disturbances, it was considered clearer to formulate separate recommendations on the causes of pain and causes of sleep disturbances.

Based on their experience and by consensus, the Committee decided to provide some context to the recommendations. The Committee explained that causes of pain that are common in the general population, including back pain, headache, non-specific abdominal pain, dental pain and dysmenorrhea, are also common in children and young people with cerebral palsy and the Committee highlighted this in their recommendations. In addition, the Committee highlighted the fact that the recognition of such conditions in this population can be difficult due to potential problems of communication, perception and recognition. Despite the lack of good quality evidence to support this, it was the unanimous view of the Committee. The Committee therefore wanted to ensure that the common causes of pain in the general population were not overlooked in children and young people with cerebral palsy.

When discussing the evidence for causes of pain, the Committee agreed that it was important to explain to parents and carers and people with cerebral palsy, as appropriate, that many children and young people with cerebral palsy experience pain and that this tends to be more common in those with severe degreed of motor impairment.

Based on the evidence presented and on their own experience, the Committee made a recommendation regarding the recognition of causes of pain that are directly related to cerebral palsy and its complications, including musculoskeletal problems, increased muscle tone, constipation, vomiting and gastro-oesophageal reflux. The Committee believed that these conditions are often under-recognised, particularly in those with difficulties of communication and impaired cognition.

Children and young people with cerebral palsy often require interventions, such as botulinum toxin injections, orthotics interventions and surgery. Such treatments may be associated, with pain or discomfort. The Committee also discussed the potential discomfort associated with certain forms of physical therapy. However, they did not make recommendation regarding these interventions as they were addressed in the NICE Guideline on Spasticity in under 19s.

Regarding the causes of sleep disturbances, the Committee noted that the evidence identified did not directly report on primary causes of sleep disturbances, but rather on the prevalence of different types of sleep disturbances. However, based on their experience, the Committee agreed that causes of sleep disturbances are common in children and young people with cerebral palsy and that those common in the general population are also found in children and young people with cerebral palsy. The Committee also agreed and recommended based on their experience that health care professionals should recognise certain condition-specific causes of sleep disturbances as being common in children and young people with cerebral palsy, including sleep-induced breathing disorders such as

obstructive sleep apnoea, seizures, pain and discomfort, the need for repositioning, poor sleep hygiene, medical interventions such as overnight tube feeding and the use of orthoses, and certain comorbidities and medication associated adverse effects.

These causes were not prioritised for the review but the Committee agreed that they clearly required consideration in clinical practice.

20.5.3 Consideration of economic benefits and harms

Knowing the common causes of pain, discomfort, distress and sleep disturbance may lead to better prediction and identification (and thus more timely management) of these problems in this population and has therefore, indirectly, potentially important resource implications. However, this is an epidemiological review question and economic analysis is not applicable.

20.5.4 Quality of evidence

The quality of the evidence has been assessed by using the tool developed and published by Munn et al. 2014. Generally, the evidence included was of moderate to very low quality, and main reasons for this were that 95% confidence intervals were not reported, incomplete data reporting, and it was often unclear whether the condition was measured reliably.

20.5.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

20.5.6 Key conclusions

The Committee concluded that prevalence for a number of causes of pain and sleep disturbances in cerebral palsy is reported in the evidence, and that this increases with severity of the motor impairment. In addition, communication difficulties and perception may make the recognition of such causes more difficult. The evidence reported the following as the most common condition-specific causes of pain: musculoskeletal problems, increased muscle tone, constipation, and gut dysmotility. With regards to the most common causes of sleep disturbances, the following were identified: sleep-induced breathing disorders, seizures, pain, poor sleep hygiene, night-time interventions, and comorbidities.

20.6 Recommendations

Pain, discomfort and distress

81. Explain that most children and young people with cerebral palsy experience pain regularly, and that the prevalence of pain increases with increasing severity of motor impairment.

82. Recognise that common causes of pain in all children and young people also affect those with cerebral palsy, and that difficulties with communication and perception may make identifying the cause more challenging. Common types of pain in children and young people include:

- non-specific back pain
- headache
- non-specific abdominal pain
- dental pain
- dysmenorrhea.

83. Recognise that the most common condition-specific causes of pain in children and young people with cerebral palsy include:

- musculoskeletal problems (for example, scoliosis, hip subluxation and dislocation)
- increased muscle tone (including dystonia and spasticity)
- constipation
- vomiting and gastro-oesophageal reflux.

Sleep disturbances

84. Explain to parents or carers that, in children and young people with cerebral palsy sleep disturbances (for example, difficulties with falling asleep and staying asleep and with daytime sleepiness):

- are common
- may be caused by factors such as environment, hunger and thirst.

85. Recognise that the most common condition-specific causes of sleep disturbances in children and young people with cerebral palsy include:

- sleep-induced breathing disorders, such as obstructive sleep apnoea
- seizures
- pain and discomfort
- need for repositioning because of immobility
- poor sleep hygiene (poor night-time routine and environment)
- night-time interventions, including overnight tube feeding or the use of orthoses
- comorbidities, including adverse effects of medication.

20.7 Research recommendations

None identified for this topic.

21 Assessment of pain, distress, discomfort and sleep disturbances

Review question: What is the validity and reliability of published tools to identify and aid the understanding of discomfort, pain and/or distress and sleep disturbances in children and young people with cerebral palsy?

21.1 Introduction

Children and young people with cerebral palsy may experience discomfort, pain and or distress at different times. It is often difficult to recognise the signs and symptoms, especially in individuals with challenges in cognition and or communication. Recognition in a valid and reliable way helps the child or young person, their families and health care professionals to ensure appropriate support, care and intervention.

There are many comprehensive verbal and non-verbal tools that are used to assist in the understanding of discomfort, pain and or distress for children and young people with cerebral palsy. It is vital that any tools used are indicative of the full spectrum of pain and distress across all levels of understanding.

The Committee considered that is was important to examine all the relevant evidence with an aim to determine the validity and reliability of commonly used tools to help recognition of discomfort, pain and distress and how they may help in our understanding of the different components of pain that would facilitate specific intervention and interdisciplinary support. A comprehensive history is essential as different approaches may be needed depending on the age, level of function, communication and cognitive ability to ensure appropriate assess to relevant services.

The aim of this review is to:

- Assist parents, carers and health care professionals in the recognition of the clinical manifestation of pain, discomfort and distress in children and young people with cerebral palsy.
- To provide guidance on reliable and valid tools used to identify pain in children and young people with cerebral palsy assist in the onward specialist referral and management for those children and young people with cerebral palsy who are experiencing discomfort, pain and distress.

21.2 Description of clinical evidence

Five studies reporting on validity and reliability of 4 pain tools have been included in this review (Breau 2002; Hunt 2004; Malviya 2006; Voepel-Lewis 2002; Solodiuk 2010).

Infants, children and young people with cerebral palsy aged up to 25 years were considered to be the target population for this review. However, no studies were found specifically on a cerebral palsy population and so the Committee considered for inclusion studies that looked at a mixed population of children and young people with neurodevelopmental disorders. The number of participants in each study varied, ranging from a minimum of 24 to a maximum of 140. Participants in the included studies ranged in age from 1 year to 19 years.

Three studies were undertaken in the United States (Malviya 2006; Voepel-Lewis 2002; Solodiuk 2010); 1 was from the United Kingdom (Hunt 2004); 1 was from Canada (Breau 2002).

One study reported on validity and reliability of the NCCPC-PV (Breau 2002) in 24 nonverbal children with severe cognitive impairment, aged 3 to 19 years. One study validated the PPP (Hunt 2004) in 140 children with severe neurological and cognitive impairment, who were unable to communicate through speech or any augmentative device (43% had cerebral palsy). Two studies assessed validity and reliability of FLACC in 52 (Malviya 2006) and 79 (Voepel-Lewis 2002) children with cognitive impairment. One study reported on validity and reliability of the INRS in 50 nonverbal children with cognitive impairment (Solodiuk 2010).

With regards to the outcomes reported by the included studies, all 4 tools were tested for construct validity and interrater reliability.

No studies have been retrieved that reported on the other tools listed in the review protocol:

- Tools that are designed to identify the presence of discomfort, pain or distress as reported by the patient or by proxy of the parent/carer:
  - Wong-Baker FACES® Pain Rating Scale
  - Disdat
- Tools that are designed to identify the presence of sleep disturbance of as reported by the patient or by proxy of the parent/carer:
  - Actigraphy
  - Sleep diaries
  - Polysomnography

Given the aim of this review, validity designs were prioritised and the following were considered as the main criteria for assessing the quality of each study, as reported by Jerosch-Herold et al., 2005:

- Sample size
- Sampling methodology
- Blinding of raters
- Statistical analysis

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

21.2.1 Clinical evidence profile

A summary of the studies that were included in this review are presented in Table 92.

Table 92: Summary of included studies

Tool assessed	Study reference	Inter-rater reliability	Known groups validity	Limitations of the study	Notes
NCCPC-PV	Breau 2002	ICC: 0.82 before surgery ICC: 0.78 after surgery	• Caregiver and researcher scores were significantly greater after surgery (paired t-test p=0.003	• Scares information on sampling methodology • Small sample size	• Nurses did not use the scale in this trial • Positive correlations with the VAS

Tool assessed	Study reference	Inter-rater reliability	Known groups validity	Limitations of the study	Notes
			and p=0.01) Cronbach's alpha • 0.71 for researchers • 0.0.91 for caregivers		
PPP	Hunt 2004	ICC: 0.74 ICC in analgesic subgroup: 0.89	• PPP vs. VRS score: p<0.001 • Significant difference in scores pre- and post-analgesia (p<0.001)	• Analysis of data from the postoperative group was complicated by the variety and number of analgesia given • Observers could rewind videotapes (used to blind observers), which would not be possible under normal circumstances when using the tool.	• Health care staff were given training on how to use the scale • No significant difference between parents and professional ratings • The familiarity with the child did not influence the extent of agreement with the parent on PPP score
FLACC	Malviya 2006	ICC: 0.90 (95% CI 0.87-0.92); k = 0.44-0.57	• Decrease in FLACC scores after analgesic administration • Proved criterion validity (correlations between FLACC, parent, and child scores)	• Videotape assessments were used to blind 1 set of observers to the administration of analgesia	
	Voepel-Lewis 2002	• Correlation between observers for total score, r = 0.51 to 0.77 • Exact agreement = 35-94% for Face, Cry,	• Decrease in FLACC scores after analgesic administration, p<0.001	• Videotape assessments were used to blind 1 set of observers to the administration of analgesia	

Tool assessed	Study reference	Inter-rater reliability	Known groups validity	Limitations of the study	Notes
		Consolability • Exact agreement = 17-77% for Legs			
INRS	Solodiuk 2010	ICC: 0.65 - 0.80	• Decrease in INRS scores 1 hr after a pain management intervention) • Modest correlations between INRS and NCCPC-PV	• Data were collected over a period of several years • Sample size did not allow for extensive subgroup analysis	

CP cerebral palsy, NCCPC-PV Non-communicating Children's Pain Checklist - Postoperative Version, PPP Paediatric pain profile, FLACC Face, legs, Activity, Cry, Consolability observational tool, INRS individualised numeric rating scale, VAS visual analogue scale.

21.3 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations of tools to identify and aid understanding of discomfort, pain and/or distress were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

21.4 Evidence statements

21.4.1 NCCPC-PV

One study validated the NCCPC-PV tool in 24 participants, reporting an inter-rater reliability of 0.82 and 0.78 before and after surgery respectively. The study was limited by little sampling methodology information and small sample size.

21.4.2 PPP

One study validated the PPP tool in 140 participants, reporting an inter-rater reliability of 0.74, which was then 0.89 in a subgroup of participants who received analgesics. The study was limited by the heterogeneity in the variety and number of analgesia given to participants and because of the use of videotape to blind 1 set of observers.

21.4.3 FLACC

Two studies validated the FLACC tool in a total of 131 participants, reporting overall good reliability (ICC: 0.90), with variation in exact agreement (35-94% for Face, Cry, Consolability

and 17-77% for Legs). The study, however, used videotape to blind 1 set of observers to the administration of analgesia for the purposes of testing inter-rater reliability.

21.4.4 INRS

One study validate the INRS tool in 50 participants, reporting moderate to good reliability (ICC: 0.65 - 0.80). The study was limited because data were collected over a period of several years and the sample size did not allow for extensive subgroup analysis.

21.5 Evidence to recommendations

21.5.1 Relative value placed on the outcomes considered

The aim of this review is to:

- Assist parents, carers and health care professionals in the recognition of the clinical manifestation of pain, discomfort and distress in children and young people with cerebral palsy.
- Provide guidance on reliable and valid tools used to identify pain in children and young people with cerebral palsy.
- Assist in the onward specialist referral and management for those children and young people with cerebral palsy who are experiencing discomfort, pain and distress.

Validity and reliability of the tools were prioritised as critical outcomes for this review.

21.5.2 Consideration of clinical benefits and harms

There are numerous challenges in recognising the presence of pain, discomfort and distress in all children. This is even more apparent when a child or young person with cerebral palsy has cognitive or communication difficulties and patterns and behaviours associated with pain can present differently from the wider paediatric population.

Using tools such as pain questionnaires can help health care professionals and parents and carers to recognise appropriate behaviours and assess if pain, distress or discomfort is present. The Committee noted that pain, distress, discomfort can be expressed in various ways and may be impacted on by a variety of other factors such as psychological and emotional wellbeing, thirst, hunger, and environmental stimulus. Additionally, as their primary advocate, parents and carers may be able to recognise pain from a child and young person's cues and emotional distress and therefore play a major role in helping health, education and social care professionals recognise and assess pain and discomfort.

The Committee agreed from the evidence presented that the Paediatric Pain Profile was the only tool that was validated for use in the post-operative settings. However, the Non-Communicating Children's Pain Checklist (NCCPC-PV) and the Numeric pain rating scale (INRS) were also reported in the papers as useful tools for assessing degree of pain, distress and discomfort. The Committee accepted that clinical practice was varied and that the identified studies were of low quality, however the most important factor was that pain, discomfort and distress was looked for. The Committee agreed that all health care professionals should regularly ask a child or young person with cerebral palsy regarding the presence of any pain, discomfort or distress. The Committee agreed that pain assessment tools should be used, especially in children with no or limited communication, to help in the assessment. The Committee noted that regular reflection is necessary with regards to the presence, pattern and degree of pain as this can be challenging and can change over time. It was also noted that there is a subjective element to pain questionnaires used in non-communicating children where health care professionals or parents and carers have the ability to quantify the qualitative signs of whether the child is in pain, distress or discomfort.

The Committee noted that recognising and assessing the presence and severity of pain, discomfort and distress required not only the awareness of parents and carers but may also need onward referral to a specialist MDT for assessment of possible cause and on-going management.

The Committee noted that no evidence was retrieved and there were no tools available for the routine recognition or assessment of sleep disturbances. However, based on their clinical experience they agreed that the use of simple measures such as sleep diaries to recognise sleep difficulties were appropriate to use in routine clinical practice, alongside the primary role of the parents and carers. Additionally, the Committee noted that sleep disturbances identified from the causes of pain, distress, discomfort and sleep disturbance evidence review (see section 20) were identified by sleep questionnaires and this reinforced their view that the use of sleep questionnaires was appropriate. They pointed out that more complex measures such as polysomnography and actinography were difficult to use in routine clinical practice. Which would only be used when health care professionals think sleep disturbance is not due to pain or discomfort but due to sleep pathology.

The Committee noted that the use of pain assessment tools in hospital to help identify signs and symptoms of pain and discomfort in children and young people with cerebral palsy who cannot communicate had become widespread. However, the evidence based looking at their use in a community setting was very limited. The Committee agreed to develop and prioritise a research recommendation to assess the use of pain assessment tools by parents and carers in a community setting.

21.5.3 Consideration of economic benefits and harms

Knowing the validity and reliability of published tools to identify and aid understanding of discomfort, pain and/or distress in children and young people with cerebral palsy may lead to better identification (and thus more timely management) in this population and has therefore, indirectly, potentially important resource implications. However, this review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

21.5.4 Quality of evidence

Main reason of bias in the included studies were small sample size, unclear sampling procedure and methods used to blind observers.

21.5.5 Other considerations

The Committee recognised that specialist services are not widely available or provided for assessment and management for pain, distress, discomfort and sleep distress for children and young people with cerebral palsy.

The recommendations related to this evidence review were based on the evidence and the Committee’s clinical experience.

21.5.6 Key conclusions

The Committee concluded that NCCPC-PV, PPP, FLACC, and INRS tools showed sufficient reliability to be used in a population of children and young people with neurodevelopmental disorders, including cerebral palsy. However, each of them has different characteristics with regards to the level of participation required by parents or carers, time needed to complete the assessment, and the setting in which the tool was validated. Therefore these should be taken into consideration when deciding which tool to use.

21.6 Recommendations

86. Refer the child or young person for a specialist multidisciplinary team assessment of pain, distress and sleep if the cause of pain or distress is not clear after routine assessment.

Pain, discomfort and distress

87. Take into account that parents and familiar carers have a key role in recognising and assessing pain and discomfort in children and young people with cerebral palsy.

88. When assessing pain in children and young people with cerebral palsy:

- recognise that assessing the presence and degree of pain can be challenging, especially if there are communication difficulties or learning disabilities
- ask about signs of distress and sleep disturbances at every contact
- recognise that pain-related behaviour can present differently compared with that in the wider population.

89. Assess for other possible causes of distress in the absence of identifiable physical causes of pain and discomfort, such as:

- psychological and emotional distress
- increased sensitivity to environmental triggers
- thirst or hunger.

90. Consider using tools to identify pain or assess severity of pain in children and young people with cerebral palsy, for example:

- For children and young people with communication difficulties:
  - Paediatric Pain Profile
  - Non-communicating Children's Pain Checklist – postoperative version
- For children and young people without communication difficulties:
  - Numeric pain rating scale.

Sleep disturbances

91. When identifying and assessing sleep disturbances in children and young people with cerebral palsy:

- recognise that parents and familiar carers have the primary role in this
- consider using sleep questionnaires or diaries.

92. Always ask about pain, sleep and distress as part of any clinical consultation.

21.7 Research recommendations

6. Does use of pain assessment tools by parents and carers improve the recognition and early management of pain in children and young people with cerebral palsy in a community setting?

Table 93: Research recommendation rationale

Research question	Does use of pain assessment tools by parents and carers improve the recognition and early management of pain in children and young people with cerebral palsy in a community setting?
Why this is needed	
Importance to 'patients' or the population	The NIHR Research for Patient Benefit Programme has supported the development of an Eating and Drinking Abilities Classification System in cerebral palsy, and a study on how services meet the psychosocial support needs of children and young people with feeding difficulties and their families is currently funded.
Relevance to NICE guidance	High priority: Recognition and interventions of pain using validated pain assessments.
Relevance to the NHS	Recognise large impact on quality of life for children and young people with cerebral palsy and their families. Early recognition and intervention minimises impact on a wider society.
National priorities	
Current evidence base	Limited in community setting
Equality	Equity of pain recognition with impaired communication skills
Feasibility	Easy
Other comments	

Table 94: Research recommendation statements

Criterion	Explanation
Population	Children and young people with cerebral palsy with impaired communication skills
Intervention	Recognition of pain and discomfort by parents and carers in the community setting using validated pain assessment tools
Comparator	N/A
Outcome	Sensitivity Specificity Likelihood ratios Clinical outcomes such as quality of life scores
Study design	Prospective cohort study
Timeframe	2 years

22 Management of pain, distress and discomfort

Review question: In children and young people with cerebral palsy, which interventions are effective in managing discomfort and/or pain and distress with no apparent cause?

22.1 Introduction

Children and young people with cerebral palsy may experience pain from a range of causes and sometimes the cause may not be identifiable despite careful assessment. There is evidence that pain and discomfort have detrimental effects both on a person and their family's quality of life through its impact on health, social participation and cognitive and emotional well-being.

Clinicians are often faced with a child or young person with severe cerebral palsy in marked discomfort, but unable to communicate and talk about the nature, location or severity of the discomfort of the discomfort or pain they are experiencing. It is important that relevant members of the multidisciplinary team contribute to the assessment and to identifying appropriate and effective interventions for these children and young people. Currently a range of treatments are available and are used in practice but guidance is required on which of these are most effective.

The aim of this review is assess the clinical and cost effectiveness of interventions for managing discomfort, pain and distress with no apparent cause in children and young people with cerebral palsy.

22.2 Description of clinical evidence

No relevant clinical studies were identified for this review.

For more details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, and exclusion list in Appendix K.

22.2.1 Clinical evidence profile

No relevant clinical studies were identified for this review.

22.3 Economic evidence

No economic evaluations of interventions relevant to managing discomfort and/or pain and distress were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

This review question was not prioritised for de novo economic modelling. To aid consideration of cost-effectiveness relevant resource and cost use data are presented in Appendix G.

22.4 Evidence statements

22.4.1 Pain control

No evidence was retrieved for this outcome.

22.4.2 Distress

No evidence was retrieved for this outcome.

22.4.3 Physical function

No evidence was retrieved for this outcome.

22.4.4 Emotional function

No evidence was retrieved for this outcome.

22.4.5 Adverse events

No evidence was retrieved for this outcome.

22.4.6 Health-related quality of life

No evidence was retrieved for this outcome.

22.4.7 Parent/carer outcomes (for example anxiety)

No evidence was retrieved for this outcome.

22.5 Evidence to recommendations

22.5.1 Relative value placed on the outcomes considered

The aim of this review was to determine which interventions are more clinically and cost effective for managing discomfort, pain and distress in people with cerebral palsy.

22.5.2 Consideration of clinical benefits and harms

The Committee noted that when faced with a child experiencing pain or discomfort it was often important to use the clinical expertise of the multidisciplinary team working closely with the parents and primary carers in order to determine the likely cause, and to assess the severity and target therapy. Several existing NICE Clinical Guidelines potentially relevant to this include guidelines on constipation, gastro-oesophageal reflux disease, spasticity, headache, low back pain, and urinary tract infection have been identified as relevant to management of pain and discomfort and distress in children and young people with cerebral palsy.

The Committee discussed how in children in whom the cause of pain or discomfort was not certain, management can be challenging. Pain may arise for a wide variety of reasons and may be obscure in origin. Both acute and chronic pain can be physiological, inflammatory or neuropathic in nature and can be complicated by the central neurological impairment in cerebral palsy, where pain signals can be increased or decreased in severity. The Committee were aware that pain was predominantly associated with musculo-skeletal discomfort or associated with a comorbidity (see section 20 on causes of pain, discomfort,

distress and sleep disturbances), and therefore they agreed it was important to first think about common explanations and explore any potential triggers.

As pain is both a both a sensory and emotional experience, the Committee noted that emotional and psychological factors, such as anxiety, depression and mental health disorders can intensify pain. As pain is multi-factorial, the Committee agreed that the approach to management should consider the physical contributors but also focus on the psychological and emotional elements of the pain. This was particularly important if the cause was not apparent and amenable to treatment.

The Committee agreed, in line with existing WHO guidance (WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses) and clinical practice, that pain management should be a step-wise process. In cases where a child required analgesia this should be employed and if necessary escalated stepwise to provide adequate pain relief if possible with a reduced risk of treatment adverse effects. There should be a clear, reflective plan depending on pain duration, pattern and severity.

Subsequent to trial of analgesic management, if presumed pain and/or distress persisted, the Committee recommended monitoring the duration, pattern and severity of pain and/or discomfort and to adjust management accordingly.

In a tiered approach to pain management without obvious causation, a more detailed assessment involving a specialist pain multidisciplinary team may be required. Within the specialist management plan, further pain interventions including anti-convulsants and neuropathic pain relief could be considered.

The Committee noted that additional areas to consider are the parents' and carers' ability to cope with the child or young person's experience of pain, its duration and severity.

The Committee also noted evidence that many of the interventions routinely used in children and young people with cerebral palsy can cause an acute episode of pain. These include physical therapy, particularly stretches, the use of poorly fitting or inappropriate orthotics and equipment, botulinum toxin injections and surgical procedures. It is important to reflect with the child and young person and their families and carers that these interventions may reduce pain and discomfort in the longer term. It is obvious that all professionals involved in the care of children and young people with cerebral palsy should implement strategies to minimise the pain and discomfort caused by any intervention.

22.5.3 Consideration of economic benefits and harms

A treatment is more likely to be cost-effective if it used for the correct indication, whereas if the wrong indication is targeted there is a potential waste of resources. Therefore the cost-effectiveness of an intervention to reduce pain or distress will depend on whether the cause of pain or distress has been identified prior to the initiation of treatment; hence identifying the cause should be first action.

However recognising the cause of pain or distress can be complex and expert specialist assessment may be required. Consequently the Committee emphasised the importance of seeking the expertise of an appropriate multi-disciplinary team, or a specialist, if required. Increased referral might of course entail a need for additional resources, but this should lead to better identification, more timely management and hence a cost-effective use of NHS resources. On the other hand, the Committee noted that on occasion, health care professionals directly and regularly involved in the care of children and young people with cerebral palsy may possess expertise in this area, evading the need for further specialist assessment in all cases.

Prior to contact with a health care professional the Committee highlighted the importance of identifying sleep hygiene issues and sensory contributors such as an environments that are

excessively bright or noisy and of discussing these matters with parents or carers. Simple measures to deal with these aspects would not be costly and might have important benefits.

The Committee highlighted that if a patient was suspected of being in pain they would start a trial of analgesics for approximately 2 weeks until the cause was identified. Analgesics are relatively inexpensive at a cost of less than £1 per day hence an initial trial would not incur a significant opportunity cost if pain or distress was incorrectly targeted.

Only after an unsuccessful trial of analgesics and a reassessment considering the duration, severity and pattern of symptoms would anticonvulsants, diazepam or fentanyl patches be considered as a second line treatment. Therefore recommendations would follow a stepwise escalation generally implementing the cheapest interventions first.

Even though analgesics are associated with a lower cost it is important to reiterate that the cost-effectiveness of any interventions included in this review cannot be ascertained in the absence of clinical effectiveness data.

The Committee noted that the use of non-pharmacological treatments would depend on the cause of pain or distress. Moreover non-pharmacological treatments are unlikely to be undertaken if the cause cannot be identified.

22.5.4 Quality of evidence

No relevant studies were included for this review.

22.5.5 Other considerations

The recommendations related to this evidence review were based on the Committee's clinical experience.

22.5.6 Key conclusions

No evidence has been retrieved that answers the clinical question.

22.6 Recommendations

93. For reversible causes of pain identified in children and young people with cerebral palsy, treat the cause where appropriate using targeted interventions in line with the following NICE guidelines:

- spasticity in under 19s
- constipation in children and young people
- gastro-oesophageal reflux disease in children and young people and gastro-oesophageal reflux disease and dyspepsia in adults
- headaches in over 12s
- low back pain in adult.
- urinary tract infection in under 16s.

94. For common interventions used in the management of cerebral palsy (such as physical therapies, botulinum toxin A injections and surgery) that can cause acute pain:

- advise the child or young person and their parents or carers that these interventions may reduce discomfort in the long term
- minimise discomfort during these procedures.

95. In the absence of an identifiable cause of pain, discomfort or distress in a child or young person with cerebral palsy:

- consider a 'stepped approach' trial of simple analgesia (such as paracetamol and/or ibuprofen) for mild to moderate pain
- monitor the duration, pattern and severity of symptoms.

96. Refer the child or young person to a specialist pain multidisciplinary team for a more detailed assessment if a trial of analgesia is unsuccessful.

22.7 Research recommendations

None identified for this topic.

23 Management of sleep disturbances

Review question: In children and young people with cerebral palsy, which interventions are effective in managing sleep disturbances arising from no identifiable cause?

23.1 Introduction

Adequate sleep is recognised as a vital element in normal health and development. As such sleep disturbances can lead to a reduction in the quality of life, potentiating negative outcomes in children and young people with cerebral palsy and also directly and indirectly their parents and families.

There are a wide variety of reasons for underlying sleep disturbances in children and young people with cerebral palsy. These include the presence of increased or decreased nocturnal movements and comorbidities such as obstructive sleep apnoea or other sleep related breathing disorders, pain, epilepsy and behavioural problems. Any approach to improving sleep should start with recognising and managing these factors before focussing on specific behavioural and pharmacological approaches used in wider population groups that help sleep initiation and maintenance.

Appropriate interventions can potentially help physical and psychological wellbeing as well as individual development, function and participation. This review aims to determine which interventions are more clinically and cost effective for reducing sleep disturbances.

23.2 Description of clinical evidence

A systematic search was conducted to retrieve evidence on the clinical and cost effectiveness of interventions for reducing sleep disturbances in children and young people with cerebral palsy.

The Committee in the review protocol prioritised the following pharmacological and non-pharmacological interventions:

- Melatonin
- Sleep systems/ sleep positioning (postural devices, wedges and supports)
- Age appropriate behavioural sleep routine (termed as sleep hygiene programmes)
- Sedatives:
    - Alimemazine / Vallergan
    - Chloral hydrate
    - Clonidine

Five studies have been included in this evidence review (Appleton 2012; Coppola 2004; Dodge 2001; Lloyd 2014; Wasdell 2008). One study is a Cochrane systematic review on sleep positioning systems in children with cerebral palsy (Lloyd 2014); and 4 studies are randomised controlled trials on the use of melatonin (Appleton 2012, Coppola 2004; Dodge 2001; Wasdell 2008).With regards to the evidence retrieved for the use of sleep positioning systems, Lloyd and colleagues conducted a systematic review that included children and adolescents up to 18 years of age with cerebral palsy. Sleep patterns and sleep quality were part of the secondary outcomes analysed in this Cochrane review, as well as quality of life of the child and the family. Only 2 cross-over trials met the inclusion criteria with regards to population and outcomes considered. Sleep quality was measured by both polysomnography and video recording, or by Actigraph.

In relation to the clinical effectiveness of melatonin, no studies were identified that only looked at children and young people with cerebral palsy. However, 4 studies comparing melatonin with placebo in populations of children and young people with neurodevelopmental disorders including cerebral palsy were included, of which 3 were cross-over (Coppola 2004; Dodge 2001; Wasdell 2008), and 1 was a health technology assessment (Appleton 2012). All trials were double-blinded and placebo-controlled. Sample sizes ranged from 20 to 143, and participants were aged between 1 and 18 years.

Participants received melatonin or placebo each day during 10 days (Wasdell 2008), 4 weeks (Coppola 2004), 6 weeks (Dodge 2001), or 12 weeks (Appleton 2012). Two studies used a fixed dose of melatonin of 5 mg (Dodge 2001, Wasdell 2008); in 1 study treatment with melatonin was initiated at a daily dose of 3 mg and parents were allowed to increase the dosage up to 9 mg/d during the following 2 weeks in case of inefficacy (Coppola 2004); in 1 study (Appleton 2012) the starting dose was 0.5 mg and the dosage could be increased through 2 mg and 6 mg to 12 mg during the first 4 weeks. Time of administration of the intervention differed slightly across studies, being fixed in 1 case at 8 pm (Dodge 2001), 45 minutes before bedtime (Appleton 2012), 20 to 30 minutes the child's most desirable bedtime (Wasdell 2008), or even at bedtime (Coppola 2004).

With regards to the outcomes, all the included studies reported on:

- Total night sleep time measured either by sleep diaries (Coppola 2004; Dodge 2001; Wasdell 2008; Appleton 2012) or actigraphy (Wasdell 2008; Appleton 2012);
- Sleep latency measured either by sleep diaries (Coppola 2004; Dodge 2001; Wasdell 2008; Appleton 2012) or actigraphy (Wasdell 2008; Appleton 2012);
- Night wakes measured either by sleep diaries (Coppola 2004; Dodge 2001; Wasdell 2008; Appleton 2012) or actigraphy and CSDI score (Wasdell 2008; Appleton 2012);
- Quality of life of the parents measured by using Family Impact Module of the PedsQL (Appleton 2012)

GRADE methodology was used for this question and GRADE profiles were produced.

Data for these outcomes were meta-analysed were possible.

Appleton 2012 also reported on adverse effects, but no formal statistical evaluation was conducted.

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, forest plots in Appendix I, study evidence tables in Appendix J and exclusion list in Appendix K.

23.2.1 Summary of included studies

Table 95: Summary of included studies

Study reference	Study design	Population	Intervention	Outcomes	Quality of systematic review
Lloyd 2014	Systematic review	21 children with cerebral palsy aged 5 to 16 years 12 boys, 9 girls GMFCS levels III to V Established users of sleep positioning	Overnight use of any commercially manufactured whole body sleep positioning system, applied in any setting.	Sleep latency No statistically significant difference whether sleeping in the sleep positioning system or not. Sleep efficiency	The review includes cross-over trials, both with high risk of bias, given by unclear random sequence generation, no information on blinding of assessors, reporting bias.

Study reference	Study design	Population	Intervention	Outcomes	Quality of systematic review
		systems		No statistically significant difference whether sleeping in the sleep positioning system or not.	

1 *GMFCS gross motor function classification system*

2 **Table 96: summary of the evidence for melatonin versus placebo**

Study reference	Study design	Population	Outcomes	Risk of bias
Appleton 2012	double-blind and placebo-controlled (HTA)	A heterogeneous group comprising 146 children with a wide range of neurological and developmental disorders, including those with a specific genetic disorder but also those without a specific diagnosis.	Primary outcome total night-time sleep Secondary outcomes sleep-onset latency; night wakes; composite sleep disturbance index score adverse events.	Low
Coppola 2004	cross-over double-blind and placebo-controlled	25 children with mental retardation/learning disability aged 3-16	Sleep latency, total sleep time, number of wakes per night.	Low
Dodge 2001	cross-over double-blind and placebo-controlled	20 children with developmental disabilities aged 1-12	Sleep latency, total sleep time, number of wakes per night.	Low
Wasdell 2008	cross-over double-blind and placebo-controlled	50 children with neurodevelopmental disability aged 2-18	Sleep latency, total sleep time, number of wakes per night.	Low

23.3 3 Clinical evidence profile

4 **Table 97: evidence profile summary for sleep positioning systems**

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	No sleep positioning systems	Sleep positioning systems			
Sleep latency the time it took the child to fall asleep once put	-	-	Limited data. A small number of	21 (1 study)	very low[1,2,3]

to bed (minutes)			established users of sleep positioning systems showed no significant difference in sleep quality indicators.		
Sleep efficiency % of time in bed actually asleep	-	-	Limited data. A small number of established users of sleep positioning systems showed no significant difference in sleep quality indicators.	21 (1 study)	very low[1,3]

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).*
1 authors state that meta-analysis was not performed due to heterogeneity between the included studies given differences in measurement tools, experimental location, choice of metric, age of participants, type of motor disorder, position adopted in sleep positioning system, history of seizures, GMFCS level, and type of sleep positioning system used. Evidence was downgraded by 2 given high heterogeneity and because a ransom effect model was rejected given the small sample sizes and number of studies.
2 Not calculable.
3 although no pooled estimate was presented, 95% CI of the single estimates in the studies are very wide. Given the small sample sizes involved, it is likely that meta-analysis would have still not reduced the wide range in confidence intervals.

Table 98: evidence profile summary for melatonin versus placebo

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Control	Melatonin versus placebo		
total night time sleep sleep diaries	-	The mean total night time sleep in the intervention groups was 30.01 higher (12.29 to 47.72 higher)	300 (4 studies)	high
total night time sleep actigraphy	-	The mean total night time sleep in the intervention groups was 14.51 higher (7.69 lower to 36.72 higher)	159 (2 studies)	moderate[1]
sleep latency	-	The mean sleep latency in	297	moderate[1]

sleep diaries		the intervention groups was 32.73 lower (43.37 to 22.09 lower)	(4 studies)	
sleep latency actigraphy	-	The mean sleep latency in the intervention groups was 29.91 lower (42.16 to 17.66 lower)	149 (2 studies)	low[1,2]
night wakes sleep diaries	-	The mean night wakes in the intervention groups was 0.01 higher (0.28 lower to 0.3 higher)	190 (3 studies)	high
night wakes actigraphy	-	The mean night wakes in the intervention groups was 0.45 higher (1.56 lower to 2.46 higher)	100 (1 study)	moderate[1]
night wakes CSDI score. Scale from: 0 to 12.	-	The mean night wakes in the intervention groups was 1.00 lower (1.83 to 0.16 lower)	125 (1 study)	moderate[1]
quality of life of the parent Family Impact Module of the PedsQL. Scale from: 0 to 100.	-	The mean quality of life of the parent in the intervention groups was 3.57 higher (0.86 lower to 8 higher)	133 (1 study)	high

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*

1 evidence was downgraded by 1 due to serious imprecision as 95%CI crossed 1 default MID

2 evidence was downgraded by 1 due to serious heterogeneity (chi-squared p<0.1, I-squared inconsistency statistic of 50%-74.99%) and no plausible explanation was found with sensitivity or subgroup analysis

23.4 Economic evidence

No economic evaluations of interventions relevant to managing discomfort and/or pain and distress were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

This review question was not prioritised for de novo economic modelling. To aid consideration of cost-effectiveness relevant resource and cost use data are presented in Appendix G.

23.5 Evidence statements

23.5.1 Sleep positioning systems

23.5.1.1 Sleep latency

A systematic review including 2 cross-over trials with 21 participants found no significant difference in sleep latency between sleeping in the sleep positioning system or not.

23.5.1.2 Sleep efficiency

A systematic review including 2 cross-over trials with 21 participants found no significant difference in sleep efficiency between sleeping in the sleep positioning system or not.

23.5.1.3 Quality of life of child and family

No studies were found for this outcome.

23.5.2 Melatonin versus placebo

23.5.2.1 Total night sleep time measured by sleep diaries

Four high quality studies with 205 participants found no clinically significant difference between melatonin and placebo for total night sleep time when measured with sleep diaries.

23.5.2.2 Total night sleep time measured by actigraphy

Two moderate quality studies with 109 participants found no clinically significant difference between melatonin and placebo for total night sleep time when measured with actigraphy.

23.5.2.3 Sleep latency measured by sleep diaries

Four moderate quality studies with 205 participants found a clinically significant beneficial effect of melatonin compared with placebo for sleep latency.

23.5.2.4 Sleep latency measured by actigraphy

Two low quality studies with 99 participants found a clinically significant beneficial effect of melatonin compared with placebo for sleep latency.

23.5.2.5 Night wakes measured by sleep diaries

Three high quality studies with 95 participants found no clinically significant difference between melatonin and placebo for number of night wakes when measured with sleep diaries

23.5.2.6 Night wakes measured by actigraphy

One moderate quality study with 50 participants found no clinically significant difference between melatonin and placebo for number of night wakes when measured with actigraphy.

23.5.2.7 Night wakes measured by CSDI

One high quality studies with 125 participants found no clinically significant difference between melatonin and placebo for number of night wakes when measured with CSDI score.

23.5.2.8 Quality of life of the parents measured by using Family Impact Module of the PedsQL

One high quality study with 133 participants found no clinically significant difference between melatonin and placebo on the quality of life of the parents.

23.5.2.9 Adverse events

No formal statistical analysis was performed by the included studies; however no difference between the intervention and the control groups with regards to adverse events was reported.

23.6 Evidence to recommendations

23.6.1 Relative value placed on the outcomes considered

The aim of this review is to determine which interventions are more clinically and cost effective for managing sleep disturbance in children and young people with cerebral palsy.

The following outcomes were identified by the committee as most useful in decision making:

- Sleep quality, measured for example, by polysomnography (gold standard) or by other methods such as wrist actigraphy, sleep diaries, Sleep Habits Questionnaire
- Health-related quality of life (for example, Peds-QL, Pediatric QOL-CP module or EQ-5D)
- Other important outcomes were: adverse events, and daytime emotional wellbeing/lability.

23.6.2 Consideration of clinical benefits and harms

The Committee noted that the first and most important aspect of sleep management of any sleep disorder in children and young people with cerebral palsy is the maintenance of 'sleep hygiene'. Simple steps to manage a normal sleep routine are vital to facilitate sleep latency and maintenance.

The Committee reflected on the close correlation between pain, discomfort and sleep disturbance. In individuals with cerebral palsy there are a number of potential factors around tone, musculo-skeletal comfort, positioning, nutrition and comorbidity that can directly affect the quality of sleep.

As such, the Committee recommended that the second step of any sleep management plan should be to consider and manage treatable causes of any sleep disturbance, in particular consideration of sleep disordered breathing patterns, potential epilepsy and movement difficulties, behavioural aspects and optimising physical and psychological comfort.

The Committee noted that the evidence provided showed that sleep systems should not be used to solely manage primary sleep disorders or if there are concerns about epilepsy. However, as outlined in NICE Spasticity guidelines, they can be useful for hip placement and thereby potentially reducing pain and discomfort. They could therefore be of benefit to help in some secondary sleep disorders. Regular review of their individual applicability and tolerance is advised.

The evidence identified gave no specific backing to sedative use, though these are frequently used in primary, secondary and tertiary medical practice. A trial of sedative medication is often used in primary and secondary care to see if this helps recover an appropriate diurnal: nocturnal sleep pattern. However, as their side effect profile is marked particularly in children or young people with respiratory or ENT difficulties, the Committee agreed their continued use should not routinely be considered without seeking specialist advice.

The Committee agreed that a trial of melatonin could be considered to manage difficulties in sleep initiation / latency. However, they also agreed that it is not routinely used to manage problems of sleep duration or episodes of waking through the night. The Committee noted that 'slow release' formulations are considered as working long-term through the duration of sleep but the efficacy of these preparations is not proven.

The Committee noted an increasing use of Chloral hydrate and / or Clonidine to help with sleep initiation and maintenance, particularly in dystonic children in particular, however there was as yet no evidence base to support this.

It was noted that in adults with cerebral palsy and sleep disturbances the most common forms of management are psychological wellbeing interventions and sometimes Chlorpheniramine as a sedative.

The Committee agreed that if there were on going sleep disturbances, the child or young person should be referred to specialist sleep services for multidisciplinary team assessment and management.

Due to the lack of clarity of the effectiveness of sedatives in managing sleep disorders in children and young people with cerebral palsy, the Committee agreed to develop a research recommendation assessing the clinical and cost effectiveness of interventions (sleep hygiene, sedatives and/or melatonin) to improve sleep disturbances.

23.6.3 Consideration of economic benefits and harms

The Committee acknowledged that the cost of sleep systems vary depending on the type of equipment required. Following this discussion the Committee believed that sleep systems would not be considered cost-effective relative to the other interventions included in this review because they are not primarily used to reduce sleep disturbance. However, the Committee highlighted that interventions aimed at reducing pain, including on occasion the use of sleep systems, can reduce sleep disturbance indirectly.

The first line intervention recommended by the Committee were modifications to the patients sleep routine (sleep hygiene programmes) that would be implemented by the family or carer at home without employing NHS resources. This programme should be put in place together with consideration of management of any potential comorbidity that could affect sleep initiation and maintenance.

Following unsuccessful modifications to the patients sleep routine the Committee considered a trial of melatonin to help manage problems sleep initiation / latency. However the Committee did not feel melatonin would be considered cost-effective to manage problems of sleep maintenance or waking.

The Committee noted that the brand of melatonin used in the UK (Circadin) is a tablet preparation, but shorter release oral solutions are available from specialist order manufacturers at a higher cost. However, the Committee stated that the tablet preparation is often crushed evading the need for oral solutions that are more expensive. Advice regarding this should be provided via specialist Paediatric Pharmacy groups.

In the event of lack of efficacy of melatonin the Committee advised that specialist advice should be sought to initiate a trial of sedatives, with a defined end point. The Committee was surprised choral hydrate incurred such a high cost (143.3mg/5ml oral solution BP, 150ml, £244.26 [BNF June 2016]) when presented with a cost description of the pharmacological treatments (Appendix G); leading to a recommendation that patients should be seen by a specialist before sedatives are received to ensure the most appropriate and cost-effective treatment is administered.

Even though choral hydrate is associated with a high cost it is important to reiterate that the cost-effectiveness of any sedative included in this review cannot be ascertained in the absence of clinical effectiveness data. For this reason, the research recommendation from the Committee to consider the clinical and cost effectiveness of interventions to improve sleep disorders in children and young people with cerebral palsy will assess if benefits can justify the costs to mitigate current uncertainty in this area.

23.6.4 Quality of evidence

One systematic review and 4 randomised controlled trials were included in this review. The quality of the evidence ranged from high to low, and main reasons for bias were due to imprecision or study design.

23.6.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

23.6.6 Key conclusions

The Committee concluded that the evidence pointed to the act that sleep positioning systems seem not to have a clinically significant effect on sleep quality in children and young people with cerebral palsy who experience sleep disturbance. With regards to the use of melatonin, the intervention has a clinically beneficial effect on sleep initiation / latency, but no clinically significant difference was found for all the other outcomes related to both sleep quality and quality of life.

23.7 Recommendations

97. Optimise sleep hygiene for children and young people with cerebral palsy.

98. Manage treatable causes of sleep disturbances that are identified in children and young people with cerebral palsy.

99. If no treatable cause is found, consider a trial of melatonin[m] to manage sleep disturbances for children and young people with cerebral palsy, particularly for problems with falling asleep.

100. Do not offer regular sedative medication to manage primary sleep disorders in children with cerebral palsy without seeking specialist advice.

101. Do not offer sleep positioning systems solely to manage primary sleep disorders in children and young people with cerebral palsy.

102. Refer the child or young person to specialist sleep services for multidisciplinary team assessment and management if there are ongoing sleep disturbances.

23.8 Research recommendations

7. What is the clinical and cost effectiveness of interventions (sleep hygiene, sedatives, melatonin) to improve sleep disturbance in children and young people with cerebral palsy?

Table 99: Research recommendation rationale

Research question	What is the clinical and cost effectiveness of interventions (sleep hygiene, sedatives, melatonin) to improve sleep disturbance in children and young people with cerebral palsy?
Why this is needed	
Importance to 'patients' or the	Sleep disturbances including difficulties with falling or staying asleep and daytime sleepiness can all lead to significant reductions in quality of life for

[m] At the time of consultation (August 2016), melatonin did not have a UK marketing authorisation for use in children and young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

Research question	What is the clinical and cost effectiveness of interventions (sleep hygiene, sedatives, melatonin) to improve sleep disturbance in children and young people with cerebral palsy?
population	children and young people with cerebral palsy as well as their families. Poor sleep can also negatively impact on other comorbidities including behaviour and emotional difficulties, cognition, communication and epilepsy. Currently it is recommended firstly to identify and treat secondary causes of sleep disturbance such as pain or epilepsy. Where no cause is identified children and their families may be offered advice on sleep hygiene, a trial of melatonin or sedatives however there is minimal evidence of efficacy and safety of these interventions in the cerebral palsy population.
Relevance to NICE guidance	It is essential to explore the efficacy, acceptability and safety of these interventions to inform future updates to this NICE guidance and therefore improve quality of life and outcomes for these young people and their families.
Relevance to the NHS	Currently many of these children are trialled on different sedatives and/ or melatonin at significant cost to the NHS and potentially exposing children to side effects. The use of evidence based treatment programmes would be safer for children and may even be cost saving when considering potential gains in other areas such as reductions in behavioural and emotional difficulties. The improvements in quality of life in both the children and their families may also reduce the burden of care in primary and social care.
National priorities	N/A
Current evidence base	There is limited evidence in 4 moderate quality studies which demonstrated a clinically significant beneficial effect of melatonin compared with placebo for sleep latency however no effect was seen in sleep duration or episodic wakening. No information is available on the value of prolonged release preparations. There is no evidence to support or refute the use of sleep hygiene training or oral sedatives.
Equality	Half of all children and young people with cerebral palsy have communication difficulties and 1 in 10 are non-verbal. In addition half have learning disabilities. This group are therefore particularly vulnerable in being able to make their needs and level of distress known. Their families are also under strain caring for them. It is essential therefore that the quality of life of these children, young people and their families is optimised through ensuring effective management of sleep difficulties.
Feasibility	The proposed research would not require large numbers or long duration to assess efficacy. The expense needed to resolve the question would be warranted and appropriate guidance would prevent ineffective and potentially dangerous treatments being trialled out of desperation.
Other comments	As answering this question could potentially improve the quality of life for people with CP and their families it would be worth approaching SCOPE and carer's charities for support.

1 **Table 100: Research recommendation statements**

Criterion	Explanation
Population	Children and young people with cerebral palsy and sleep disturbances
Intervention	sleep hygiene programme standard and slow release melatonin sedative drugs
Comparator	no treatment placebo any other pharmacological or non-pharmacological intervention that is used to reduce sleep disturbance

Criterion	Explanation
Outcome	Quality of sleep using Sleep diary and Actigraphy Quality of life measures for children and young people with cerebral palsy and their families Cost effectiveness of various interventions Day time emotional wellbeing/lability Adverse effects/side effects
Study design	RCT +/– cross over
Timeframe	2 years

1

24 Assessment of mental health problems

Review question: In children and young people with cerebral palsy, what assessments are effective in identifying the presence of mental health problems?

24.1 Introduction

Children and young people with cerebral palsy are at greater risk of mental health problems such as depression and anxiety in comparison with the general age comparison population. Despite a growing awareness of this, in routine care the motor impairment is often the main focus of assessment and management, with signs and symptoms of mental health problems missed or misinterpreted.

Mental health problems may therefore not be picked up nor treated effectively early enough in their presentation and thus they may continue into adulthood. The presence of communication and/or cognitive difficulties can make the identification of mental health problems in the child/young person especially challenging.

There are many mental health assessment tools that are used in general clinical practice but not all of these are appropriate for use in children and young people with cerebral palsy, particularly if there are difficulties in communication and cognition and therefore current clinical practice varies to a great degree. It is essential that assessments that are sensitive to the symptoms of mental health problems in children and young people with cerebral palsy are identified for use in practice to help identification, allow timely, appropriate treatment thereby enabling improved outcomes.

The aim of this review is to determine what assessments are effective in identifying the presence of mental health problems in cerebral palsy.

24.2 Description of clinical evidence

The included studies aimed to assess reliability and validity of the following tools (Table 101).

Table 101: Description of tools assessed

Tool name	Key features
CHQ (child health questionnaire)	• CHQ is a measure of the physical and psychological health of children 5 years of age and older. • CHQ assesses physical functioning, behaviour, mental health, general health, social and family functioning, family cohesion, self-esteem, pain,and the impact of health issues on parental time and emotions. • Comprises 13-single and multi-item child health scales and was developed for children in the general population and for children with chronic conditions. • The parent form is available in 2 lengths - the CHQ-PF50 and the CHQ-PF28.
CHQ-PF50	• CHQ-PF50 has 13 single and multi-item scales that assess child health status over "the last four weeks", and a further global item assessing change in health "over the last year". • Assesses both physical and psychosocial well-being. • Responses are scored for each domain, producing a figure between 0 and 100, with higher scores indicating better health and well-being. Scales generate 2 summary scores, representing physical health (PhS) and psychosocial (PsS).
SDQ (strengths and difficulties	• The SDQ consists of 25 items, of which 4 record problem domains, each including 5 items, and 1 prosocial domain (scale) including 5 items.

Tool name	Key features
questionnaire)	• Each item can be answered with "not true", "somewhat true", or "certainly true" rated 0-2 for negatively worded items, and inversely 2-0 for positively worded items. • The problem domains are hyperactivity problems, conduct problems, emotional problems and peer problems. Prosocial behaviour consists of items such as being helpful and kind. Combining the 4 problem subscales (0-10) computes the Total Difficulties Score (TDS) (0-40). • The SDQ also includes an impact score (IS) which measures the impact of mental health problems. For each of the subscales, a score at or above the 90th percentile of the controls was defined as screened positive and a TDS at or above the 90th percentile as risk of having psychiatric disorder.

Five studies (Beckung 2008; McCollough 2009; McCollough 2008; Bjorgaas 2013; Parkes 2008) were included in this review that aimed to determine what assessments are effective in identifying the presence of mental health problems in cerebral palsy. Three studies were undertaken in the United Kingdom (McCollough 2009; McCollough 2008; Parkes 2008); 1 in Sweden (Beckung 2008); and 1 in Norway (Bjorgaas 2013).

The total sample size ranged between 56 and 818 children and young people with cerebral palsy and their families. Participants in the included studies ranged in age from 2 year to 18 years.

Three studies looked at the usefulness of the Child Health Questionnaire (CHQ) scale in a cerebral palsy population (Beckung 2008; McCollough 2009; McCollough 2008), and in particular, Beckung 2008 studied the association between this tool and GMFCS levels. The McCollough 2008 paper is a review that includes a total of 13 different studies reporting on the validity and reliability of CHQ. Ten of the included studies were based in the US, 2 in Australia, and 1 in Brazil.

The 2 remaining studies assessed the use of SDQ in a population of children with cerebral palsy, by reporting on its reliability (Parkes 2008) or by comparing it to the Kiddie-SADs instrument (Bjorgaas 2013).

No studies have been retrieved that reported on the other tools listed in the review protocol:

- Self‑report Mood and Feelings Questionnaire (MFQ)
- Hospital anxiety and depression scale (HADs)
- Beck Youth Inventories
- CP Child - Quality of Life Questionnaire
- Child Behaviour Checklist (CBCL)
- General Health Questionnaire (GHQ – DoH)

Validity designs were prioritised, and the following were considered as the main criteria for assessing the quality of each study, as reported by Jerosch-Herold 2005:

- Sample size
- Sampling methodology
- Blinding of raters
- Statistical analysis

For full details see protocol in Appendix D. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

24.2.11 Clinical evidence profile

2 Table 102 and Table 103 below present the mental health assessment tools and CHQ and
3 gross motor function classification system (GMFCS) levels correlation as reported by
4 Beckung 2008, respectively.

5

1 **Table 102: Clinical evidence: mental health assessment tools**

<table>
<tr><th>Tool assessed</th><th>Study reference</th><th>Results</th><th>Limitations of study</th></tr>
<tr><td>CHQ (Child Health Questionnaire)</td><td>McCollough 2009</td><td>For the total sample, 3 scales had a α-value below the 0.70 threshold. In relation to "behaviour", internal consistency declined by GMFCS levels, being adequate for children in levels I and II, but decreasing to 0.32 for children in Level 0. 5 scales had α-values 0.80 or higher. These scales were relatively stable across all levels of the GMFCS.
<table>
<tr><td>CHQ domain</td><td colspan="6">Scale reliability by GMFCS level</td></tr>
<tr><td></td><td>I</td><td>II</td><td>III</td><td>IV</td><td>V</td><td>Total sample</td></tr>
<tr><td>Mental health</td><td>0.77</td><td>0.63</td><td>0.70</td><td>0.76</td><td>0.69</td><td>0.72</td></tr>
</table></td><td rowspan="2">• The study included parent report alone. Child self-report (where possible) may have produced different findings.
• Not relevant whether observer/tester were appropriately trained or certified.
• There is no evidence of test-retest reliability
• Intertester reliability is not relevant for this questionnaire (i.e. is a self-administered questionnaire)</td></tr>
<tr><td>CHQ (Child Health Questionnaire)</td><td>McCollough 2008</td><td>
<table>
<tr><td>Reliability</td><td></td><td>PsH</td><td>PsS</td></tr>
<tr><td colspan="4">Internal consistency</td></tr>
<tr><td>McCarthy 2002</td><td>Cronbach ∝</td><td>0.81</td><td>-</td></tr>
<tr><td>Morales 2006</td><td>Cronbach ∝</td><td>0.60</td><td>-</td></tr>
<tr><td>Wake 2003</td><td>Cronbach ∝</td><td>∝ reported as ranging 0.75-0.97 across all scales</td><td></td></tr>
<tr><td colspan="4">Concurrent Validity</td></tr>
<tr><td>Adams 2005</td><td>Kendalls'</td><td>-0.01</td><td>0.09</td></tr>
<tr><td>McCarthy 2002</td><td>Spearman partial (GMFM)</td><td>-0.12</td><td>-</td></tr>
<tr><td>Morales 2006</td><td>Pearson's (GMFM)</td><td>-0.13</td><td>0.00</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Tool assessed</th><th>Study reference</th><th>Results</th><th>Limitations of study</th></tr>
<tr><td>SDQ (strengths and difficulties questionnaire)</td><td>Bjorgaas 2013</td><td>
<table>
<tr><th></th><th>Sensitivity</th><th>Specificity</th><th>PPV</th><th>NPV</th></tr>
<tr><td>Emotional symptoms vs. emotional disorders</td><td>1.00</td><td>0.79</td><td>0.36</td><td>1.00</td></tr>
<tr><td>Conduct problems vs. conduct disorder/ODD</td><td>0.50</td><td>0.67</td><td>0.13</td><td>0.93</td></tr>
<tr><td>Hyperactivity problems vs. ADHD/ADD</td><td>0.13</td><td>0.87</td><td>0.50</td><td>0.49</td></tr>
<tr><td>Total Difficulties Score vs. any psychiatric disorder</td><td>0.85</td><td>0.55</td><td>0.71</td><td>0.73</td></tr>
<tr><td>Peer problems vs. any psychiatric disorder</td><td>1.0</td><td>0.25</td><td>0.63</td><td>1.0</td></tr>
<tr><td>Impact score vs. any psychiatric disorder</td><td>0.74</td><td>0.65</td><td>0.74</td><td>0.65</td></tr>
</table>
</td><td>• The version of Kiddie-SADS used in the present study did not contain a section on ASD, which is a weakness since all children diagnosed with a psychiatric disorder screened positive for peer problems.
• Children with GMFCS V and intellectual disability were not included.
• Not relevant whether the observers/testers are appropriately trained or certified.
• Power of the study was not reported, but sample size is estimated to be reduced.</td></tr>
<tr><td>SDQ (strengths and difficulties questionnaire)</td><td>Parkes 2008</td><td>Validation of the SDQ instrument:
• The coefficients were generally satisfactory (mean 0.69) and all coefficients were similar to the author's validation study (Goodman 2001) with the exceptions of the conduct domain which was lower (0.46 compared to 0.63) and the prosocial behaviour domain which was higher (0.81 compared to 0.65).</td><td>• No relevant whether observer/tester were appropriately trained or certified.
• Test-retest reliability was not reported.
• Intertester reliability doesn't apply.</td></tr>
</table>

CP cerebral palsy, GMFCS gross motor function classification system, NPV negative predictive value, PPV positive predictive value, ADHD attention deficit hyperactivity disorder, ADD attention deficit disorder, ODD oppositional defiant disorder, ASD autism spectrum disorder, PsS health and psychosocial subscale, PhS physical subscale.

Table 103: Clinical evidence: CHQ and GMFCS levels correlation as reported by Beckung 2008

CHQ Dimension	GMFCS I	II	III	IV	V	P values
Physical functioning	94	94	100	78	46	0.0001
Bodily pain	80	70	70	60	60	0.0001
Behaviour	73	73	73	77	79	0.002
Mental health	75	75	75	75	75	0.96
Self-esteem	75	75	75	79	75	0.74
General Health	68	64	64	63	47	0.0001
Parent Impact-emotional	75	75	71	75	67	0.95
Parent impact-time	94	89	78	89	78	0.0001
Family activities	88	79	75	75	71	0.0001
Physical summary scale	51	47	49	41	32	0.0001
Psychosocial summary scale	49	49	50	52	52	0.04

CHQ child health questionnaire, GMFCS gross motor function classification system.

24.3 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations of tools to identify the presence of mental health problems were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

24.4 Evidence statements

24.4.1 Child Health Questionnaire (CHQ)

Two studies reported on the usefulness of the CHQ scale in a population of 2047 participants. Reliability ranged between 60% and 97%, and it varied between different GMFCS levels between 63% and 77%. The evidence did not show a statistically significant correlation between the mental health domain of the CHQ tool and GMFCS levels.

24.4.2 Strengths and Difficulties Questionnaire (SDQ)

Two studies reported on the usefulness of the SDQ scale in a total population of 874 participants. One of the 2 studies reported that sensitivity ranged between 13% and 100% depending on the domain assessed, with the domain ‘emotional symptoms’ scoring the highest. Specificity ranged between 25% and 87%. With ‘hyperactivity problems’ scoring the highest. The other study reported a reliability score of 69% for this scale.

24.4.3 Self-report Mood and Feelings Questionnaire (MFQ)

No evidence was retrieved for this tool.

24.4.4 Hospital anxiety and depression scale (HADs)

No evidence was retrieved for this tool.

24.4.5 Beck youth inventories

No evidence was retrieved for this tool.

24.4.6 CP Child - quality of life questionnaire

No evidence was retrieved for this tool.

24.4.7 GHQ - DoH

No evidence was retrieved for this tool.

24.5 Evidence to recommendations

24.5.1 Relative value placed on the outcomes considered

The aim of this review was to determine what assessments are effective in identifying the presence of mental health problems in cerebral palsy.

Sensitivity and specificity of the tools were prioritised as critical outcomes for decision-making.

24.5.2 Consideration of clinical benefits and harms

The Committee agreed that most commonly seen mental health problems in children and young people with cerebral palsy had been covered by NICE guidelines and the Committee made a recommendation to that effect.

The Committee decided it was important to provide some context and point out that children and young people with cerebral palsy have an increased prevalence of mental health problems, due to a number of factors including the primary interplay of the cerebral lesions and secondary social and environmental interaction. They noted that there was a lack of evidence on the prevalence of mental health problems in cerebral palsy. The Committee discussed how mental health problems are generally under recognised in the cerebral palsy population, particularly in individuals with problems of cognition and communication. Furthermore, the Committee agreed that children and young people with cerebral palsy have an increased prevalence of autism, ADHD as well as behaviours that challenge which can be triggered by other problems, such as the presence of chronic pain and sleep difficulties.

The Committee agreed that early recognition of mental health problems should be conducted in all settings, as some of the early signs might be more evident in non-medical situations. For example, the social and environmental challenges within education setting and family situation can be very different. The Committee therefore made a recommendation to this effect, in that all members of the health, social and educational multidisciplinary teams should consider, assess, or flag up problems and or concerns and reflection on these areas should occur at each consultation.

The Committee, however, recognised that assessment of these disorders can be challenging, especially in those children and young people who cannot communicate or have cognitive difficulties. Therefore, the Committee recommended that both health practitioners and carers should reflect on other possible causes for change in emotional state and/or behaviour such as acute or chronic pain, physical symptoms or social factors. These factors sometimes lead to misinterpretation of the signs and symptoms for mental health problems.

The Committee discussed the importance of early identification and timing of assessment, as they agreed that often mental health issues are only considered at the ‘annual review’. The Committee recommended referral for a specialist assessment when there are concerns about a mental health and psychological state is present.

With regards to the tools that aid identification of mental health problems, the Committee examined the evidence presented and agreed to recommend those validated in the literature, without being too prescriptive. This has been done to reflect the need to have everyone in the multidisciplinary team feeling confident and able/competent to record signs and symptoms that could indicate a mental health disorder. The Committee agreed that because it depends on who is doing the assessment, training in the use of standardised assessment tools is also equally important.

The Committee discussed how there was a lack of evidence about the prevalence of mental problems in this population, particularly in young people and young adults. They noted that improved guidance would allow greater access to suitable services for young people and young adults with cerebral palsy and therefore developed and prioritised a research recommendation to assess the prevalence of mental health problems in young people (up to the age of 25) with cerebral palsy.

24.5.3 Consideration of economic benefits and harms

Knowing the prevalence of mental health problems and the tools to identify them in children and young people with cerebral palsy may lead to better prediction, identification (and thus more timely management) and possibly prevention of mental health problems in this population. This has therefore, indirectly, potentially important resource implications. However, this review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

24.5.4 Quality of evidence

Main reason of bias in the included studies were no evidence on test/retest reliability and underpowered studies.

24.5.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee’s clinical experience.

24.5.6 Key conclusions

The Committee noted that the overall prevalence of mental health disorders in children and young people with cerebral palsy is higher than in the general population. Additionally, common impairments seen in children and young people with cerebral palsy, such as learning disabilities or communication difficulties, could jeopardise an accurate diagnosis. For this reason, the Committee noted that an early recognition was essential and that a referral should be done in cases where difficulties were present. The screening tools identified by the evidence have been validated in the cerebral palsy population and present with good sensitivity and specificity, therefore are considered to be effective for recording signs and symptoms that could indicate a mental health disorder.

24.6 Recommendations

103. Follow the relevant NICE guidelines when identifying and managing mental health problems and psychological and neurodevelopmental disorders in children and young people with cerebral palsy:

- depression in children and young people
- depression in adults
- generalised anxiety disorder and panic disorder in adults
- challenging behaviour and learning disabilities
- antisocial behaviour and conduct disorders in children and young people
- mental health problems in people with learning disabilities[n]
- autism in under 19s and autism in adults.
- attention deficit hyperactivity disorder.

104. Take into account that parents and familiar carers have a central role in recognising and assessing emotional difficulties and mental health problems in children and young people with cerebral palsy.

105. Recognise that children and young people with cerebral palsy have an increased prevalence of:

- mental health and psychological problems, including depression, anxiety and conduct disorders
- behaviours that challenge, which may be triggered by pain, discomfort or sleep disturbances
- neurodevelopmental disorders, including autism spectrum disorders (ASD) and attention deficit hyperactivity disorder (ADHD).

106. Recognise that emotional and behavioural difficulties (for example, low self-esteem) are reported in up to 1 in 4 children and young people with cerebral palsy.

107. Any multidisciplinary team should:

- recognise that mental health problems and emotional difficulties can be as important as physical health problems for children and young people with cerebral palsy
- explore such difficulties during consultations
- recognise that assessing psychological problems can be challenging in children and young people with communication difficulties or learning disabilities.

108. Think about and address the following contributory factors if a change in emotional state occurs in a child or young person with cerebral palsy:

- pain or discomfort (see sections 20.6, 21.6 and 22.6)
- frustration associated with communication difficulties
- social factors, such as a change in home circumstances or care provision.

[n] Publication expected September 2016; the consultation draft of the guideline can be viewed here

109. Use validated tools, such as the Child Health Questionnaire and the Strengths and Difficulties Questionnaire, to assess mental health problems in children and young people with cerebral palsy.

24.74 Research recommendations

8. What is the prevalence of mental health problems in young people (up to the age of 25) with cerebral palsy?

Table 104: Research recommendation rationale

Research question	What is the prevalence of mental health problems in young people (up to the age of 25) with cerebral palsy?
Why this is needed	
Importance to 'patients' or the population	There is a lack of evidence with regards to the prevalence of behavioural and mental health disorders in young people with cerebral palsy. There are a number of factors in young people with cerebral palsy that predispose to them being at greater risk of having behavioural and MH disorders. The presence of these difficulties has a marked impact on the individual's quality of life and challenges of care. Altered guidance would allow greater access of young people to suitable services. In addition, given the link between mental and physical health, improvement in mental health care could potentially influence physical health and comorbidity.
Relevance to NICE guidance	High priority: the research is essential to inform future updates of key recommendations in the guidance. The current committee were presented with little quality evidence to base the guidelines Knowledge of prevalence of mental health disorders influence many aspects of health and social care covered in this and a number of other guidelines.
Relevance to the NHS	The results may highlight the importance of routine screening tools for mental health problems in young people and young adults with cerebral palsy particularly at the point of transition. This may result in increased recognition of specific need within this population, subsequent interventions and development of specialist services for young adults with cerebral palsy.
National priorities	Not applicable
Current evidence base	There is little information about the prevalence of mental health disorder across all severities of cerebral palsy in adolescents and young adults. There is little evidence regarding the full range of factors that make certain individuals more at risk within this group
Equality	Knowledge of prevalence within the population of young people and young adults with cerebral palsy will guide any equalities considerations.
Feasibility	Prospective cohort study or cross sectional study of sufficient size to give sufficient power. Point prevalence means that this could be conducted over a short period.
Other comments	May be methodological problems in finding measures for participants with communication difficulties and/or cognitive impairment.

Table 105: Research recommendation statements

Criterion	Explanation
Population	Young people and young adults with cerebral palsy
Intervention	Behavioural rating scales
Comparator	N/A

Criterion	Explanation
Outcome	Prevalence of : Conduct disorders Anxiety Depression Neuro-developmental disorders including ADHD and autism
Study design	UK Prospective cohort study or cross sectional study of sufficient size to give sufficient power.
Timeframe	1-2 years

1

2

25 Management of mental health problems

Review question: What is the clinical and cost effectiveness of interventions to manage mental health problems in children and young people with moderate to severe cerebral palsy (GMFCS III-V)?

25.1 Introduction

Mental health problems in children and young people with moderate to severe cerebral palsy may be difficult to detect and treat appropriately. Mental health challenges often causes more distress for the child and family than their existing physical, developmental or cognitive disabilities and can markedly adversely affect the course of their holistic care. The higher prevalence of cognitive and communication difficulties in this group, together with potential drug interactions and side effect profiles mean that some forms of treatment may not be suitable, accessible or effective.

To compound this, the availability of suitable treatments for this group varies greatly and little is understood, even in specialist practice about which treatment to select from the range available. There is also the need to ensure treatments are cost effective within our health care system.

The first point of any pathway is to ensure information and guidance is provided for families, young people and practitioners regarding any appropriate management, particularly which treatments are both clinically and cost effective for children and young people with cerebral palsy. Therefore the scope of this review was focussed on these areas.

25.2 Description of clinical evidence

Two studies, a full RCT paper and an abstract for RCT, were included in the review (Whittingham 2014; Whittingham 2014). The 2 trials used the same population, study design and methods, but reported on different outcomes.

The aim of the studies was to investigate whether the parenting intervention, such as Stepping Stones Triple P (SSTP) and parent Acceptance and Commitment Therapy (ACT) improves child functional performance, child quality of life and parental psychological adjustment in families of children with cerebral palsy. Specifically, the participants were randomised in 3 groups:

1. The SSTP consisted of 6 (2 hour) group sessions plus 3 (30 minute) telephone consultations and was delivered by psychologists with accreditation in SSTP. SSTP sessions included strategies for building a positive parent-child relationship, encouraging desirable behaviour, teaching new skills and behaviours, managing misbehaviour, and managing high-risk situations. Parents made specific goals for change and were supported in enacting plans for managing challenging parenting situations.
2. Intervention SSTP + ACT: the ACT sessions (two 2-hour group sessions) preceded SSTP. ACT sessions included identifying values, mindfulness, cognitive diffusion (distancing from thoughts), acceptance of emotions, and making specific goals for acting on values.
3. Waiting list (WL)

The sample size in both studies was of 67 parents of children with a diagnosis of cerebral palsy, of whom 97% were reported to be mothers (mean age 38.7 ± 7.1 years). Among children, 64.2% were boys (mean age 5.3 ± 3 years).

Families where the parental role is only temporary (for example short-term foster placements) were not considered for this study.

4. The following relevant outcomes have been reported by the 2 papers:

- Child functional performance as measured by the Paediatric Evaluation of Disability Inventory (PEDI)
- Parental psychological adjustment measured by the Depression Anxiety Stress Scale (DASS)
- Child quality of life as measured by the Cerebral Palsy Quality of Life Scale (CP-QOL, parent report)
- Child behavioural and emotional problems as measured by the Eyberg Child Behaviour Inventory (ECBI)
- Strengths and Difficulties Questionnaire (SDQ), which produces 5 subscales (emotional symptoms, conduct problems, inattention/hyperactivity, peer problems, and prosocial behaviour).

Evidence from these are summarised in the clinical GRADE evidence profile below (Table 50: , Table 108, Table 109, Table 110).See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

25.2.15 Summary of included studies

A summary of the studies that were included in this review are presented in Table 106.

Table 106: Summary of included studies

Study	Intervention/Comparison	Population	Outcomes	Comments
Whittingham 2014 (full RCT)	Stepping Stones Triple P (SSTP) and parent Acceptance and Commitment Therapy (ACT)	67 parents of children with a diagnosis of CP	- Child behavioural and emotional problems as measured by the Eyberg Child Behaviour Inventory (ECBI) - Strengths and Difficulties Questionnaire (SDQ)	Limitations: • Participants blinded to treatment allocation- unclear • Individuals administering care blinded to treatment allocation - unclear • Investigators blinded to intervention - unclear • Investigators blinded to confounding factors - unclear Indirectness Does the study match the review protocol in terms of: •Population: yes (but only few participants with severe CP). •Intervention: not as specific as detailed in review protocol •Outcomes: yes •Indirectness: some Other information •Data extraction done with a structured abstract. Full version not available. •Whittingham 2014 and the present study used the same population and intervention, but not the
Whittingham 2014 (RCT abstract)	Stepping Stones Triple P (SSTP) and parent Acceptance and Commitment Therapy (ACT)	67 parents of children with a diagnosis of CP	- Child functional performance as measured by the Paediatric Evaluation of Disability Inventory (PEDI) - Parental psychological adjustment measured by the Depression Anxiety Stress Scale (DASS) - Child quality of life as measured by the Cerebral Palsy Quality of Life Scale (CP-QOL, parent report)	

Study	Intervention/Comparison	Population	Outcomes	Comments
				same outcome measures thus results vary.

CP cerebral palsy, RCT randomised controlled trial.

25.32 Clinical evidence profile

Table 107: Summary clinical evidence profile for SSTP compared to WL for mental health problems in cerebral palsy

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	WL	SSTP		
ECBI intensity	-	The mean ECBI intensity in the intervention groups was 15.43 higher (0.78 to 30.08 higher)	42 (1 study)	low[1,2]
ECBI problem	-	The mean ECBI problem in the intervention groups was 6.04 higher (2.20 to 9.89 higher)	42 (1 study)	low[1,2]
SDQ emotional symptoms	-	The mean SDQ emotional symptoms in the intervention groups was 1.33 higher (0.45 to 2.21 higher)	42 (1 study)	low[1,2]
SDQ conduct problems	-	The mean SDQ conduct problems in the intervention groups was 0.85 higher (0.23 lower to 1.72 higher)	42 (1 study)	low[1,2]
SDQ hyperactivity	-	The mean SDQ hyperactivity in the intervention groups was 0.73 higher (0.40 lower to 1.86 higher)	42 (1 study)	low[1,2]
SDQ peer problems	-	The mean SDQ peer problems in the intervention groups was 0.77 higher (0.10 lower to 1.65 higher)	42 (1 study)	low[1,2]
SDQ prosocial	-	The mean SDQ prosocial in the intervention groups was 0.44 lower (1.68 lower to 0.78 higher)	42 (1 study)	low[1,2]
SDQ impact	-	The mean SDQ impact in the intervention groups was 0.67 higher (1.14 lower to 2.50 higher)	42 (1 study)	low[1,2]

SDQ Strengths and Difficulties Questionnaire; ECBI Eyberg Child Behaviour Inventory; WL waiting list; SSTP Stepping Stones Triple P; ACT parent Acceptance and Commitment Therapy.

The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).
1 evidence was downgraded by 1 dues to unclear blinding of participants and investigators
2 majority of evidence has only 1 indirect aspect of PICO (intervention not clearly specified in the protocol)

Table 108: Summary clinical evidence profile for SSTP + ACT versus WL for mental health problems in cerebral palsy

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Control	SSTP + ACT versus WL		
DASS depression	-	The mean DASS depression in the intervention groups was 5.33 higher (95% CI not calculable)	45 (1 study)	low[1,2]
DASS stress	-	The mean DASS stress in the intervention groups was 5.50 higher (95% CI not calculable)	45 (1 study)	low[1,2]
CP-QOL acceptance	-	The mean CP-QOL acceptance in the intervention groups was 9.01 lower (95% CI not calculable)	45 (1 study)	low[1,2]
CP-QOL functioning	-	The mean CP-QOL functioning in the intervention groups was 8.72 lower (95% CI not calculable)	45 (1 study)	low[1,2]
ECBI intensity	-	The mean ECBI intensity in the intervention groups was 24.12 higher (10.22 to 38.03 higher)	45 (1 study)	low[1,2]
ECBI problem	-	The mean ECBI problem in the intervention groups was 8.30 higher (4.63 to 11.97 higher)	45 (1 study)	low[1,2]
SDQ emotional symptoms	-	The mean SDQ emotional symptoms in the intervention groups was 0.37 higher (0.46 lower to 1.21 higher)	45 (1 study)	low[1,2]
SDQ conduct problems	-	The mean SDQ conduct problems in the intervention groups was 0.43 higher (0.41 lower to 1.26 higher)	45 (1 study)	low[1,2]
SDQ hyperactivity	-	The mean SDQ hyperactivity in the intervention groups was 1.66 higher (0.55 to 2.77 higher)	45 (1 study)	low[1,2]
SDQ peer problems	-	The mean SDQ peer problems in the intervention	45 (1 study)	low[1,2]

		groups was 0.64 higher (0.18 lower to 1.46 higher)		
SDQ prosocial	-	The mean SDQ prosocial in the intervention groups was 0.16 lower (1.33 lower to 0.78 higher)	45 (1 study)	low[1,2]
SDQ impact	-	The mean SDQ impact in the intervention groups was 1.00 higher (0.66 lower to 2.67 higher)	45 (1 study)	low[1,2]

SDQ Strengths and Difficulties Questionnaire; ECBI Eyberg Child Behaviour Inventory; WL waiting list; SSTP Stepping Stones Triple P; ACT parent Acceptance and Commitment Therapy; DASS Depression Anxiety Stress Scales.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 dues to unclear blinding of participants and investigators
2 majority of evidence has only 1 indirect aspect of PICO (intervention not clearly specified in the protocol)

Table 109: Summary clinical evidence profile for SSTP + ACT compared to SSTP only for mental health problems in cerebral palsy

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	SSTP only	SSTP + ACT		
ECBI intensity	-	The mean ECBI intensity in the intervention groups was 8.69 higher (5.65 lower to 23.04 higher)	43 (1 study)	low[1,2]
ECBI problem	-	The mean ECBI problem in the intervention groups was 2.26 higher (1.61 lower to 6.12 higher)	43 (1 study)	low[1,2]
SDQ emotional symptoms	-	The mean SDQ emotional symptoms in the intervention groups was 0.95 lower (1.81 to 0.09 lower)	43 (1 study)	low[1,2]
SDQ conduct problems	-	The mean SDQ conduct problems in the intervention groups was 0.42 lower (1.28 lower to 0.44 higher)	43 (1 study)	low[1,2]
SDQ hyperactivity	-	The mean SDQ hyperactivity in the intervention groups was 0.93 higher (0.17 lower to 2.04 higher)	43 (1 study)	low[1,2]
SDQ peer problems	-	The mean SDQ peer problems in the intervention groups was 0.13 lower (0.98 lower to 0.61 higher)	43 (1 study)	low[1,2]
SDQ prosocial	-	The mean SDQ prosocial in the intervention groups was 0.29 higher (0.91 lower to 1.49 higher)	43 (1 study)	low[1,2]

SDQ impact	-	The mean SDQ impact in the intervention groups was 0.33 higher (1.42 lower to 2.07 higher)	43 (1 study)	low[1,2]

SDQ Strengths and Difficulties Questionnaire; ECBI Eyberg Child Behaviour Inventory; WL waiting list; SSTP Stepping Stones Triple P; ACT parent Acceptance and Commitment Therapy.
**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 dues to unclear blinding of participants and investigators
2 majority of evidence has only 1 indirect aspect of PICO (intervention not clearly specified in the protocol)

Table 110: Summary clinical evidence profile for SSTP + ACT compared to SSTP only at 6 months follow up for mental health problems in cerebral palsy

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	SSTP only	SSTP + ACT		
ECBI intensity Follow-up: 6 months	-	The mean ECBI intensity in the intervention groups was 15.3 lower (36.74 lower to 6.14 higher)	28 (1 study)	very low[1,2,3]
ECBI problem Follow-up: 6 months	-	The mean ECBI problem in the intervention groups was 2.61 lower (7.32 lower to 2.1 higher)	28 (1 study)	very low[1,2]
SDQ emotional symptoms Follow-up: 6 months	-	The mean SDQ emotional symptoms in the intervention groups was 0.08 higher (1.04 lower to 1.2 higher)	28 (1 study)	very low[1,2,4]
SDQ conduct problems Follow-up: 6 months	-	The mean SDQ conduct problems in the intervention groups was 0.31 higher (0.46 lower to 1.08 higher)	28 (1 study)	very low[1,2,3]
SDQ hyperactivity Follow-up: 6 months	-	The mean SDQ hyperactivity in the intervention groups was 0.36 lower (2.17 lower to 1.45 higher)	28 (1 study)	very low[1,2,3]
SDQ peer problems Follow-up: 6 months	-	The mean SDQ peer problems in the intervention groups was 0.78 lower (2.14 lower to 0.58 higher)	28 (1 study)	very low[1,2,3]
SDQ prosocial Follow-up: 6 months	-	The mean SDQ prosocial in the intervention groups was 0.26 lower (2.26 lower to 1.74 higher)	28 (1 study)	very low[1,2,4]
SDQ impact Follow-up: 6 months	-	The mean SDQ impact in the intervention groups was 0.67 lower (1.67 lower to 0.33 higher)	28 (1 study)	very low[1,2,3]

SDQ Strengths and Difficulties Questionnaire; ECBI Eyberg Child Behaviour Inventory; WL waiting list; SSTP Stepping Stones Triple P; ACT parent Acceptance and Commitment Therapy.

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 dues to unclear blinding of participants and investigators
2 majority of evidence has only 1 indirect aspect of PICO (intervention not clearly specified in the protocol)
3 evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID
4 evidence was downgraded by 2 due to very serious imprecision as 95%CI crossed 2 default MIDs

25.4 Economic evidence

No economic evaluations of interventions to manage mental health problems were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

This review question was not prioritised for de novo economic modelling. To aid consideration of cost-effectiveness relevant resource and cost use data are presented in Appendix G.

25.5 Evidence statements

25.5.1 SSTP compared to WL for mental health problems in cerebral palsy

One RCT with 67 participants found a statistically significant difference[o] in child behaviour problems in the SSTP group, when compared to waiting list (control group). Similarly, a statistically significant difference in emotional symptoms measured with SDQ scale was found between SSTP group and control. No difference was found in all other domains of the SDQ scale (conduct problems, hyperactivity, peer problems, prosocial, and impact).

25.5.2 SSTP + ACT versus WL for mental health problems in cerebral palsy

One RCT with 67 participants found a statistically significant difference in depression and stress when measured by the DASS scale in the SSTP +ACT group, when compared to waiting list (control group). Similarly, a statistically significant difference in acceptance and functioning, and in behaviour problems when measured by the CP-QOL scale and ECBI scale respectively in the SSTP +ACT group, when compared to waiting list (control group). A statistically significant difference was also found for the hyperactivity domain of the SDQ scale, favouring the intervention group. No difference was found in all other domains of the SDQ scale (emotional symptoms, conduct problems, peer problems, prosocial, and impact).

25.5.3 SSTP + ACT compared to SSTP only for mental health problems in cerebral palsy

One RCT with 67 participants found a statistically significant difference in emotional symptoms measured with SDQ scale between SSTP + ACT group and SSTP only group. No difference was found between the 2 groups in all other domains of the SDQ scale (hyperactivity, conduct problems, peer problems, prosocial, and impact) and ECBI scale.

[o] When possible, clinical beneficial effects were always reported and captured in the evidence statements. However, when the data did not allow for calculation/use of MIDs, the statistical significance was reported in the statements instead.

25.5.4.1 SSTP + ACT compared to SSTP only at 6 months follow up for mental health problems in cerebral palsy

25.5.4.1.1 ECBI intensity

One very low quality evidence RCT with 67 participants found that there might be a clinically harmful effect of SSTP +ACT compared to SSTP alone, but there is uncertainty around the estimate.

25.5.4.2.1 ECBI problem

One very low quality evidence RCT with 67 participants found that there is no clinically significant difference between the 2 interventions for this outcome.

25.5.4.3.1 SDQ emotional symptoms, conduct problems, hyperactivity, prosocial, impact

One very low quality evidence RCT with 67 participants found that there is no clinically significant difference between the 2 interventions for this outcome.

25.5.4.4.1 SDQ peer problems

One very low quality evidence RCT with 67 participants found that there might be a clinically harmful effect of SSTP +ACT compared to SSTP alone, but there is uncertainty around the estimate.

25.5.5 Adverse effects (side effects of meds – sedation, drowsiness, change in movement, worsening of seizures)

No evidence was found for this outcome.

25.5.6 Suicide risk

No evidence was found for this outcome.

25.5.7 Sleep quality

No evidence was found for this outcome.

25.6 Evidence to recommendations

25.6.1 Relative value placed on the outcomes considered

The aim of this review was to assess the clinical and cost effectiveness of interventions to manage mental health problems in children and young people with moderate to severe cerebral palsy (GMFCS III-V). The Committee indicated the following as the critical outcomes for decision-making:

- Health related quality of life
- Emotional health
- Adverse effects

25.6.2 Consideration of clinical benefits and harms

The Committee noted that the interventions included in the evidence are also used in the general population, and they are not specific to the cerebral palsy population.

The Committee agreed that if emotional and behavioural difficulties persist or there are concerns about the mental health of the child or young person with cerebral palsy, they should be referred for specialist psychological assessment and on-going management.

The Committee recognised that there was a lack of support for families and carers. Therefore, they agreed that when setting any mental health management plan it was essential to include parents and carers in goal setting and treatment protocols, as well as considering the specific needs of parents in coping with their child's mental health problems and behavioural difficulties.

The Committee also recognised that there were challenges specific to the cerebral palsy population, for example the specific central nervous system impairment as well as the prevalence of comorbidities, cognitive, communication difficulties and social care needs. Based on their experience, it was the view of the Committee that these have a great impact in the management of mental health problems and any challenge provided to care should be minimised by using individualised approaches.

The Committee agreed to refer to existing NICE guidelines on specific mental health problems (for example, Depression in children and young people and Depression in adults) for both pharmacological and psychological interventions. Because of the risk of movement abnormalities due to the side effect profile, the approach to psychotropic drug use in children and young people with disability must be cautious. In particular, the Committee recognised the importance of specifying that psychotropic drug treatment should not be considered without seeking specialist advice. This is because of potential comorbidities, Central Nervous System interactions and side effects that can occur particularly in the presence of cerebral palsy.

Emotional areas of the brain are closely related, anatomically, physiologically and biochemically, to motor areas of the brain from anatomical, physiological and biochemical basis and therefore careful assessment of all developmental areas is necessary before initiating any pharmacological treatment which should be regularly reviewed. An approach of 'start slow, go slow and avoidance of multiple drug prescription' was considered to be vital.

25.6.3 Consideration of economic benefits and harms

An intervention is more likely to be cost-effective if it used for the correct indication. If the wrong indication is targeted this will lead to a wasteful use of NHS resources; not only with regards to the intervention, but also, potentially, further downstream costs from adverse effects and reductions in quality of life. Therefore, the cost-effectiveness of an intervention to manage mental health problems will depend on whether the correct mental health problem has been identified prior to the initiation of treatment; hence accurate identification of the cause should be the first action.

The Committee acknowledged that pharmacological treatments (particularly tablet or capsule preparations of antidepressants) were relatively cheap compared to psychotherapy sessions. However, the Committee was uncomfortable recommending psychotropic drug treatments for children and young people with cerebral palsy given their potential misuse, side effects and drug interactions.

Consequently, the Committee made a recommendation to only consider pharmacological treatments upon specialist advice as inappropriate treatments could lead to further challenges particularly in the areas of communication and mobility. Moreover, pharmacological treatments that are recommended in other mental health related NICE guidance may not be as appropriate for some children and young people with cerebral palsy, because of their specific areas of brain impairment, which is why specialist advise should always be sought.

Overall, the Committee considered that although it is important to recognise and manage mental health difficulties, with the evidence provided they were unable to recommend any specific intervention. All programmes should be individualised to the patient, their family and their carers, taking into account the factors outlined above, including the pattern and severity of movement disorder, communication difficulties, comorbidities, social care needs, educational needs and any potential drug interactions.

There is in particular a paucity of information about young adult mental health difficulties in children and young people with cerebral palsy. Management should therefore continue to reflect the general principles as outlined above and set out in a variety of other NICE guidelines.

25.6.4 Quality of evidence

One RCT (2 papers) was included in the review. The quality of the evidence for this review ranged from low to very low. Main reasons of bias were: lack of or unclear blinding of investigators, difficulty assessing the imprecision of the estimates due to lack of information reported (95% CI, standard deviations, exact p-values).

25.6.5 Other considerations

The recommendations related to this evidence review were based on the Committee's clinical experience.

25.6.6 Key conclusions

The Committee concluded that knowing the cause of mental health problems is key to informing management. For this reason, the Committee were unable to use the findings from the clinical evidence review to inform their recommendations, as management would be individualised to the patient, potentially requiring specialist psychological assessment.

25.7 Recommendations

110. Refer the child or young person for specialist psychological assessment and ongoing management if emotional and behavioural difficulties persist or there are concerns about their mental health.

111. Work in partnership with the child or young person with cerebral palsy, and their parents and primary carers, when assessing and managing mental health problems and setting goals.

112. When making an individual management plan to address the mental health needs of a child or young person with cerebral palsy, take into account ways of providing support to parents or carers.

113. Recognise that there are specific challenges in managing and minimising the impact of mental health problems in children and young people with cerebral palsy. These include:

- communication difficulties
- comorbidities, particularly epilepsy and pain
- side effects and drug interactions of multiple medications (polypharmacy)
- specific social care needs.

25.8 Research recommendations

None identified for this topic.

26 Management of sensory and perceptual difficulties

Review question: In children and young people with cerebral palsy, what interventions are effective for managing difficulties in registering and processing of sensory and perceptual information?

26.1 Introduction

Many children and young people with cerebral palsy present with difficulties with registration and processing of sensory and perceptual information which may lead to functional difficulties that are not explained by alterations in muscle tone alone. There is little understanding of how impairment in the motor system directly or indirectly affects sensory and perceptual processing. Such difficulties include challenges in organising and planning movements, difficulties with navigating environments, dressing, self-care, handwriting, attention and concentration, as well as understanding multistep instructions.

Difficulties may arise from impairment of 1 or more of the sensory systems as part of the cerebral palsy: vision, hearing, touch, taste, smell, balance (the vestibular system) or position feedback / proprioception (knowing where one's body parts are in relation to one another). Or it may arise from difficulty in the way that sensory information is perceived and processed. These sometimes remain unrecognised or may not be identified until school age when children begin to learn to read, write and are expected to organise themselves within the classroom environment. This can lead to frustration and unwanted behaviours as children may fall behind their peers without strategies in place to move forwards; in some cases sensory and perceptual difficulties can be more limiting on function and independence than physical difficulties.

There is limited recognition and understanding of sensory and perceptual difficulties in children and young people with cerebral palsy despite their impact on function, independence and wellbeing. The aim of this evidence review is to assess interventions that are effective in managing difficulties in registering and processing of sensory and perceptual information in children and young people with cerebral palsy.The following sensory domains will be targeted:

- Tactile
- Vestibular
- Proprioception (somatosensory)
- Visual
- Auditory
- Gustatory
- Olfactory.

26.2 Description of clinical evidence

Four studies were included in this systematic review that aimed to identify interventions that are effective for the management of difficulties in processing sensory and perceptual information in children and young people with cerebral palsy.

Three randomised controlled trials (RCTs) (James 2015; Kuo 2016; Law 2011) and 1 pre- and post-intervention study (Bumin 2001) reported on the 4 following comparisons:

- Sensory-perceptual motor training versus home-based programme

- Child-focused versus context-focused approach
- Web-based multimodal therapy versus standard care
- Hand-arm intensive manual therapy (HABIT) + tactile training versus HABIT alone
- All studies included children with cerebral palsy, and sample sizes ranged between 20 and 270 participants.
- Follow-up times varied between immediate post-intervention measurement and 9 months.
- A range of scales was used in the studies to report on the following outcomes indicated in the protocol:
- Improvement in processing sensory and perceptual information
- Goal attainment scales
- Quality of life, reported as participation and activities of daily living

The evidence did not show results for improvement in psychological wellbeing (anxiety and depression) or wellbeing of parents/carers.

For full details see review protocol in Appendix E. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

See Appendix H for the GRADE profiles and Table 112, Table 113, Table 114 and Table 115 for the summarised GRADE clinical evidence profile of the included studies.

26.2.18 Summary of included studies

A summary of the studies that were included in this review are presented in Table 111.

Table 111: Summary of included studies

Study	Intervention/Comparison	Population	Outcomes	Comments
Bumin, 2001	The intervention group received SPM training individually and in groups. The control group received a home-based programme.	N=41 children with spastic diplegic CP	Sensory integration as measured by The Ayres SCSIT Activities of daily living as measured by the PAT	Pre/post-test study design. No follow-up.
James, 2015	Mitii, a web-based multimodal therapy programme and standard care (consultative sessions with medical and allied health professionals).	N=270 children and young people with unilateral CP	AMPS Self-perceived occupational performance, as measured by the COMP Visual perception as measured by the TVPS-3	RCT. Measures taken at baseline and 20 weeks after intervention.
Kuo, 2016	HABIT, which is a form of intensive bimanual training. HABIT + T; with specific training components that encompassed tactile discrimination and matching.	N= 20 children and young people with congenital USCP	Tactile spatial resolution as measured by the GOT Sterognosis, as measured by the Manual Form Perception Test Static TPD, performed by using Disk-criminator Tactile perception, as measured by the SWM	RCT with pre-test and immediate post-test measures.
Law, 2011	Child-focused approach group: children were provided therapy tailored	N=128	Capability and performance of functional tasks as measured by the	RCT with 6 and 9 months follow up.

Study	Intervention/Comparison	Population	Outcomes	Comments
	to their specific impairments. Context- focused approach: by using the Canadian Occupational Performance Measure, parents were asked to identify in their children motor-based tasks in which their children had difficulty accomplishing.		PEDI GMFM-66 Dimensions of empowerment in the parents, as measured by The Family Empowerment Scale Participation in everyday activities Assessment of preschool children's participation	

CP cerebral palsy, RCT randomised controlled trial, GMFM gross motor function measure, PEDI Paediatric Evaluation of Disability Inventory scale, SWM Semmes-Weinstein, SPM sensory – perceptual motor, SCSIT Southern California Sensory Integration Test, PAT Physical Activity Test, AMPS assessment of motor and process skills, COMP Canadian Occupational Performance Measure, MiTii 'Move it to Improve it', TVPS – 3 Test of Visual Perceptual Skills, HABIT Hand-arm intensive manual therapy, USCP unilateral spastic cerebral palsy, GOT grating Orientation Task.

26.37 Clinical evidence

Table 112: Clinical evidence summary for sensory-perceptual motor training compared to home-based programme

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	Home-based programme	Sensory-perceptual motor training		
Individual versus group - double tactile stimuli perception (DTS) The Ayres Southern California Sensory Integration Test (SCSIT)	-	The mean individual versus group - double tactile stimuli perception (DTS) in the intervention groups was 1 lower (2.99 lower to 0.99 higher)	32 (1 study)	very low[1,2]
Individual versus group - localization of tactile stimuli (LTS) The Ayres Southern California Sensory Integration Test (SCSIT)	-	The mean individual versus group - localization of tactile stimuli (LTS) in the intervention groups was 1.29 higher (2.49 lower to 5.07 higher)	32 (1 study)	very low[1,2]
Individual versus group - graphestesia (GRA) The Ayres Southern California Sensory Integration Test (SCSIT)	-	The mean individual versus group - graphestesia (GRA) in the intervention groups was 0.25 lower (1.49 lower to 0.99 higher)	32 (1 study)	very low[1,3]
Individual versus group - kinaesthesia (KIN) The Ayres Southern	-	The mean individual versus group - kinaesthesia (KIN) in the intervention groups was	32 (1 study)	very low[1,2]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
California Sensory Integration Test (SCSIT)		11.68 lower (20.51 to 2.85 lower)		
Individual versus group - finger identification (FI) The Ayres Southern California Sensory Integration Test (SCSIT)	-	The mean individual versus group - finger identification (FI) in the intervention groups was 1.44 higher (0.42 lower to 3.3 higher)	32 (1 study)	very low[1,2]
Individual versus group - manual form perception (MFP) The Ayres Southern California Sensory Integration Test (SCSIT)	-	The mean individual versus group - manual form perception (MFP) in the intervention groups was 0.06 higher (0.3 lower to 0.42 higher)	32 (1 study)	very low[1,3]
Individual versus group - design copying (DC) The Ayres Southern California Sensory Integration Test (SCSIT)	-	The mean individual versus group - design copying (DC) in the intervention groups was 0.06 higher (1.27 lower to 1.39 higher)	32 (1 study)	very low[1,3]
Individual versus group - position in space (PS) The Ayres Southern California Sensory Integration Test (SCSIT)	-	The mean individual versus group - position in space (PS) in the intervention groups was 0.38 higher (1.16 lower to 1.92 higher)	32 (1 study)	very low[1,2]
Individual versus group - imitation of posture (IP) The Ayres Southern California Sensory Integration Test (SCSIT)	-	The mean individual versus group - imitation of posture (IP) in the intervention groups was 0.62 higher (0.62 lower to 1.86 higher)	32 (1 study)	very low[1,2]
Individual versus group - motor accuracy (MAC) The Ayres Southern California Sensory Integration Test (SCSIT)	-	The mean individual versus group - motor accuracy (MAC) in the intervention groups was 4.48 lower (15.77 lower to 6.81 higher)	32 (1 study)	very low[1,2]
Individual versus group - right-left discrimination (RLD) The Ayres Southern California Sensory Integration Test (SCSIT)	-	The mean individual versus group - right-left discrimination (RLD) in the intervention groups was 1.25 lower (3.14 lower to 0.64 higher)	32 (1 study)	very low[1,2]
Individual versus group - physical	-	The mean individual versus group - physical	32	very low[1,3]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
activity test (PA)		activity test (PA) in the intervention groups was 7.31 lower (19.34 lower to 4.72 higher)	(1 study)	

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 2 due to moderate selection bias, weak study design, unclear blinding, weak data collection methods, moderate attrition bias, unclear intervention integrity.
2 evidence was downgraded by 1 due to serious imprecision as 95%CI crossed 1 default MID
3 evidence was downgraded by 2 due to very serious imprecision as 95%CI crossed 2 default MIDs

Table 113: clinical evidence summary for child-focused versus context-focused approach

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	context-focused approach	Child-focused		
paediatric evaluation of disability inventory (PEDI) - Self-care (functional skill scale) at 6 mo Follow-up: 6 months	-	The mean paediatric evaluation of disability inventory (PEDI) - self-care (functional skill scale) at 6 mo in the intervention groups was 2.49 higher (3.25 lower to 8.23 higher)	128 (1 study)	low[1,2]
paediatric evaluation of disability inventory (PEDI) - Self-care (functional skill scale) at 9 mo. Follow-up: 9 months	-	The mean paediatric evaluation of disability inventory (PEDI) - self-care (functional skill scale) at 9 mo. in the intervention groups was 0.11 higher (6.22 lower to 6.44 higher)	128 (1 study)	moderate[1,2]
paediatric evaluation of disability inventory (PEDI) - Self-care (caregiver assistance scale) at 6 mo. Follow-up: 6 months	-	The mean paediatric evaluation of disability inventory (PEDI) - self-care (caregiver assistance scale) at 6 mo. in the intervention groups was 0.58 lower (9.2 lower to 8.04 higher)	128 (1 study)	moderate[1]
paediatric evaluation of disability inventory (PEDI) - Self-care (caregiver assistance scale) at 9 mo. Follow-up: 9 months	-	The mean paediatric evaluation of disability inventory (PEDI) - self-care (caregiver assistance scale) at 9 mo. in the intervention	128 (1 study)	moderate[1]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
		groups was 1.28 higher (7.78 lower to 10.34 higher)		
paediatric evaluation of disability inventory (PEDI) - Mobility (functional skill scale) at 6 mo. Follow-up: 6 months	-	The mean paediatric evaluation of disability inventory (PEDI) - mobility (functional skill scale) at 6 mo. in the intervention groups was 1.17 higher (7.27 lower to 9.61 higher)	128 (1 study)	moderate[1]
paediatric evaluation of disability inventory (PEDI) - Mobility (functional skill scale) at 9 mo. Follow-up: 9 months	-	The mean paediatric evaluation of disability inventory (PEDI) - mobility (functional skill scale) at 9 mo. in the intervention groups was 1.52 higher (7.26 lower to 10.3 higher)	128 (1 study)	moderate[1]
paediatric evaluation of disability inventory (PEDI) - Mobility (caregiver assistance scale) at 6 mo. Follow-up: 6 months	-	The mean paediatric evaluation of disability inventory (PEDI) - mobility (caregiver assistance scale) at 6 mo. in the intervention groups was 0.42 higher (9.64 lower to 10.48 higher)	128 (1 study)	moderate[1]
paediatric evaluation of disability inventory (PEDI) - Mobility (caregiver assistance scale) at 9 mo. Follow-up: 9 months		The mean paediatric evaluation of disability inventory (PEDI) - mobility (caregiver assistance scale) at 9 mo. in the intervention groups was 3.18 higher (7.25 lower to 13.61 higher)	128 (1 study)	moderate[1]
Gross Motor Function Measure (GMFM) - at 6 mo Follow-up: 6 months	-	The mean gross motor function measure (GMFM) - at 6 mo in the intervention groups was 1.44 lower (16.63 lower to 13.75 higher)	128 (1 study)	moderate[1]
Gross Motor Function Measure (GMFM) - at 9 mo Follow-up: 9 months	-	The mean gross motor function measure (GMFM) - at 9 mo in the intervention groups was 2.73 higher (2.33 lower to 7.79 higher)	128 (1 study)	low[1,2]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
family empowerment scale (FES) - at 6 mo Follow-up: 6 months	-	The mean family empowerment scale (FES) - at 6 mo in the intervention groups was 0.07 higher (0.1 lower to 0.24 higher)	128 (1 study)	low[1,2]
family empowerment scale (FES) - at 9 mo Follow-up: 9 months	-	The mean family empowerment scale (FES) - at 9 mo in the intervention groups was 0.15 higher (0.01 lower to 0.31 higher)	128 (1 study)	low[1,2]
assessment of preschool children's participation - APCP play at 6 mo. Follow-up: 6 months	-	The mean assessment of preschool children's participation – APCP play at 6 mo. in the intervention groups was 0.08 higher (0.45 lower to 0.61 higher)	128 (1 study)	moderate[1]
assessment of preschool children's participation - APCP play at 9 mo. Follow-up: 9 months	-	The mean assessment of preschool children's participation - APCP play at 9 mo. in the intervention groups was 0.18 lower (0.7 lower to 0.34 higher)	128 (1 study)	moderate[1]
assessment of preschool children's participation - APCP skill development at 6 mo. Follow-up: 6 months	-	The mean assessment of preschool children's participation - APCP skill development at 6 mo. in the intervention groups was 0.05 lower (0.45 lower to 0.35 higher)	128 (1 study)	moderate[1]
assessment of preschool children's participation - APCP skill development at 9 mo. Follow-up: 9 months	-	The mean assessment of preschool children's participation - APCP skill development at 9 mo. in the intervention groups was 0.02 higher (0.36 lower to 0.4 higher)	128 (1 study)	moderate[1]
assessment of preschool children's participation - APCP social activities at 6 mo. Follow-up: 6 months	-	The mean assessment of preschool children's participation - APCP social activities at 6 mo. in the intervention groups was 0 higher (0.36 lower to 0.36	128 (1 study)	moderate[1]

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
		higher)		
assessment of preschool children's participation - APCP social activities at 9 mo. Follow-up: 9 months	-	The mean assessment of preschool children's participation - APCP social activities at 9 mo. in the intervention groups was 0.02 higher (0.33 lower to 0.37 higher)	128 (1 study)	moderate[1]
assessment of preschool children's participation - APCP active physical activities at 6 mo. Follow-up: 6 months	-	The mean assessment of preschool children's participation - APCP active physical activities at 6 mo. in the intervention groups was 0.07 higher (0.35 lower to 0.49 higher)	128 (1 study)	moderate[1]
assessment of preschool children's participation - APCP active physical activities at 9 mo. Follow-up: 9 months	-	The mean assessment of preschool children's participation - APCP active physical activities at 9 mo. in the intervention groups was 0.09 higher (0.39 lower to 0.57 higher)	128 (1 study)	moderate[1]

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 due to high level of performance bias and moderate level of detection bias.
2 evidence was downgraded by 1 due to serious imprecision as 95%CI crossed 1 default MID

Table 114: clinical evidence summary for web-based multimodal therapy compared to standard care

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	standard care	Web-based multimodal therapy		
Assessment of Motor and Process Skills (AMPS) - motor skills Follow-up: 3 months	-	The mean assessment of motor and process skills (AMPS) - motor skills in the intervention groups was 0.27 higher (0.02 to 0.52 higher)	102 (1 study)	low[1,2]
Assessment of Motor and Process Skills (AMPS) - processing skills Follow-up: 3 months	-	The mean assessment of motor and process skills (AMPS) - processing skills in the intervention groups was 0.31 higher (0.14 to 0.48 higher)	102 (1 study)	low[1,2]
Canadian	-	The mean Canadian	102	low[1,2]

Occupational Performance Measure (COPM) Follow-up: 3 months		occupational performance measure (COPM) in the intervention groups was 1.28 higher (0.68 to 1.88 higher)	(1 study)	
Test of Visual Perceptual Skill (non-motor) 3rd edition (TVPS-3) Follow-up: 3 months	-	The mean test of visual perceptual skill (non-motor) 3rd edition (TVPS-3) in the intervention groups was 8.83 higher (1.83 to 15.83 higher)	102 (1 study)	low[1,2]

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 due to unclear/unknown performance bias and detection bias.
2 evidence was downgraded by 1 due to serious imprecision as 95%CI crossed 1 default MID

Table 115: clinical evidence summary for hand-arm intensive manual therapy compared to hand-arm intensive manual therapy + tactile training

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk		
	hand-arm intensive manual therapy + tactile training	Hand-arm intensive manual therapy		
Grating Orientation Task (GOT)	-	The mean grating orientation task (GOT) in the intervention groups was 0.46 higher (0.06 to 0.86 higher)	20 (1 study)	low[1,2]
Sterognosis	-	The mean sterognosis in the intervention groups was 1.17 lower (2.41 lower to 0.07 higher)	20 (1 study)	low[1,2]
Two-point discrimination thumb, mm (TPD)	-	The mean 2-point discrimination thumb, mm (TPD) in the intervention groups was 0.03 higher (0.04 lower to 0.1 higher)	20 (1 study)	low[1,2]
Semmes-Weinstein monofilaments (SWM)	-	The mean semmes-weinstein monofilaments (SWM) in the intervention groups was 1.1 lower (2.98 lower to 0.78 higher)	20 (1 study)	low[1,2]

**The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).*
1 evidence was downgraded by 1 due to unclear/unknown performance bias, attrition bias, and detection bias.
2 evidence was downgraded by 1 due to serious imprecision as 95%CI crossed 1 default MID

26.4 Economic evidence

No economic evaluations of interventions to manage difficulties in registering and processing of sensory and perceptual information were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

This review question was not prioritised for de novo economic modelling. However, the interventions under consideration vary in the resources and costs required, for example sensory integration could be implemented at home by the family or carer, whereas regular occupational or psychological sessions would incur high staff costs. According to NHS Reference Costs 2015 the cost per occupational therapy attendance is £67 (WF01A, Non-Admitted Face to Face Attendance, Follow-up, 651) whilst the cost per psychotherapy attendance is £174 (WF01A, Non-Admitted Face to Face Attendance, Follow-up, 713).

26.5 Evidence statements

26.5.1 Sensory-perceptual motor training versus home-based programme

Very low quality evidence from 1 study with 41 participants found that there is no clinically significant difference between sensory-perceptual motor training and home-based programme when measuring improvement in processing sensory and perceptual information using the Ayres Southern California Sensory Integration Test.

26.5.2 Child-focused versus context-focused approach

Moderate quality evidence from 1 study with 128 participants found that there is no clinically significant difference between child-focused and context-focused approach when measuring: 1) Gross Motor Function, 2) improvement in self-care or mobility using the Paediatric Evaluation of Disability Inventory scale, 3) improvement using the Family Empowerment scale, and 4) improvement in participation using the Assessment of Pre-school Children Participation scale, at either 6 months or 9 months follow-up.

26.5.3 Web-based multimodal therapy versus standard care

Low quality evidence from 1 study with 270 participants found that there is a clinically beneficial effect of web-based multimodal therapy compared to standard care for improvement in: 1) motor and processing skills (both measured with the Assessment of Motor and Processing Skills scale) and 2) the Canadian Occupational Performance scale at 3 months follow-up.

The same study reported no clinically significant difference between web-based multimodal therapies compared to standard care when measuring visual perceptual skills at 3 months follow-up.

26.5.4 Hand-arm intensive manual therapy (HABIT) + tactile training versus HABIT alone

Low quality evidence from 1 study with 20 participants found that there is a clinically beneficial effect of tactile training in addition to manual therapy compared to manual therapy alone for improvement in grating orientation task.

The same study demonstrated no clinically significant difference between tactile training in addition to manual therapy compared to manual therapy alone when measuring stereognosis, the 2-point discrimination, and cutaneous sensation levels (using Semmes-Weinstein monofilaments test).

26.6 Evidence to recommendations

26.6.1 Relative value placed on the outcomes considered

The aim of this review was to identify interventions that are effective for the management of difficulties in processing sensory and perceptual information in children and young people with cerebral palsy. The Committee identified the following as the critical outcomes for decision-making:

- improved sensory and perceptual function
- health related quality of life
- improved psychological wellbeing

26.6.2 Consideration of clinical benefits and harms

The Committee acknowledged the evidence presented and was not aware of any important study missed, however they also agreed that the population of interest was not always well defined in the included studies.

With regards to the interventions reported in the included studies, the Committee agreed that they did not reflect current practice in the population of children and young people with cerebral palsy. The Committee noted that the evidence was of too low quality and non-specific to allow them to recommend any particular therapeutic approach. Equally, they thought that the specific interventions reviewed were best applied in a research rather than a clinical setting.

However, the Committee noted some key principles that could be applied to rehabilitation or treatment plans and agreed to incorporate these in the recommendations for this review. The Committee agreed not to recommend any particular interventions or associated resources used in current UK clinical practice as these would be individualised to the patient. This is because sensory and perceptual problems vary considerably in their complexity and presentation.

Firstly, the Committee wanted to highlight that children and young people with cerebral palsy may have sensory and perceptual issues which compound their physical difficulties. However, they noted that in practice it is often difficult to separate signs and symptoms of sensory and motor impairment. For this reason, it is important for clinicians to not only focus on motor difficulties during assessment, but to consider sensory difficulties and their possible impact on function, activity and participation. Given the complexity of most cases and the number of comorbidities involved, the assessment of such problems is not easy in cerebral palsy, and therefore undertaking research and measuring clinically beneficial effects is challenging. The Committee wanted to reiterate the importance of regular assessment of children with motor disabilities, in particular the need for considering and looking for potential sensory processing problems. The Committee highlighted how there was be considerable variation in understanding and practice with regards to this aspect of management. Therefore, they agreed that a recommendation was needed to inform what this is, why it is important, and what the impact is.

The Committee recognised that there was a paucity of evidence about specific clinical interventions that work for this population, and decided that this should also be explained to families. In particular, the web-based approach presented was carried out in a limited population of children with gross motor function classification system (GMFCS) levels I and II. Therefore, though they considered it was important to develop its potential further, the Committee did not feel confident to generalise this intervention to the whole cerebral palsy population. The Committee however, noted that interventions that reflect on a combination of challenges such as motor, sensory, communication and cognition should be functionally oriented in their implementation.

The Committee discussed the importance of a multi-disciplinary approach to these difficulties, as well as the need to allow the young person to choose and be aware of his/her choices and what the problems may be. In addition, they recognised the importance of explaining to parents and carers why their child may be having these difficulties, for example by explaining that many factors usually contribute to the overall picture and it is not only due to motor control, tightness or weakness.

The Committee discussed that a wide variety of interventions without clear evidence base were being used in clinical practice in children and young people with cerebral palsy and these difficulties. Therefore, the Committee agreed to develop a research recommendation to assess the clinical and cost effectiveness of interventions to manage specific sensory and perceptual difficulties.

26.6.3 Consideration of economic benefits and harms

The Committee highlighted that parents and carers sometimes focus on low quality evidence to request interventions that are costly and potentially ineffective. Consequently, the Committee made a recommendation to explain to parents and carers that there is a lack of evidence to support specific interventions.

On the other hand, the Committee agreed that if sensory and perceptual problems were not identified and managed appropriately, there may be further downstream difficulties that could, for example, negatively impact on areas such as eating and drinking, communication and education. The Committee recognised that when sensory and perceptual problems are targeted correctly, therapy can improve a patient's health-related quality of life, potentially leading to a cost-effective use of NHS resources.

The Committee acknowledged that there was strong evidence to suggest web based interventions were effective in managing difficulties in registering and processing of sensory and perceptual information. They also agreed web based interventions could be implemented at home at zero monetary cost, providing a cost-effective intervention. However, the Committee noted web based interventions would be limited to GMFCS levels I and II.

Consequently, the Committee recommended a functional approach led by occupational therapists, physiotherapists and/or psychologists. The Committee were unable to describe the resource use these sessions would incur as the health care professional leading those sessions and frequency they are performed would depend on the complexity and goals of the patient.

Overall, the Committee considered the benefits of an individualised approach to outweigh the costs of therapy, given that sensory and perceptual problems are correctly identified.

26.6.4 Quality of evidence

Quality of the evidence ranged between moderate and very low, due mainly to selection bias, detection bias and performance bias. When possible, clinical beneficial effects were always reported and captured in the evidence statements. However, when the data did not allow for calculation or use of MIDs, the statistical significance was reported in the statements instead.

26.6.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

26.6.6 Key conclusions

The Committee concluded that many children and young people with cerebral palsy will have sensory or perceptual difficulties; these should be considered when functional difficulties are greater than those expected from the child's or young person's physical examination.

Sensory and perceptual difficulties can compound physical difficulties and should be considered within the context of motor and cognitive function.

A functional, goal-orientated, individualised programme should be developed in partnership with the child or young person and/or their parents and carers to take into account the complexity and variety of the way in which these difficulties present.

There is a lack of evidence to support specific interventions; parents and carers should be aware of this and that some interventions are based on no evidence when making decision about different types of treatment.

26.7 Recommendations

114. Explain to children and young people with cerebral palsy and their parents or carers that difficulties with learning and movement may be exacerbated by difficulties with registering or processing sensory information. These may include:

- primary sensory disorders, such as the way visual or hearing information is processed
- complex disorders of sensory processing and perception, such as planning movements.

115. For children and young people with cerebral palsy who have difficulties with processing sensory and perceptual information:

- agree a functional, goal-orientated, individualised programme in partnership with parents or carers
- explain to parents or carers that there is a lack of evidence to support specific interventions.

26.8 Research recommendations

9. What is the clinical and cost effectiveness of interventions to manage specific sensory and perceptual difficulties?

Table 116: Research recommendation rationale

Research question	What is the clinical and cost effectiveness of interventions to manage specific sensory and perceptual difficulties?
Why this is needed	
Importance to 'patients' or the population	Many children and young people with cerebral palsy present with difficulties in registering and processing sensory and perceptual information which may lead to functional difficulties that are not explained by alterations in muscle tone alone. There is insufficient understanding of how motor impairment impacts on sensory and perceptual processing. Although these difficulties impact on many daily activities and independence skills they are under recognised; there is limited evidence about the prevalence and impact of sensory and perceptual difficulties in this population and insufficient evidence about interventions. A wide variety of interventions without clear evidence base are used in clinical

Research question	What is the clinical and cost effectiveness of interventions to manage specific sensory and perceptual difficulties?
	practice in children and young people with cerebral palsy and these difficulties. The disparity in their use can be confusing for children and young people with cerebral palsy and their families and clinicians.
Relevance to NICE guidance	There is a need for evidence based interventions in this area. This would be used to inform future updates of key recommendations in this guideline.
Relevance to the NHS	Identifying and addressing these difficulties will impact on therapy provision and resources however this would be offset by increased social participation, quality of life and improved workplace productivity in the future. No economic evaluations of interventions to manage difficulties in registering and processing of sensory and perceptual information were identified in the literature search conducted for this guideline.
National priorities	N/A
Current evidence base	Four studies (3 RCTs and 1 pre- and post-intervention study) of very low, low and moderate evidence were identified for the NICE guideline review. The identified studies did not necessarily look at the most commonly used interventions available. One study did not look specifically at perceptual and sensory difficulties. There is therefore limited evidence to determine the effectiveness of sensory and perceptual interventions in children and young people with cerebral palsy. Relevant research to resolve this uncertainty is needed.
Equality	N/A
Feasibility	
Other comments	Due to the nature of the interventions well designed non-experimental descriptive studies to evaluate patient experience and expert opinions may be required to understand the nature of these difficulties prior to randomised controlled trials or large cohort studies to understand both the prevalence of and effects of interventions in this population.

1

2 **Table 117: Research recommendation statements**

Criterion	Explanation
Population	Children and young people with cerebral palsy with sensory and perceptual difficulties
Intervention	A variety of specific interventions: Sensory integration (traditional method) (sight, sound, taste, smell, touch, balance, body position, tactile, sensory diet, sensory lifestyle) Goal-directed therapy /Activity focussed and goal directed therapy/Task-orientated therapy Occupational therapy (Activity analysis, CO-OP approach (cognitive orientation to daily occupational performance) Computer based programmes (for example, videogame therapy, computer enhanced therapy to improve balance) Neuro-psychological and educational psychological support (behavioural training)
Comparator	Comparative outcomes vs no interventions or vs interventions listed above
Outcome	QoL for children and young people with cerebral palsy and parents/carers Participation Motor planning tools

Criterion	Explanation
	Improvement in psychological wellbeing Wellbeing of parents/carers Goal attainment scales
Study design	RCT
Timeframe	2 years

1

27 Other comorbidities in cerebral palsy

Review question: In infants, children and young people with cerebral palsy what is the prevalence of important comorbidities with a view to informing early identification?

27.1 Introduction

Children and young people with cerebral palsy have complex and wide ranging needs. It is essential that health care professionals are aware of the variety of comorbidities commonly associated with cerebral palsy to enable these to be identified early and appropriately managed.

Current clinical practice varies considerably and often there is a focus on management of the obvious motor impairment while other issues go unrecognised and unmanaged. Developmental comorbidities can cause unnecessary distress and reduced participation for children and young people with cerebral palsy and their families and carers. More obviously clinical comorbidities have a direct impact on the health of the child or young person and therefore their quality of life.

Some comorbidities such as learning disabilities and emotional difficulties may not be readily diagnosed in early childhood. Health care professionals need to be aware of a change in potential developmental and clinical comorbidities becoming important as the child grows and develops.

Under-recognition is as a problem in specific areas including identification of behavioural, cognitive and learning difficulties, sensory impairment including hearing and vision, communication difficulties as well as more medical issues, such as vomiting and reflux, constipation and epilepsy.

An increased understanding of the nature and prevalence of these comorbidities will aid in early recognition and guide appropriate management, and where necessary onward specialist referral.

The objective of this systematic review is:

- To determine the prevalence of the most commonly occurring comorbidities associated with cerebral palsy and relevant subgroups
- To assist health care professionals in recognising important comorbidities in children and young people with cerebral palsy and identifying subgroups most at risk
- To improve onward specialist referral and management
- For parental information and reassurance.

27.2 Description of clinical evidence: cognitive and learning disabilities

Four studies have been included for this review that reported prevalence data of cognitive and learning disabilities among children with cerebral palsy. One study (Surman 2009) used data from the UK Collaborative Network of Cerebral Palsy Registers and Surveys (UKCP) registry, which included 5019 children born between 1976 and 1999 and did not report results by subgroups. The UKCP comprised of 5 registers in the UK: Cerebral Palsy Register for Scotland, Northern Ireland Cerebral Palsy Register, 4child (which was the Oxford Register of Early Childhood Impairment), Mersey Region Register and the North of England Collaborative Cerebral Palsy Survey. One paper (Michelsen 2014) used data from 9 European registries in the Study of Participation of Children with Cerebral Palsy Living in Europe (SPARCLE) and included 667 children who have been followed up from birth until the

age of 13 to 17 years. Cognitive impairment was measured by intellectual quotient (IQ) and reported by disease severity using the Gross Motor Function Classification System (GMFCS) levels. Results for severe learning disability were reported by 1 paper (Himmelmann 2009) that used data from the Surveillance of Cerebral Palsy in Europe (SCPE) registry and included 578 children with diskenetic cerebral palsy born between 1976 and 1996. One study (Delacy 2016) used data from the Australian Cerebral Palsy register (ACPR) and included 2982 children with cerebral palsy. Cognitive impairment was reported by intellectual status and GMFCS levels and intellectual status and cerebral palsy subtype.

Individual reviews were undertaken for each of the comorbidities listed in the protocol and the results are reported below Specific criteria for study inclusion have been applied in order to analyse the most relevant data for informing the recommendations. UK based registry data have been prioritised, as these papers best represent the population of interest. The Committee were interested also in the prevalence of comorbidities reported by subgroups (cerebral palsy type, motor problems distribution, and GMFCS levels), therefore non-UK studies reporting this information have been included when needed.

The quality of each study was assessed using the tool developed and published by Munn 2014.

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

27.2.10 Summary of included studies

A summary of the studies that were included in this review and their results for cognitive and learning disabilities are presented in Table 118.

Table 118: Included studies for cognitive and learning difficulties

Study	Register	Dates	N	Overall results	Results per subgroup	Notes	Quality of the study
Surman 2009	UKCP (collates core data items from 5 colaborating registers).	born 1976 - 1999	Data available for cognitive impairmet, n= 3884; data available for severe cognitive impairment, n=3826.	cognition problems: 1848/3884 (48%, 95% CI 46 - 49) Severe cognitive problems: 1025/3826 (27%, 95% CI 25-28).	No	Cognition was reported by upper and lower limb function impairment. However, not by GMFCS levels, type of motor disorder or distribution of motor problem (as defined in protocol). Scottish register excluded for cognition due to incompleteness of data.	MODERATE - study subjects and subgroups not described in details
Michelsen 2014	SPARCLE study. 8/14	Follow up from birth (betwe	667	IQ< 50 = 28%, IQ 50 - 70	GMFCS I or II and IQ >70 = 33%.		LOW - unclear definition of

Study	Register	Dates	N	Overall results	Results per subgroup	Notes	Quality of the study
	registries from SCPE + database from NW Germany	en 1991 - 1997) until age 13 to 17		= 26% IQ >70 = 46%	GMFCS III, IV or V and IQ >=70: 13%. GMFCS I or II and IQ < 70: 19%. GMFCS III, IV or V and IQ < 70: 35%		CP and unclear measurement of the comorbidity - 95% CI not reported
Delacy 2016	ACPR	Born 1996-2005	3466 (2982 analysed)	Moderate to severe intellectual impairment: 671/3466 (22.7%, 95% CI 19.2-26.2)	Moderate to severe intellectual level by GMFCS level: GMFCS I or II = 7% to 15% GMFCS III and IV = 25%-34% GMFCS level V = 55% Moderate to severe intellectual level and CP subtype: Mono/hemiplegia = 11% Diplegia = 15% Tri/quadriplegia and intellectual level =42% Dyskinesia and intellectual level = 27% Ataxia and intellectual level= 17% Hypotonia and intellectual level= 54%	Moderate to severe intellectual level defined as an IQ < 50	HIGH
Himmelmann 2009.	SCPE	Dyskenetic CP born 1976-1996	578	Only in dyskinetic CP	Severe learning disability: n (%) = 245 (52)	The occurrence of severe learning disability was similar in	LOW - No subgroups described in details - 95% CI not

Study	Register	Dates	N	Overall results	Results per subgroup	Notes	Quality of the study
						children with mild or severe motor impairment, while in children with moderate motor impairment a higher percentage of children with dyskinetic CP had severe learning disability (p<0.01)	provided

CP cerebral palsy, UKCP UK Collaborative Network of Cerebral Palsy Registers and Surveys, SPARCLE Study of Participation of Children with Cerebral Palsy Living in Europe, IQ intelligence quotient, GMFCS gross motor function classification system, SCPE Surveillance of Cerebral Palsy in Europe, ACPR Australian cerebral palsy register.

27.3 Evidence statements

27.3.1 Cognitive and learning disabilities

One moderate quality study with 3884 patients found that the prevalence of cognitive difficulties in children with cerebral palsy was 48%.

One low quality study with 667 patients found that the prevalence of cognitive and learning disabilities in children with cerebral palsy ranged from 26% to 48% depending on the children's IQ level; for IQ < 70, 19% and 35% of children in the I-II and III-IV-V GMFCS groups had cognitive and learning disabilities, respectively.

One low quality study with 578 patients found that the prevalence of severe learning disability defined as IQ < 50 in children with cerebral palsy was 52%.

One high quality study with 3466 patients found that the prevalence of moderate to severe intellectual status defined as IQ < 50 ranged from 7% to 55% and was associated with the GMFCS levels. Moderate to severe cognitive impairment was more common in children classified to higher GMFCS levels and those with hypotonic cerebral palsy or spastic quadriplegia.

27.4 Description of clinical evidence: Constipation

One study (Odding 2005) has been included for this review that reported prevalence data of constipation among children with cerebral palsy. The study analysed data from 6 European registries, and reported prevalence of constipation for children born between 1965 and 2004. No results for important subgroups have been found.

27.4.1 Summary of included studies

A summary of the studies that were included in this review and their results for constipation are presented in Table 119.

Table 119: Included studies for constipation

Study	Register	Dates	N	Overall results	Results per subgroup	quality of the study
Odding 2005	SCPE: 6/14 SCPE countries + Netherlands	1965 - 2004	N/A only percentages from registries provided	constipation: 59%	No	VERY LOW - study subjects not described in details - no standard criteria applied for measurement of the comorbidity - 96% CI not provided

SCPE Study of Participation of Children with Cerebral Palsy Living in Europe, CI confidence interval, N/A not applicable

27.5 Evidence statements

27.5.1 Constipation

One very low quality study based on European registry data (sample size not reported) found that the prevalence of constipation in children with cerebral palsy was 59%.

27.6 Description of clinical evidence: Communication difficulties

Three studies have been included for this review that reported prevalence data of communication difficulties in children with cerebral palsy. One study (Nystrad 2014) used European registry data for 594 children with cerebral palsy who were born between 1991 and 1997. One study (Odding 2005) analysed data from the 6 European registries plus 1 register from the Netherlands, including children with cerebral palsy born between 1965 and 2004; this study reported results separately for hemiplegic (unilateral), diplegic (bilateral LL>UL), 'tetraplegic' (quadriplegic / bilateral LL+UL), and dyskinetic children with cerebral palsy. One study (Delacy 2016) used Australian registry data for 3070 children and young people with cerebral palsy who were born between 1996 and 2005. Results were reported by speech status and GMFCS levels and by speech status and cerebral palsy subtype.

27.6.1 Summary of included studies

A summary of the studies that were included in this review and their results for communication difficulties are presented in Table 120.

Table 120: Included studies for communication difficulties

Study	Register	Dates	N	Overall results	Results per subgroup	Notes	Quality of the study

Nystrad 2014	SPARCLE study (8/14 registries from SCPE + 1 database from NW Germany)	Follow up from birth (between 1991 - 1997) until age 8 – 12 (SPARCLE1) and 13 to 17 (SPARCLE2)	594	8 – 12 years: Normal: 341/594 (57%) Communication difficulties but uses speech 102/594 (17%) Uses non-speech for formal communication: 73/594 (12%) no formal communication 78/594 (13%) 13 – 17 years: Normal: 349/594 (59%) Communication difficulties but uses speech 91/594 (15%) Uses non-speech for formal communication: 77/594, (13%) no formal communication 73/594 (12%) missing 4/594 (1%) % who remained stable between childhood and adolescence: 82% kappa statistic 0.90 (95% CI: 0.82 – 0.98) showing agreement between impairment in childhood and adolescence (no change) % who changed for better: 10% % who changed for worse: 7% % who changed 1 level (for example normal to communication difficulties but uses speech): 14% % who changed 2 levels or more: 1%	No	8/14 registers from SCPE and an additional database from North West Germany. Both SPARCLE1 and 2 same participants but followed up at different times. Details of assessment of communication and speech not provided.	VERY LOW - study subjects not described in details - no standard criteria applied for measurement of the comorbidity - 96% CI not provided

Odding 2005	SCPE: 6/14 SCPE countries + Netherlands	1965 - 2004	N/A -only percentages from registries provided	Overall prevalence of speech impairment: 42 - 81%	Speech impairment: hemiplegic 30%, diplegic 20%, tetraplegic 85%, dyskinetic 95%	There is some overlap between Nystrad 2014 and Odding 2005	VERY LOW - unclear definition of CP and unclear measurement of comorbidities - no subgroups described in details - 95% CI not reported
Delacy2016	APCR	1996-2005	3466 (3070 analysed)	Some speech impairment: 1133/3466 (36.9%, 95% CI 34.6-39.3) Non-verbal: 733/3466 (23.8%, 95% CI 21.5-26.1)	Some impairment of speech and GMFCS level: GMFCS level I and II= 37%-46% GMFCS level III and IV=43-46% GMFCS level V= 10% Non-verbal children by GMFCS level: GMFCS level I and II= 2%-8% GMFCS level III and IV=19% - 45% GMFCS level V= 87% Some impairment of speech and CP subtype:	Non-verbal speech status defined as non-verbal referred to no or severely limitedverbal expressive communication at 5 years. Some impairment referred to any speech impairment or delay regardless of cause or the presence of intellectual impairment.	HIGH

					Mono/hemiplegia= 36% Diplegia = 39% Tri/quadriplegia =28% Dyskinesia=40 % Ataxia= 64% Hypotonia=37% Non-verbal children and CP subtype : Mono/hemiplegia= 4% Diplegia = 9% Tri/quadriplegia =61% Dyskinesia=54 % Ataxia= 19% Hypotonia=58		

CP cerebral palsy, SPARCLE Study of Participation of Children with Cerebral Palsy Living in Europe, SCPE Surveillance of Cerebral Palsy in Europe, N/A non-applicable, ACPR Australian cerebral palsy register, GMFCS gross motor function classification system.

27.7 Evidence statements

27.7.1 Communication difficulties

One very low quality study with 594 patients found that the prevalence of communication difficulties in children with cerebral palsy aged 8 to 12 years was 43%. 12% used non-speech methods for communication and 13% had no formal communication. In patients aged 13 to 17 years, there was little change with 41% having communication difficulties with similar rates of non-speech communication (13%) and no formal communication (12%).

One very low quality study based on European registry data (sample size not reported) found that the prevalence of speech impairment in children with cerebral palsy ranged overall from 42% to 81% and varied as follows with cerebral palsy type:

- 30% in patients with hemiplegic (unilateral) cerebral palsy
- 20% in patients with diplegic (bilateral LL>UL) cerebral palsy
- 85% in patients with ‘tetraplegic’ (quadriplegic / bilateral LL+UL) cerebral palsy

- 95% in patients with dyskinetic cerebral palsy

One high quality study with 3466 patients based on an Australian cerebral palsy register found communication difficulties in 61% of the cerebral palsy cohort and almost 24% were essentially non-verbal at 5 years of age. Increasing proportions of both speech impairment and non-verbal status were seen in increasing GMFCS level. The cerebral palsy subtypes of hypotonia (95%), dyskinesia (94%), and spastic quadriplegia (bilateral LL+UL) (89%) showed the highest proportions of speech impairment.

27.8 Description of clinical evidence: Behavioural difficulties

One study (Parkes 2008) has been included for this review that reported prevalence data of behavioural difficulties in children with cerebral palsy. The study used data from European registries and included 818 children with cerebral palsy born between 1991 and 1997. Results on emotional and behavioural symptoms have been reported. Emotional and behavioural symptoms were measured by the parent-form Strengths and Difficulties Questionnaire (SDQ). This has 4 domains: emotion, conduct, hyperactivity, peer problems (all combined - total difficulty score (TDS)). A TDS > 16 was considered to be abnormal.

27.8.1 Summary of included studies

A summary of the studies that were included in this review and their results for behavioural difficulties are presented in Table 121.

Table 121: Included studies for behavioural problems

Study	Register	Dates	N	Overall results	Results per subgroup	Quality of the study
Parkes 2008	SPARCLE study (8/14 registries from SCPE + 1 database from NW Germany)	Follow up from birth (between 1991 - 1997) until age 13 to 17 (SPARCLE2)	818	Total difficulty score assessed using the parent-form Strengths and Difficulties Questionnaire (SDQ): 26% (95% CI 24 - 28) Score by domains: Peer problems: 32% (95% CI 30 – 35%) Hyperactivity: 31% (95% CI: 29 – 33%) Emotion: 29% (95% CI 26 – 31%) Conduct: 17% (95% CI 15 – 19%)	No	HIGH - no major limitations identified

CP cerebral palsy, SPARCLE Study of Participation of Children with Cerebral Palsy Living in Europe, CI confidence intervals, SCPE Surveillance of Cerebral Palsy in Europe.

27.9 Evidence statements

27.9.1 Behavioural problems

One high quality study based on European registry data with a total of 818 patients found that the overall prevalence of emotional and behavioural symptoms using the Strengths and

Difficulties Questionnaire in children with cerebral palsy was 26%. When looking at the specific domains, 32% of the patients with cerebral palsy presented with peer problems, 31% showed hyperactivity, 29% had emotional difficulties, and 17% showed conduct problems.

27.10 Description of clinical evidence: Vomiting, regurgitation and reflux

One study (Odding 2005) has been included for this review that reported prevalence data of vomiting among children with cerebral palsy. The study analysed data from 6 European registries, and reported prevalence of vomiting for children born between 1965 and 2004. No results for important subgroups were reported.

27.10.1 Summary of included studies

A summary of the studies that were included in this review and their results for vomiting, regurgitation and reflux are presented in Table 122.

Table 122: included studies for vomiting, regurgitation and reflux

Study	Register	Dates	Total number participants	Overall results	Results per subgroup	quality of the study
Odding 2005	SCPE: 6/14 SCPE countries + Netherlands	1965 - 2004	N/A - only percentages from registries provided	vomiting: 22%	No	VERY LOW - study subjects not described in details - no standard criteria applied for measurement of the comorbidity - 96% CI not provided

SCPE Surveillance of Cerebral Palsy in Europe, N/A non-applicable, CI confidence interval.

27.11 Evidence statements

27.11.1 Vomiting, regurgitation and reflux

One very low quality study based on European registry data (sample size not reported) found that the prevalence of vomiting in children with cerebral palsy was 22%.

27.12 Description of clinical evidence: Hearing impairment

Three studies have been included that presented prevalence data of hearing impairment in children with cerebral palsy. One study (Surman 2009) used data from the UKCP registry, which included 5019 children born between 1976 and 1999. As this paper did not report results by subgroups, 1 additional study has been considered. Shevell 2009 used data from the Quebec Cerebral Palsy Register to identify children over a 4-year birth interval (1999-2002) with cerebral palsy. Results for severe auditory impairment have been reported by GMFCS levels and cerebral palsy type. One study (Delacy 2016) used data from the Australian cerebral palsy register and reported on 3069 with known hearing status born between 1996 and 2005.

27.12.11 Summary of included studies

A summary of the studies that were included in this review and their results for hearing impairment are presented in Table 123.

Table 123: included studies for hearing impairment

Study	register	dates	N	overall results	Subgroups	quality of the study
Surman 2009	UKCP (collates core data from 5 collaborating registers)	Born 1976-1999	Data available for hearing impairment = 4566; data available for severe hearing impairment = 4536	Hearing impairment: 356/4566 (8%, 95% CI 7 - 9) Severe hearing impairment: 104/4536 (2%, 95% CI 2 - 3)	No	MODERATE - study subjects and subgroups not described in details
Shevell 2009	Quebec CP register	1999-2002 birth cohorts	301 (243 analysed)	Severe auditory impairment, 23 (6.7%)	N, (%) GMFCS I = 6 (6) GMFCS II = 3 (13) GMFCS III = 4 (13) GMFCS IV = 7 (16) GMFCS V = 8 (21) Spastic quadriplegia = 12 (14) Spastic hemiplegia = 4 (5) Spastic diplegia = 3 (6) Dyskinetic = 6 (38) Ataxic-hypotonic = 3 (33)	LOW - study subjects not described in details - 95% CI not provided
Delacy 2016	ACPR	Born 1996-2005	3466(3069 analysed)	Some hearing impairment: 274/3466 (8.9%, 95% CI 7.9-9.9)	Some hearing impairment and GMFCS level: GMFCS level I and II= 5%-9%	HIGH

				Bilateral deafness: 106/3466 (3.4%, 95% CI 2.6-4.3)	GMFCS level III and IV=10-11% GMFCS level V=16% Bilateral deafness and GMFCS level: GMFCS level I and II= 2% GMFCS level III and IV=3%- 4% GMFCS level V= 9% Some hearing impairment and CP subtype: Mono/hemiplegia= 6% Diplegia= 8% Tri/quadriplegia =13% Dyskinesia=11 % Ataxia=8% Hypotonia=12 % Bilateral deafness and CP subtype: Mono/hemiplegia= 2% Diplegia= 2% Tri/quadriplegia =5% Dyskinesia=10 % Ataxia=8% Hypotonia=6%	

CP cerebral palsy, UKCP UK Collaborative Network of Cerebral Palsy Registers and Surveys, GMFCS gross motor function classification system, ACPR Australian cerebral palsy register, CI confidence interval.

27.13 Evidence statements

27.13.1 Hearing impairment

One moderate quality study with 3884 patients found that the prevalence of hearing impairment and severe hearing impairment was 8% and 2%, respectively in children with cerebral palsy.

One low quality study with 243 patients found that the prevalence of severe auditory impairment varied depending on the GMFCS level and type of cerebral palsy, with children in GMFCS levels IV-V showing a higher prevalence (16% and 21% respectively). Children with dyskinetic or ataxic-hypotonic also showed a high prevalence of severe auditory impairment, 38% and 33% respectively, while in children with spastic cerebral palsy the prevalence ranged from 6% to 14%.

One high quality study with 3466 patients found that the prevalence of patients with unaided loss of 25 to70dB in the better ear or inability to hear whispers ranged between 5% and 16% depending on GMFCS levels. The proportion of patients with hearing impairment increased by GMFCS level. The proportion of patients with bilateral deafness as defined as unaided loss of > 70 dB increased by GMFCS level. The dyskinetic subtype showed the highest proportions of hearing impairment.

27.147 Description of clinical evidence: Visual impairment

Three studies have been included that presented prevalence data of visual impairment in children with cerebral palsy. One study (Surman 2009) used data from the UKCP registry, which included 5019 children born between 1976 and 1999. As this paper did not report results by subgroups, 1 additional study was considered. Shevell 2009 used data from the Quebec Cerebral Palsy Register to identify children over a 4-year birth interval (1999-2002) with cerebral palsy. Results for severe visual impairment have been reported by GMFCS level and cerebral palsy subtype. One study (Delacy 2016) used data from the Australian cerebral palsy registry, which included 3466 children with cerebral palsy born between 1996 and 2005. This study reported its results by GMFCS level and cerebral palsy subtype.

27.14.17 Summary of included studies

A summary of the studies that were included in this review and their results for visual impairment are presented in Table 124.

Table 124: Included studies for visual impairment

Study	register	dates	N	overall results	subgroups	quality of the study
Surman 2009	UKCP (collates core data items from 5 colaborating registers).	Born 1976-1999	Data available for visual impairmetn = 4492; data available for severe visual impairment = 4204	Visual impairment: 1929/4492 (43%, 95% CI 42 - 44) Severe visual impairment: 425/4204 (10%, 95% CI 9 - 11)	No	MODERATE - study subjects and subgroups not described in details
Shevell 2009	Quebec CP register	1999-2002 birth cohorts	301 (243 analysed)	Severe visual impairment by GMFCS level, n (%) Cortical blindness by neurologic subtype, n (%)	N, (%) GMFCS I = 4 (4) GMFCS II = - (-) GMFCS III = 1 (3) GMFCS IV = 5 (12) GMFCS V = 13 (33) Cortical blindness: Spastic quadriplegia = 18 (21) Spastic hemiplegia = 2 (3) Spastic diplegia = 1 (4) Dyskinetic = 1 (7) Ataxic-hypotonic = 1 (11)	LOW - study subjects not described in details - 95% CI not provided

Delacy 2016	ACPR	1996 – 2005	3466 (2953 analysed)	Some visual impairment: 897/3466 (30.3%, 95% CI 26.4-34.3) Functionally blind: 162/3466 (5.5%, 95% CI 4.8-6.3)	GMFCS level I and II= 21%-28% GMFCS level III and IV=39%- 42% GMFCS level V= 44% Functionally blind and GMFCS level: GMFCS level I and II= 2% GMFCS level III and IV=2%- 7% GMFCS level V= 24% Some visual impairment and CP subtype: Mono/hemiplegia= 25% Diplegia= 28% Tri/quadriplegia=39 % Dyskinesia=30% Ataxia=34% Hypotonia=47% Functionally blind children and CP subtype: Mono/hemiplegia= 1% Diplegia= 2% Tri/quadriplegia=16 % Dyskinesia=6% Ataxia=1% Hypotonia=10%	MODERATE

CP cerebral palsy, UKCP UK Collaborative Network of Cerebral Palsy Registers and Surveys, GMFCS gross motor function classification system, ACPR Australian cerebral palsy register, CI confidence interval

27.15 Evidence statements

27.15.1 Visual impairment

One moderate quality study with 3884 patients found that the prevalence of visual impairment and severe visual impairment was 43% and 10%, respectively in children with cerebral palsy.

One low quality study with 243 patients found that the prevalence of severe visual impairment varied depending on the GMFCS level, with children in GMFCS levels IV-V showing a higher prevalence (12% and 33% respectively). The same study found that the prevalence of cortical visual impairment (referred to in the study as cortical blindness) varied depending on cerebral palsy subtype, being 21% in children with spastic quadriplegia (bilateral spastic cerebral palsy UL+LL), 3% in spastic hemiplegia (unilateral spastic cerebral palsy), 4% in spastic diplegia (bilateral spastic cerebral palsy LL>UL), 7% in dyskinetic cerebral palsy, and 11% in children with ataxic-hypotonic cerebral palsy.

27.16 Description of clinical evidence: Epilepsy

Four studies have been included that presented prevalence data of epilepsy in children with cerebral palsy. One study (Surman 2006) used data from the UKCP registry, which included 6910 children born between 1960 and 1997. As this paper did not report results by subgroups, 2 additional studies have been considered. One paper (Sellier 2012) used data from the SCPE register and included 9137 children with cerebral palsy born between 1976 and 1998; results for history of epilepsy have been presented by type of cerebral palsy. One study (Delacy 2016) used data from the Australian cerebral palsy registry and included 3466 children and young people with cerebral palsy. Results of this study were reported by GMFCS levels and cerebral palsy subtype.

27.16.1 Summary of included studies

A summary of the studies that were included in this review and their results for epilepsy are presented in Table 125.

Table 125: Included studies for epilepsy

study	register	dates	N	overall results	subgroups	quality of the study
Surman 2006	CP register, UK (UKCP = 5 CP registers)	1960-1997 birth cohorts	6910	18-33% had epilepsy	No	MODERATE - study subjects and subgroups not described in details
Sellier 2012	SCPE	1976-1998 birth cohorts	9137	history of epilepsy = 3424 (35%)	CP type n (%): bilateral spastic = 1854 (36.6) unilateral spastic = 691 (25.6) dyskinetic = 342 (51.6) ataxic = 100 (27.2)	MODERATE - 95% CI not reported
Delacy 2016	ACPR	1996-2005	3466 (3173 analysed)	Epilepsy resolved by age 5y: 116/3466 (3.6%, 95% CI 3.0-4.3) Epilepsy: 883/2466 (22.8%, 95% CI 24.8-30.9)	Epilepsy resolved by 5y and GMFCS level: GMFCS level I and II= 3% GMFCS level III and IV=4%-5% GMFCS level V= 4% Epilepsy and GMFCS level: GMFCS	HIGH

					level I and II= 13%-22% GMFCS level III and IV=22%-43% GMFCS level V= 65% Epilepsy resolved by 5y and CP subtype: Mono/hemiplegia= 4% Diplegia= 2% Tri/quadriplegia=5% Dyskinesia= 4% Ataxia=4% Hypotonia=5% Epilepsy and CP subtype: Mono/hemiplegia= 22% Diplegia= 14% Tri/quadriplegia=53% Dyskinesia= 35% Ataxia=21% Hypotonia=43%	

CP cerebral palsy, UKCP UK Collaborative Network of Cerebral Palsy Registers and Surveys, SCPE Surveillance of Cerebral Palsy in Europe, Y years, APCR Australian cerebral palsy registry.

27.17 Evidence statements

27.17.1 Epilepsy

Two studies of moderate quality with a total of 16047 patients found that the overall prevalence of epilepsy in children with cerebral palsy ranged between 18% and 35%. When looking at prevalence of epilepsy by cerebral palsy subtype, children with dyskinetic cerebral palsy had the highest prevalence of epilepsy (51.6%), followed by children with bilateral spastic cerebral palsy (36.6%), children with ataxic cerebral palsy (27.2%), and children with unilateral spastic cerebral palsy (25.6%).

27.18 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations on comorbidities with a view to informing early identification were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

27.19 Evidence to recommendations

27.19.1 Relative value placed on the outcomes considered

The objective of this systematic review was to determine the prevalence of the most important comorbidities associated with cerebral palsy and relevant subgroups, in order to assist health care professionals in recognising important comorbidities and identifying subgroups most at risk; the aim was also to improve onward specialist referral and management and inform parents and carers.

27.19.2 Consideration of clinical benefits and harms

It was the Committee's view that in addition to the specific recommendations on information to be provided to children and young people with cerebral palsy and their families and carers, health care professionals should regularly assess for clinical and developmental comorbidities, manage them, and when necessary refer to specialist teams for ongoing assessment and management. The Committee recommended that all regions in England and Wales should have clearly defined network of care that covers the developmental and clinical comorbidities commonly observed in children and young people with cerebral palsy.

Visual impairment

The Committee noted that the likelihood of visual impairment increased by GMFCS level, however impairment may be present in all severities. The Committee highlighted that visual impairment may occur at any part of the visual pathway and processing (eye to brain). Visual impairment in lower severities (GMFCS level I and II) may go unnoticed by health care professionals.

The Committee discussed the importance of distinguishing between visual and cortical visual impairment (CVI). Visual impairment is any loss of vision caused by problems at any point of the visual system from eye, eye muscles/astigmatism, optic nerve and pathways all the way back to the visual cortex. Cortical visual impairment results from problems in the visual cortex. Some evidence was presented which showed that the prevalence of CVI (reported as cortical blindness) varied between cerebral palsy type.

The Committee noted that recognition of the impairment is difficult to pick up in the early stages of visual impairment, particularly if there are problems with communication or learning. Recognition often only occurs when children are of school age, as the impairment becomes more apparent in the learning process. Therefore, the Committee agreed that it was important to regularly assess children and young people with cerebral palsy.

Hearing impairment

The Committee noted that Shevell 2009 reported that 28 children and young people with cerebral palsy had severe hearing impairment (defined as <70dB), in a sample of 243 (11.5%). In conjunction with evidence from Surman 2009 showing that 8% of children and

young people with cerebral palsy had hearing impairment, the Committee recommended to be aware that 1 in 10 children and young people with cerebral palsy had hearing impairment. Therefore, the Committee agreed that it was important to regularly assess children and young people with cerebral palsy.

Cognitive and learning disabilities

The Committee noted that it was important to make a distinction between learning disabilities and specific learning difficulties (such as dyslexia or dyscalculia). In line with the NICE guideline on Challenging behaviour and learning disabilities, learning disabilities can be defined by 3 core criteria: lower intellectual ability (usually an IQ<70), significant impairment of social or adaptive functioning, and onset in childhood. Learning difficulties do not affect intellect. The evidence reported both cognitive and learning disabilities mainly in terms of IQ levels. For example, it was noted by the Committee that a child may have an IQ > 70, and so not be diagnosed with a learning disability, but may still have problems in school due to specific learning difficulties. The Committee interpreted the results reported by Michelsen 2014 as follows: GMFCS I and II = 52% of total population. Of these, 33/52 had IQ => 70 and 19/52 had IQ < 70. Of the total participants, 48% had GMFCS levels III, IV and V, of which 13/48 had IQ => 70 and 35/48 had IQ < 70. This has been reflected in the recommendation made by the Committee.

Communication difficulties

The Committee noted that children and young people with learning disabilities (cognitive disability) would be likely to have communication difficulties. However, they noted that motor speech disorders (dysarthria) do not necessarily completely correlate with cognitive disability. The Committee noted that expressive communication includes speech production, language (putting sentences together) and use of formal methods of communication. Non-verbal formal communication methods may include manual signing, pictures or symbols, or speech generating devices (augmentative and alternative communication). Based on the evidence presented and on their clinical experience, the Committee decided to develop recommendations on the association between communication difficulties and both the severity and type of cerebral palsy, as the evidence showed that children with dyskinetic or severe bilateral cerebral palsy may be more at risk of having speech difficulties or being non-verbal.

Recommendations arising from the review of communication comorbidities were incorporated into the sections on speech, language and communication. The Committee highlighted the importance of continued monitoring of changes in communication skills. They also noted that communication ability and support needs change over time.

Behavioural difficulties

The Committee noted that the assessment used, SDQ, in the study (Parkes 2008) was not a robust measure of behaviour and there are other measures which are used more in practice such as the Child Behaviour Checklist. The SDQ is parent reported and only provides the parent perception of behavioural experiences and not the child's perception. The SDQ additionally shows correlation of percentage of parent reported behavioural experiences with the population norm. However, the Committee agreed that the study provided useful information which is representative of their experiences in clinical practice, such as around 2-3 in 10 report behavioural difficulties, and considered it was appropriate to advise parents on these findings.

The Committee also pointed out that behavioural difficulties can be associated with other comorbidities and environmental factors such as frustration and boredom.

The Committee considered that it was important to reiterate that behavioural difficulties should be managed routinely by district multidisciplinary services, but onward referral to specialist teams should occur if the difficulties persist.

Vomiting, regurgitation and reflux

The Committee noted that vomiting and frequency of vomiting was not described or defined within the study (Odding 2005). No evidence was retrieved for regurgitation and reflux, yet the Committee noted that all fore gut dysmotility (vomiting, regurgitation and reflux) is frequently present in children and young people with cerebral palsy. Given the limitations of the evidence, and based on their clinical experience, the Committee agreed that parents and carers should be informed that vomiting, regurgitation and reflux are a known problem in infants, children and young people with cerebral palsy.

Constipation

The Committee wanted to raise awareness that constipation is prevalent within children and young people with cerebral palsy and based on the evidence identified agreed to recommend to inform parents that constipation occurs in around 3 in 5 children and young people with cerebral palsy.

Epilepsy

The Committee noted that based on published prevalence data and their clinical knowledge, the prevalence of diagnosed epilepsy in the general paediatric population is around 1 in 200.

The evidence showed that 1 in 3 children with cerebral palsy had epilepsy. Evidence was presented to the Committee that reported prevalence of epilepsy by severity and motor distribution of cerebral palsy. Of these, the moderate to high quality studies showed that the prevalence of epilepsy is increased in different subtypes, particularly in those with dyskinetic cerebral palsy. However, the Committee were keen to underline that health care professionals should not misinterpret dyskinetic movements with epilepsy.

27.19.3 Consideration of economic benefits and harms

Knowing the prevalence of important comorbidities may lead to increased vigilance and thus more timely management and has therefore, indirectly, potentially important resource implications. However, this was an epidemiological review question and economic analysis to assess cost-effectiveness is not applicable as it does not involve a comparison of competing alternatives. Even so, the assessment, monitoring, referral and management of the comorbidities all have cost implications. The Committee recognised that if comorbidities are not identified and management appropriately, they can negatively impact on a child or young person's wellbeing, function and participation, and increase their risk of complications leading to additional treatment costs and reductions in their quality of life. Estimating the costs to manage those comorbidities would go beyond the scope of the guideline, but it was clear from the Committee that such costs would offset the potential downstream costs from delayed or inappropriate management.

27.19.4 Quality of evidence

The quality of the evidence has been assessed by using the tool developed and published by Munn 2014.

Prevalence data can be sourced from various study designs. Therefore, studies have been assigned high quality and downgraded based on the limitations identified. The methodological tool validated by Munn 2014 assesses critical issues of internal and external

validity that must be considered when addressing validity of prevalence data. The criteria address the following issues:

- Ensuring a representative sample
- Ensuring appropriate recruitment
- Ensuring an adequate sample size
- Ensuring appropriate description and reporting of study subjects and setting
- Ensuring data coverage of the identified sample is adequate
- Ensuring the condition was measured reliably and objectively
- Ensuring appropriate statistical analysis
- Ensuring confounding factors/subgroups/differences are identified and counted for.

27.19.5 Other considerations

The Committee noted that many other comorbidities such as malnutrition and obesity, bladder dysfunction, respiratory diseases, dental problems, delayed puberty, autism, gastro-oesophageal reflux disease (GORD), and dysautonomic dysfunctions can be associated with cerebral palsy in children and young people. It was beyond the scope of the guideline development to look at all comorbidities.

The Committee also noted that many comorbidities, in particular constipation is frequently seen as an underlying cause for pain in children and young people with cerebral palsy and so the evidence reviews on assessment and management of pain, discomfort, and distress are also closely related. Please see sections 21 and 22.

The Committee agreed that the management of the comorbidities included in in this evidence review will be covered by the following NICE guidelines:

- NICE guidelines on gastro-oesophageal reflux disease in children and young people and gastro-oesophageal reflux disease and dyspepsia in adults
- NICE guideline on constipation in children and young people.
- NICE guideline on epilepsies: diagnosis and management.

The Committee also agreed that it was crucial to cross-refer to the NICE guideline on spasticity in under 19s.

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

27.19.6 Key conclusions

The Committee concluded that several comorbidities can be associated with cerebral palsy in children and young people, and that the prevalence of such co-existing disorders often varies with the severity and type of cerebral palsy.

Children and young people often have more than 1 comorbidity and these often have a compounding impact on each other and implications for management.

27.20 Recommendations

116. Assess children and young people with cerebral palsy regularly for developmental and clinical comorbidities, and recognise that these can have an important impact on wellbeing, function and participation.

117. Manage comorbidities, and refer the child or young person for further specialist care if necessary (for example, if a management programme is unsuccessful).

118. Ensure that the child or young person has access to a multidisciplinary team that:

- is able to meet their individual needs
- can provide the following expertise, through a local network of care:
  - paediatric medicine
  - adult medicine (as appropriate)
  - nursing care
  - physiotherapy and occupational therapy
  - orthotics and rehabilitation (as appropriate)
  - speech and language therapy
  - dietetics
  - psychology
  - social care.

119. Ensure that routes for accessing specialist teams involved in managing comorbidities associated with cerebral palsy are clearly defined on a regional basis.

Visual impairment

120. Talk to children and young people and their parents or carers about visual impairment that can be associated with cerebral palsy. Information that may be useful to discuss includes the following:

- visual impairment occurs in around 1 in 2 children and young people with cerebral palsy
- it may occur in children and young people with any functional level or motor subtype, but prevalence increases with increasing severity of motor impairment
- it may include impairment of control of eye movements, ocular function and cerebral visual processing
- regular ongoing visual assessment is necessary.

121. Regularly assess children and young people with cerebral palsy for signs of cortical visual impairment, bearing in mind that this:

- occurs in around 1 in 5 children and young people with cerebral palsy
- may occur in children and young people with any functional level or motor subtype but prevalence increases with increasing severity of motor impairment
- may be difficult to recognise in the early stages.

Hearing impairment

122. Talk to children and young people and their parents or carers about hearing impairment that can be associated with cerebral palsy. Information that may be useful to discuss includes the following:

- hearing impairment occurs in around 1 in 10 children and young people with cerebral palsy

- it may occur in children and young people with any functional level or motor subtype but prevalence increases with increasing severity of motor impairment
- it is more common in people with dyskinetic or ataxic cerebral palsy than in those with spastic cerebral palsy
- regular ongoing hearing assessment is necessary.

Cognitive and learning disabilities

123. Talk to children and young people and their parents or carers about learning disabilities that can be associated with cerebral palsy (for example, problems with knowledge acquisition, memory and understanding and use of language). Information that may be useful to discuss includes the following:

- learning disabilities occur in around 1 in 2 children and young people with cerebral palsy
- severe learning disabilities (IQ below 50) occur in around 1 in 2 of these
- learning disabilities can be associated with any functional level, but prevalence increases with increasing severity of motor impairment:
  - GMFCS level I or II: around 1 in 3 have an IQ below 70
  - GMFCS level III, IV or V: around 2 in 3 have an IQ below 70.

Communication difficulties

124. Talk to children and young people and their parents or carers about communication difficulties that can be associated with cerebral palsy. Information that may be useful to discuss includes the following:

- communication difficulties occur in around 1 in 2 children and young people with cerebral palsy
- at least 1 in 10 need augmentative and alternative communication (signs, symbols and speech generating devices)
- around 1 in 10 children and young people cannot use formal methods of augmentative and alternative communication because of cognitive and sensory impairments communication difficulties
- communication difficulties may occur with any functional level or motor subtype, but are more common in children and young people with dyskinetic or severe bilateral spastic cerebral palsy
- communication difficulties do not necessarily correlate with learning disabilities.

Behavioural difficulties

125. Talk to children and young people and their parents or carers about behavioural difficulties that can be associated with cerebral palsy. Information that may be useful to discuss includes that around 2–3 in 10 children and young people with cerebral palsy have 1 or more of the following:

- emotional and behavioural difficulties that have an effect on the child or young person's function and participation
- problems with peer relationships
- difficulties with attention, concentration and hyperactivity
- conduct behavioural difficulties.

126. Support children and young people with cerebral palsy and their families and carers to recognise behavioural problems.

127. Manage routine behavioural problems within the multidisciplinary team, and refer the child or young person to specialist services if problems persist.

Vomiting, regurgitation and reflux

128. Advise parents or carers that vomiting, regurgitation and gastro-oesophageal reflux are common in infants, children and young people with cerebral palsy. If there is a marked change in the pattern of vomiting, assess for a clinical cause.

129. For guidance on identifying and managing gastro-oesophageal reflux disease, see the NICE guidelines on gastro-oesophageal reflux disease in children and young people and gastro-oesophageal reflux disease and dyspepsia in adults.

Constipation

130. Recognise that around 3 in 5 children and young people with cerebral palsy have chronic constipation, and:

- discuss this with children and young people and their parents or carers
- carry out regular clinical assessments for constipation.

131. For guidance on identifying and managing constipation in under 18s, see the NICE guideline on constipation in children and young people.

Epilepsy

132. Advise children and their parents or carers that epilepsy may be associated with cerebral palsy. Information that may be useful to discuss includes the following:

- epilepsy occurs in around 1 in 3 children with cerebral palsy
- it may occur in children and young people with any functional level or motor subtype but prevalence increases with increasing severity of motor impairment
- it is reported in around 1 in 2 children with dyskinetic cerebral palsy.

133. Ensure that dyskinetic movements are not misinterpreted as epilepsy in children with cerebral palsy.

134. For guidance on identifying and managing epilepsy, see the NICE guideline on epilepsies: diagnosis and management.

135. For guidance on managing problems with movement and posture in children and young people with cerebral palsy, see the NICE guideline on spasticity in under 19s.

27.21 Research recommendations

10. What is the clinical and cost effectiveness of early interventions to improve cognitive learning/ability in children and young people with cerebral palsy?

Table 126: Research recommendation rationale

Research question	What is the clinical and cost effectiveness of early interventions to improve cognitive learning/ability in children and young people with cerebral palsy?
Why this is needed	
Importance to 'patients' or the population	Cognitive outcome in children with cerebral palsy is a major determinant of long term function, participation and experience. It has an impact on education, the child's ability to communicate and engage with therapy.
Relevance to NICE guidance	In this guideline, we identified cognitive deficits as significant comorbidity. However, we have not been able to recommend specific interventions that can be used.
Relevance to the NHS	Children who are at high risk of developing cerebral palsy often receive anticipatory therapeutic input targeting the infant such as early sensory stimulation or specific parental education and psychosocial support. It would be very cost effective if we know which infants to target and how and for how long, for best possible long term outcome. It would be cost effective to know what intervention would be most effective in different subgroups of cerebral palsies.
National priorities	It would contribute towards long term planning of services around children with cerebral palsy in health, social care, education and in the voluntary sector.
Current evidence base	The evidence that early intervention and which components of early intervention are able to improve developmental outcome, both cognitive and motor, in children with cerebral palsy is very limited. More research is urgently needed.
Equality	Children with cerebral palsy should also benefit from research input, which has been largely lacking in this population.
Feasibility	This would need to be a fairly long term, multicentre study involving all subgroups of children with cerebral palsy, with clearly identified interventions.
Other comments	

Table 127: Research recommendation statements

Criterion	Explanation
Population	Children with cerebral palsy who have impaired verbal communication skills.
Intervention	Compare and contrast – RCT of 3 subgroups that are stratified to motor subtype and severity: Children without specific targeted intervention Children who have a targeted programme of early sensory stimulation Parental education programme including psycho-social support
Comparator	Compare and contrast the groups
Outcome	Children development including motor, communicative and cogitative parameters
Study design	Multicentre randomised controlled trial

Criterion	Explanation
Timeframe	3 years

28 Social care needs

Review question: What are the specific social care needs of children and young people with cerebral palsy and their family members and carers?

28.1 Introduction

It can be exceptionally demanding for families to manage the complex health, social and care needs of a child and young person with cerebral palsy. Children and young people with cerebral palsy and their families need an optimal level of support from a variety of agencies. Both parents and professionals report that it is often a challenge to be able to identify what social care support is available and even more difficult to access it.

The families need an early detailed assessment of their needs, ideally at the time of diagnosis. Recognised good practice is that families are given the information about what resources are available at that point. However, if it is too early for them to consider the implications at that point it is imperative they can access services at a later stage. This assessment should include information on support packages and respite.

Although in some parts of the UK all members of multidisciplinary teams across health, education and social services are communicating and working well together, this is unfortunately not happening universally. Lack of appropriate, timely support increases isolation and impacts on many other social difficulties for children and young people with cerebral palsy and their families. Children with Disabilities Social Workers have a statutory responsibility to offer support but access to them is variable.

There may be additional expense in caring for a child with cerebral palsy, and many families find it difficult to meet costs and maintain employment. Families can feel isolated; and they need to be provided with a framework to talk to, communicate and share concerns with other families in a similar situation.

The provision of information and appropriate equipment to enable participation should be maintained throughout the whole care pathway. There are times, particularly when rehabilitating after an intervention, when specific support may become necessary. Services should be proactive in ensuring that health and social networks are focussed on the individual's challenges at these points of care.

The aim of this evidence review is to identify the specific social care needs of children and young people with cerebral palsy and their parents and carers.

28.2 Description of clinical evidence

Qualitative studies were selected for inclusion for this review. We looked for studies that collected data using qualitative methods (such as semi-structured interviews, focus groups, and surveys with open-ended questions) and analysed data qualitatively (including thematic analysis, framework thematic analysis, content analysis etc.). Survey studies restricted to reporting descriptive data that were analysed quantitatively were excluded.

Findings/themes were summarised from the literature and were not restricted to only those identified as likely themes by the Committee in the evidence review protocol. The majority of themes listed in the protocol were identified in the studies, apart from the need for social care assessments at the time of diagnosis. An additional theme: 'personal support needs' including the subthemes 'familial support' and 'emotional support' was identified in the literature and included as it is an area where social care workers can provide support.

A total of 5 studies were included in this review. As per the protocol, studies from the UK were prioritised to reflect the UK social care setting. However, non-UK studies were considered for inclusion. The following provides a brief description of the included studies:

- Two studies (Lawlor 2006; Mir and Tovey 2003) were conducted within the UK. Of these, 1 study (Lawlor 2006) was conducted in Northeast England and interviewed parents to examine the factors influencing social participation of children with cerebral palsy. One study (Mir and Tovey) was conducted in the north of England with participants from South Asia and explored the experiences of South Asian parents in caring for their children with cerebral palsy.
- One study (McManus 2006) was conducted in 5 European countries: Denmark, France, Italy, Ireland and Sweden and reported environmental concerns of parents with children who have cerebral palsy.
- One study (Capjon and Bjork 2010) was conducted in Norway, specifically in a population of children whom have multilevel surgery (a series of procedures, bony, soft tissue or both, for connection of deformities in children with cerebral palsy). Both parents and children were interviewed to obtain evidence on post-surgery rehabilitation. This study was included as no studies from the UK reported social care needs for cerebral palsy children who have had multilevel surgery.
- One study (Shimmel 2013) was conducted in Canada and included evidence of physical participation from both children with cerebral palsy and their parents. This study was included as it provided additional evidence for a number of themes.

Two studies (Lawlor 2006 and Mir and Tovey 2003) collected evidence by interviews. One study (Capjon and Bjork 2010) collected evidence by semi-structured interviews. The remaining studies (McManus 2006; Shimmel 2013) used in depth discussion groups or a mixture of focus groups and interviews.

For full details please see protocol in Appendix E. A brief description of the studies is provided in Table 128. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

28.2.1 Summary of included studies

Five themes were identified: physical environmental needs, familial and emotional support needs, services providing support and condition related needs.

A summary of the studies that were included in this review are presented in Table 128.

Table 128: Summary of included studies

Study	Study design/ methods	Population	Aims	Comments
Capjon and Bjork 2010	Semi-structured interviews	N= 8 spastic CP children and their parents. Norway.	To explore post-operative family situation, rehabilitation and interdisciplinary cooperation for ambulant children with CP, after multilevel surgery.	- Data collection and analysis clearly reported. - Role and potential influences of researchers unclear
Lawlor 2006	Interviews	N = 13 families of children with CP, identified from Northeast of England	To ascertain from families of children with cerebral palsy the features of such environments which	- out of 28 respondents, 12 families participated - Data collection

Study	Study design/ methods	Population	Aims	Comments
		Collaborative CP Survey.	facilitate or restrict participation.	and analysis clearly reported. - Role of and potential influences of researchers described.
McManus 2006	Discussion group	Parents of 28 children with CP from 5 countries; Denmark, France, Italy, Ireland and Sweden.	To inform the content of a questionnaire relevant to the environment of children with CP living in Europe	- Aim not directly related to aim of this evidence review. - Data collection not clearly described
Mir and Tovey 2003	Interviews	N = 20 carers of children with CP. South Asian community in northern England. 13 Pakistani and 7 Indian, were interviewed. Of the 14 women and 6 men, 16 were Muslim, 3 Sikh, and 1 Hindu.	To explore South Asian carers' perceptions of causation of CP or their views on the quality of social service support.	- Data collection and not clearly described. - Role and potential influences of researchers unclear
Shimmel 2013	focus groups and interviews	N = 15 children with CP between age of 10 – 18 years and their parents. Canada.	To identify factors in children with CP that make it easy or hard to be physically active.	- Data collection and not clearly described. - Role and potential influences of researchers unclear

CP cerebral palsy

28.3 Clinical evidence profile

Individual studies were assessed for methodological limitations using an adapted Critical Appraisal Skills Programme (CASP 2006) checklist for qualitative studies, where items in the original CASP checklist were adapted and fitted into 5 main quality appraisal areas according to the following criteria:

- Aim (description of aims and appropriateness of the study design)
- Sample (clear description, role of the researcher, data saturation, critical review of the researchers' influence on the data collection)
- Rigour of data selection (method of selection, independence of participants from the researchers, appropriateness of participants)
- Data collection analysis (clear description, how are categories or themes derived, sufficiency of presented findings, saturation in terms of analysis, the role of the researcher in the analysis, validation)
- Results / findings (clearly described, applicable and comprehensible, theory production)

An adapted GRADE approach was then used to then assess the evidence by themes. Similar to GRADE in effectiveness reviews this includes 4 domains of assessment and an overall rating:

- Limitations across studies for a particular finding or theme (using the criteria described above)
- Coherence of findings (equivalent to heterogeneity but related to unexplained differences or incoherence of descriptions)
- Applicability of evidence (equivalent to directness, i.e. how much the finding applies to our review protocol)
- Saturation or sufficiency (this related particularly to interview data and refers to whether all possible themes have been extracted or explored)

The clinical evidence profile for this review question (social care needs) is presented diagrammatically in a theme map in Figure 5 in the adapted GRADE approach for qualitative findings in Table 129 - Table 131.

Figure 5: Theme map for social care needs

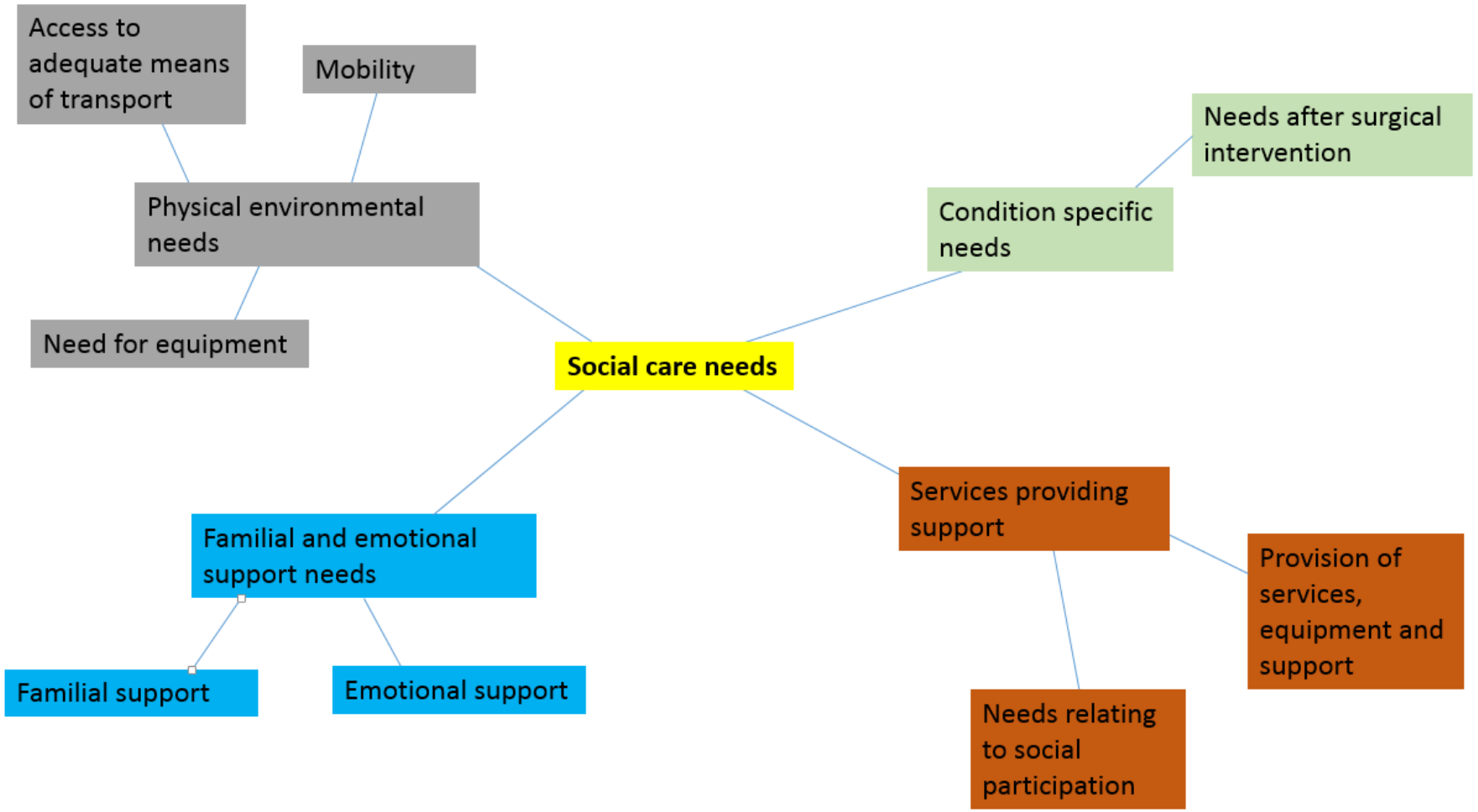


Table 129: Summary of clinical evidence (adapted GRADE approach for qualitative findings) – theme: Physical environmental needs

Physical environment					
Study information			**Quality assessment**		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
Sub-theme 1: Access to adequate means of transport					
3 (Lawlor 2006; McManus 2006; Shimmel 2013)	1 interviews, 1 interviews and focus groups, 1 discussion group	• 2 studies reported on the use of private transport as a facilitator for greater participation, access to transport and use of public transport in a cerebral palsy population. • **Use of private transport** • 2 studies (Lawlor 2006; McManus 2006) reported the benefits of having private transport, such as the family car and private taxis. The studies reported that private transport allowed individuals to travel, visit people and participate in work, school and social activities. Additionally, in Denmark, private transport was facilitated as there is no registration tax and they receive financial aid for special fitting of the car. " • *Before we had the car we used taxis or we didn't go anywhere. We've had a car for about 4 years and we go everywhere in it, it's much easier" (Child 11 father)* • However, the studies also reported barriers to the use of private transport including poor parking facilities, planning journeys ahead and needing extra time for loading equipment: • *"Parking at the shops is terrible; a lot of people use the disabled spaces. Builders' wagons use them. Traffic wardens just ignore it. If they put more pressure on them it might make a difference" (Child 5 father).* • Use of public transport • 2 studies (Lawlor 2006, McManus 2006) reported the benefits of accessing and using public transport, highlighted in the UK and France. One mother reported that her child	Limitation of evidence	Major limitations	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Saturated	

Physical environment					
Study information			**Quality assessment**		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		likes to use the Metro and has no problems *"getting on and off" (Child 7 mother).* • However, 3 studies ((Lawlor 2006; McManus 2006; Shimmel 2013) reported barriers to the use of public transport, including lack of available transit systems (Canada), lack of wheelchair adapted transport such as wheelchair friendly taxis and buses (Ireland, Sweden, Italy) and physical barriers including steps, narrow aisles and lack of lifts (UK). As 1 parent from Sweden said: *"Wheelchairs are not allowed on trams"* and arrangements for booking disability friendly transport *"never work".*			
Sub-theme 2: Mobility					
2 (Lawlor 2006; McManus 2006)	1 interviews, 1 discussion group	**Structural adaptions** 2 studies (Lawlor 2006; McManus 2006) reported that structural adaptions in the environment (both at home and in community) facilitate mobility of children with cerebral palsy and access to facilities. One family also reported that adaptions to the home had to be altered as the child grows due to change in needs. *"She has a downstairs bedroom, bathroom, shower and toilet. It's purpose built for her and we were involved in the plan. We have an intercom" (Child 6 father, UK).* However, families from 2 studies (Lawlor 2006; McManus 2006) reported that there was a lack of structural adaptions in health care services, local amenities and leisurely activities including going to the beach. Steps, lack of lists or ramps and poor path pathing were barriers to mobility, particularly when using wheelchairs. *"The GP has a slope up into the surgery, the doors aren't good because the first door opens inwards and the second door opens outwards into the foyer so that's very difficult to deal with" (Child 1 mother, UK).* Similarly, in relation to accessibility	Limitation of evidence	Moderate limitations	Low
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Unclear	

Physical environment					
Study information		**Description of theme or finding**	**Quality assessment**		
Number of studies	**Design**		**Criteria**	**Rating**	**Overall**
		to shops: *"If we do get in, he can't move around inside the shop" (one mother of child with cerebral palsy, Denmark).*			
Sub-theme 3: Need for equipment					
2 (Lawlor 2006; McManus 2006)	1 interviews, 1 discussion group	**Equipment for daily living** Two studies (Lawlor 2006; McManus 2006) reported that equipment including: wheelchairs, walking frames, hoists and motorised tricycles facilitated daily living of both the child and parent. Furthermore, 1 study (Lawlor 2006) reported that outdoor electric wheelchair as opposed to manual or indoor electric wheelchair was seen as an invaluable equipment facilitating parent and child to develop independence and participate in activities while reducing the required level of support and supervision. One mother (of child 3) stated *"…his electric chair is a real help".* **Listening to the child's needs** One study (McManus 2006) reported the importance of listening to the child's requests for equipment's and adaptions. One parent said "the child is the motor of the change" (France) meaning that understanding the child's needs allows the child to gain a better understanding of their space and thereby 'autonomy and independence'.	Limitation of evidence	Moderate limitations	Low
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Unclear	

1 **Table 130: Summary of clinical evidence (adapted GRADE approach for qualitative findings) – theme: Familial and emotional**
2 **support needs**

Study information		**Description of theme or finding**	**Quality assessment**		
Number of studies	**Design**		**Criteria**	**Rating**	**Overall**

Study information		Description of theme or finding	Quality assessment		
Number of studies	**Design**		**Criteria**	**Rating**	**Overall**
Sub-theme 1: Need for familial support					
2 (Lawlor 2006; McManus 2006)	1 interviews, 1 discussion group	• **Supporting parents in daily living** • One study (Lawlor 2006) reported that the child's grandparents play an essential role in providing support for the child's parents, allowing them to work: *"We're very fortunate in that we have two sets of grandparents very close by. If we didn't have the grandparents I don't know what we'll do, one of us wouldn't be able to work" (Child 9 father).* • Similarly, 1 study (McManus 2006) reported that the family as a whole is involved in support, particularly emotional support for the child with cerebral palsy but also for the parents: *"Every family member is involved in the life of a child with cerebral palsy" (1 parent).* •	Limitation of evidence	Moderate	Low
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Unclear	
Sub-theme 2: Need for emotional support					
2 (McManus 2006, Mir and Tovey 2003)	1 discussion group, 1 interviews	**Emotional impact of cerebral palsy** One study (Mir and Tovey 2003) reported the emotional impact of cerebral palsy on both mother and child. The mother devoted 'enormous energy to the goal of making her daughter "normal"' resulting in emotional damage to the child with cerebral palsy. *"She sometimes talks about being different to me. [cries]…One day she said to me 'I wish I was dead. Then you would have a daughter who could walk nicely and could do everything'…I said to her 'We don't want another daughter, we want you, you will get better, we'll do exercises every day and you will get better.' Then she started to cry." (Harpreet, carer for her 11 year old child).* **Emotional support from family** One study (McManus 2006) reported that the family as a whole is involved in emotional support for the child with cerebral palsy but also for the parents: *"Every family member is involved in*	Limitation of evidence	Moderate	Very low
			Coherence of findings	Unclear	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Unclear	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		the life of a child with cerebral palsy" (1 parent). **Faith and spiritualty** One study (Mir and Tovey 2003) reported that faith played an important role in accepting and adjusting to their role as carers. *"Since Nadeem was born we have become more religious, our prayer has become more focused".(Qamar, parent of child with CP)*			

1 **Table 131: Summary of clinical evidence (adapted GRADE approach for qualitative findings) – theme: Services providing support**

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
Sub-theme 1: Need for adequate services, equipment and support					
3 (Lawlor 2006; McManus 2006; Mir and Tovey 2003)	2 interviews, 1 discussion group	• **Respite care** • The studies (Lawlor 2006; McManus 2006; Mir and Tovey 2003) reported the benefits of having respite care in providing a 'break' for parents but also in allowing their child with cerebral palsy to socially engage. All the studies reported satisfaction with respite and respite care staff (UK, northern England south Asian community and Sweden). • *"Unit X is a residential unit at the school and [child 4] actually goes there one night a week to give him a bit of development and independence" (Child 4 mother).* • Additionally, 1 study (McManus 2006) reported that respite care in the home was a source of support and practical help, but can provide difficulty if there is staff turnover: "it is very good with a helping person at home but it is difficult when there is a change in staff". • **Support in the home and school** • Two studies (Lawlor 2006, McManus 2006) reported difficulties in receiving support in the home: *"we can't get a*	Limitation of evidence	Moderate	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Saturated	

Study information			Quality assessment		
Number of studies	Design	Description of theme or finding	Criteria	Rating	Overall
		teenager to baby-sit our son, due to the requirements for a specialized sitter. This is very expensive, often too expensive to have time off" (parent, Ireland). Additionally, 1 parent reported that *"to invite a friend with a disability demands that you are prepared to take care of two disabled children, we do not always have the energy for that".* • Additionally, support in daily living and activities was reported from 1 study (Lawlor 2006) and which parents feel the need for support in bathing, toileting, dressing, feeding and lifting. "*In the mornings I can't hoist [child 8] because he's so stiff until he's had his medication, so I lift him, give him his breakfast, give him his medication and time to relax" (Child 7 mother).* • One study (Lawlor 2006) reported inadequate care in schools: *"I worry about what he is doing at school. I make all sorts [of food for him], nurses can't do the same as me, they don't keep an eye on whether he has eaten or fallen. When he comes home from school he seems so hungry as though he's not eaten all day" (Riffat, parent of child with cerebral palsy).* • **Services providing equipment** • Two studies (Lawlor 2006; McManus 2006) reported delays in services providing equipment: *"One of the services that is a problem is wheelchair services. Everything takes forever. It's taken about 3 or 4 years to get the electric wheelchair organized. It's the waiting for assessment, waiting for money, waiting for approval, the paperwork to go through" (Child 10 father).* • **Financial support** • Two studies (Lawlor 2006; McManus 2006) reported significant financial implications in having a child with cerebral palsy which includes extra costs of adaptions to house, equipment and other expenses including travel.			

Study information		Description of theme or finding	Quality assessment		
Number of studies	**Design**		**Criteria**	**Rating**	**Overall**
		Some parents reported lack of financial support and raising money for their child's equipment, in 1 case raising *"£3000 for an electric chair"* (Child 3 mother). One parent reported lack of governmental financial support and the need for support from non-governmental organisations (NGOs): "*..but we had to fight to get [Motability allowance], we had the Disabled Children's Foundation involved. It took a long time to get it*'. *(Child 5 father).* • **Lack of information relating to financial support** • Two studies (Lawlor 2006; McManus 2006) reported an inadequate level of information available for financial support: *"I didn't even know you could apply for a benefit. It was the Health Visitor who told me about the Disability Living Allowance and made me fill the forms out, I wouldn't have bothered but she was adamant'" - Child 12 mother.* • **Access to schools catering for special education needs** • One study (McManus 2006) reported that Danish and Irish parents felt that schools which cater for special education needs are located far away from their home. Parents reported that due to this, their child's friends also lived far away. • However, parents in Italy reported that they appreciated the lack of schools providing support for special education needs as it allowed their child to integrate and improve social participation.			
Sub-theme 2: Needs relating to social participation					
2 studies (McManus 2006; Shimmel 2013)	1 in depth discussion group, 1 focus groups and interviews	**Role of the school** One study (McManus 2006) reported that parents feel that the school is the principal factor to improve social participation. Parents in Italy appreciated the lack of schools catering for special education needs as it allowed their child to integrate and improve social participation. However,	Limitation of evidence	Low	Low
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		Danish and Irish parents reported that schools catering for special education needs are located far away from their home and due to this, their child's friends lived far away. **Role of siblings within schools** One study (McManus 2006) reported that parents feel that siblings play an important role in allowing their child with cerebral palsy to become socially integrated and accepted in the school. **Physical activity may be time consuming** One study (Shimmel 2013) reported that parents find it challenging to make time for their children to be physically active or to participate in more time consuming activities. One parent stated: *"Any activity for disabled kids, a team sporting activity, if you're doing it, is an all-day activity".* **Performing physical activity** One study (Shimmel 2013) reported that children with cerebral palsy have preferences for physical activity, especially in relation to peer's perceptions of the condition. One child preferred to perform physical activities alone: "*for me I like working alone because that takes away the outside barriers, it's just me and the exercises, there's no people picking me last or anything" (14 year old, GMFCS I).* Additionally, 1 parent reported that their child does not experience a sense of belonging when performing physical activity: *"This is why [name of son] doesn't really fit into anywhere, he doesn't fit into the sports with the kids with the wheelchairs because he says "I don't have a wheelchair, I don't want to be with kids with wheelchairs, I don't need a wheelchair." But he does sports with kids with nothing wrong with them, he's not as good as them or there's problems so he doesn't really fit into either." (Parent of 14 year old, GMFCS I).*	Sufficiency or saturation	Unclear	

Study information			Quality assessment		
Number of studies	Design	Description of theme or finding	Criteria	Rating	Overall
		Pain as a barrier to physical activity One study (Shimmel 2013) reported that pain is a barrier to performing activities the child enjoys: *"…In yoga you are bending every which-way and when I like bend the wrong way, my muscles go into a Charlie horse and that is extremely painful" (17 year old, GMFCS IV).*			

28.41 Economic evidence

This review question is not relevant for economic analysis because it does not involve a decision between alternative courses of action.

No economic evaluations on social care needs were identified in the literature search conducted for this guideline. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

28.57 Evidence statements

A number of themes emerged from the interviews, focus groups and discussion group studies. . These themes centred around making living with cerebral palsy manageable for the child or young person, coping strategies for parents and children with cerebral palsy and personal preferences. The 4 overall themes were: physical environmental needs, physical support needs, services providing support and condition specific needs.

Three studies reported on the theme physical environmental needs. Two studies reported evidence from children and young people with cerebral palsy and their parents and 1 study reported evidence from children with cerebral palsy. This theme included the subthemes: access to adequate means of transport (moderate quality evidence), mobility and need for equipment (both low quality evidence). These sub themes showed that children and young people with cerebral palsy and their parents experience difficulties with availability of different modes of transports available, mobility (getting around), requiring adaptions to the home and environment as well as provision of specific equipment including wheelchairs and hoists.

Three studies reported on the theme of personal support needs. This theme included a subtheme of need for familial support (low quality evidence) and need for emotional support (very low quality evidence). Within the subtheme of need for emotional support, 1 study conducted in the South Asian community within northern England reported that parents found that faith and spirituality plays an important role in accepting and adjusting to their role as carers.

In total, 4 studies reported on the theme of services providing support. This theme included the subtheme: need for adequate services, equipment and support (moderate quality) which was reported by 3 studies. This subtheme found that respite care, support in the home and school, services providing equipment, financial support and lack of information relating to financial support were all important for children and young people with cerebral palsy and their parents and carers. An additional subtheme identified was needs relating to social participation (low quality evidence). This subtheme reported from 2 studies reported that children and young people with cerebral palsy and their parents found the role of the school, siblings within schools, time required for physical activity, performing physical activity and pain as a barrier to physical activity were all areas which were important for social participation.

One study reported on the theme of condition related needs. This theme included 1 subtheme: needs after surgery (low quality evidence). This subtheme found that children and young people with cerebral palsy undergoing multilevel orthopaedic surgery have specific needs during the rehabilitation period, including revision of equipment to help with personal care and mobility physiotherapy and training. Parents of these children also reported their experiences with rehabilitation. A main barrier that arose was that parents found that coping with their child’s pain was their greatest challenge and felt they received an inadequate level of care support during this period.

28.6 Evidence to recommendations

28.6.1 Relative value placed on the outcomes considered

Evidence on all of the themes relevant to the evidence review were considered important by the Committee. The themes emerging from this evidence review related to the social care needs of children with cerebral palsy and their carers and it is important to note that information regarding condition specific needs and services providing support is covered in section 11 of the guideline on 'Information and support'. However, within the theme of services providing support, the subtheme of need for adequate services, equipment and support reported that parents felt there was a lack of information relating to financial support.

28.6.2 Consideration of clinical benefits and harms

The Committee considered that it was crucial to recommend a minimal level of support available for children and young people with cerebral palsy. The Committee discussed that social support at the time of diagnosis may not be universally available or it may be too emotional for the families to accept support at that stage. Therefore, the Committee recommended that on-going access to a team of health and social care professionals should be available to children with cerebral palsy and their families, so that the child, young person or family can access information and support at the time most relevant for them. On-going access to care should include accessing resources, including financial support, social care, education, participation. The Committee pointed out that welfare rights and charities could also provide financial information and support.

The Committee noted that there was disparity in the UK in terms of social care provision as some areas have social care workers within the multidisciplinary team while other areas do not. There was also a lack of resources available for social care workers, particularly during the transition period (18 – 25 years). The Committee felt that it was important for there to be integrated team working across health and social care teams as part of the multidisciplinary team.

The Committee noted that psychological support for families was very important in terms of helping the mechanisms of coping and acceptance, however they also agreed that the support available was variable and often limited. It was also noted that every local authority has a legal duty of providing care to children and their families in their area.

In terms of helping access to the physical environment, the Committee noted that it was a legal requirement to cater towards people with disabilities in the local community (including local amenities such as shops). This includes improving access and mobility support in the community, such as by providing wheelchair ramps. Additionally, there are statutory provisions such as the 'Blue Badge' which allows access to parking facilities for people with disabilities.

In particular the Committee, led by the child and young person and carer representatives, discussed that there can be limited access to appropriate toileting facilities for children and young people with cerebral palsy in the local Community, though this was not reported in the evidence. Though there are many areas with good provision of such need, this is not universally the case throughout the UK and the Committee felt that this should be addressed.

The Committee acknowledged that information specifically about services and resources available to help access to the physical environment might be limited or not directly available to children and young people with cerebral palsy. The Committee recommended that health care; education and social care professionals should address the specific appropriate, individual needs of transport, mobility, specialist equipment to help with care, participation and toileting facilities for children and young people with cerebral palsy. The Committee considered it was important to highlight that the network of care should provide ongoing

access to a team of health and social care professionals experienced in the care of children and young people with cerebral palsy beyond a focus on mobility and posture. The network team should provide access to health and social care professionals with experience in accessing wider resources for children and young people with cerebral palsy and their families, particularly in the following areas; social care and respite; financial support, educational provision, independent living as well as the problems highlighted previously of physical access.

From the experience of the Committee, support networks available for children with cerebral palsy and their families can be wider than immediate family and can include advocacy groups, charities, other carers and health professionals. For support networks and emotional support, the Committee also recognised the important role of parents, siblings and families as a whole, together with other families in similar circumstances and other carers including nurses and school staff. Parents and professionals recognise that caring for a child or young person with cerebral palsy can also impact on their siblings, who often require their own support. Although it is important to consider the views of the whole family, all professionals should not only consider the parents' needs but also respect the individual child or young person's wishes and respond appropriately.

It was noted that from the evidence that the family unit was shown to be important for providing emotional and support for daily living. Additionally, based on the evidence and from their experience, the Committee considered it was important to recognise the importance of social, cultural, spiritual and religious networks in providing support to children and young people with cerebral palsy and their families.

The Committee noted that respite care was very important in providing support to children and young people with cerebral palsy, their families and carers, including care in the home, NHS establishments or other setting. The Committee felt that health and social care professionals should assess the need for respite care and when appropriate facilitate access to respite care.

With regards to condition specific needs, the Committee also noted that individual tailored health and social care pathways to manage pain and rehabilitation are often important after a major surgical intervention (for example after multilevel orthopaedic surgery, spinal surgery, neurosurgical intervention or gastrostomy placement). Often the re-fitting of equipment and orthoses need to be considered urgently as part of rehabilitation.

28.6.3 Consideration of economic benefits and harms

This review question was not relevant for economic analysis because it does not involve a decision between alternative courses of action. Even so, the provision of any identified social care would incur opportunity costs.

The Committee believed that there are not enough resources devoted to social care needs. It was particularly noted that providing respite care and specialist equipment for all eligible children and young people with cerebral palsy would exceed current social care budgets. Following this, the Committee noted that reviewing the needs of children and young people with cerebral palsy would optimise their functional participation and subsequently their health-related quality of life. However, the benefits of providing such needs has not been assessed; hence, the cost-effectiveness of providing these needs cannot be ascertained. Consequently, the Committee wanted to make recommendations that identified the minimum level of support children and young people with cerebral palsy, families and carers should expect to receive. Bringing social care to this standard would incur large implementation costs; however, early and on-going assessment could both increase the quality of life of children and young people with cerebral palsy and their families and also minimise potential risk of emergency provision.

The Committee also noted that social care needs were sometimes only assessed at the onset of diagnosis in UK clinical practice today. They also stated that the assessment of ongoing needs depended hugely by area, clinician preference, functional ability and/or age. However the child or young person with cerebral palsy's needs and the needs of their family changed over time requiring on-going assessment and psychological support independent of those factors. Moreover, when social care needs are re-assessed at any point after the initial assessment this generally occurs when a specific need is identified. Access is often delayed, potentially leading to further downstream costs if that need is thereby exacerbated.

Ideally the Committee wanted each district multidisciplinary team to have access to a social worker as this would improve the care pathway, increase satisfaction with the level of care received and facilitate timely access to social care services. This may have a significant cost implication as social care staff levels may need to increase as their numbers are thought to be insufficient for a rearrangement in order to provide even the minimum appropriate level of social care.

It was agreed that families need information they can access at the onset of their pathway, after diagnosis has been made. Moreover access to this information needs to be provided in a number of different ways including verbal, written and digital forms. Timely information should be provided to families by their health care professionals as families may not know and may not think to ask what information is available to them especially at key times such as transition. This may incur training costs as the Committee felt health care professionals may not universally be up-to-date on what levels of social care are available for children and young people with cerebral palsy, or be competent to identify when social care needs exist.

28.6.4 Quality of evidence

The quality of the evidence ranged from moderate to very low. The main reasons for downgrading the evidence was data collection and/or analysis was not reported clearly and role and potential influences of researchers described.

28.6.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

28.6.6 Key conclusions

The Committee discussed the following themes identified in the clinical evidence review: physical environmental needs, familial and emotional support needs, services providing support and condition related needs. In light of these themes and their own clinical experience, the Committee agreed that addressing individual needs will promote functional participation, concluding that regular reassessment is needed as social care needs change over time.

28.7 Recommendations

136. Recognise the importance of social care needs in facilitating participation and independent living for children and young people with cerebral palsy.

137. Assess the care needs of every child with cerebral palsy, and of their parents or carers, at diagnosis and reassess regularly if appropriate.

138. Provide information on the following areas of care at diagnosis of cerebral palsy and as appropriate thereafter:

- social care services
- financial support, welfare rights and charities
- support groups (including emotional support for the child or young person and their families and carers, including siblings).

139. Address and review the specific needs of the child or young person with cerebral palsy in relation to accessing their physical environment (for example, home, school, healthcare, workplace, community), in order to optimise their functional participation. Think about the following aspects:

- mobility
- equipment, particularly wheelchairs and hoists
- transport
- toileting and changing facilities.

140. Ensure effective communication and integrated team working between health and social care providers.

141. When assessing care needs, take into account the role of any social, cultural, spiritual or religious networks that support the child or young person with cerebral palsy and their family.

142. Take into account that English may not be the first language of children and young people with cerebral palsy or their parents or carers. Provide an interpreter if necessary. Follow the principles in the NICE guideline on patient experience in adult NHS services.

143. Explore with the child or young person and their parents or carers the value of respite services, such as carer support either at home or in another setting.

144. Ensure that individual, tailored care pathways (including pain management, rehabilitation and equipment) are in place after any major surgical intervention for children and young people with cerebral palsy (see also the NICE guideline on spasticity in under 19s).

28.8 Research recommendations (refer to NICE's guide for research recommendation development

None identified for this topic.

29 Transition to adult services

Review question: What are the specific elements of the process of transition from paediatric to adult services that are important for young people with cerebral palsy and their family members and carers?

29.1 Introduction

Transitioning young people from paediatric health services to adult-based healthcare systems and between the respective education and social services is a recognised challenge, however due to the complexities of their neurodisability this is often an extremely difficult, and sometimes distressing time for young people with cerebral palsy and their families. The issues are multifaceted and include the local availability of appropriate adult services and management by multiple professionals/disciplines; various concurrent care packages; the difficulties of finding suitable education placements and respite for adolescents; the recognition of the importance of family members and/or carers; funding issues; and critically the co-ordination of management of comorbidities.

Clearly it is recognised that transition is not simply an onward transfer of care but should be a purposeful, planned, individualised process which requires co-ordinated and joined up working between paediatric and adult based health and social services. However, many young people with cerebral palsy, their families and carers feel let down by the current process and report that they feel abandoned at a time when they are facing significant life challenges.

Effective transition is important for all young people with health needs, as outlined in the NICE guideline on transition from children's to adult's services. However, they were specifically focused on aspects that are particularly important or unique for young people with cerebral palsy, their families and carers.

The aim of this review is to identify elements of the transition process (for example involvement in transition planning) from paediatric to adult services from perspectives of young people with cerebral palsy and their family and carers.

29.2 Description of clinical evidence

Qualitative studies were selected for inclusion for this review. We looked for studies that collected data using qualitative methods (such as semi-structured interviews, focus groups, and surveys with open-ended questions) and analysed data qualitatively (including thematic analysis, framework thematic analysis, content analysis etc.). Survey studies restricted to reporting descriptive data that were analysed quantitatively were excluded.

Findings/themes were summarised from the literature and were not restricted to only those identified as likely themes by the Committee in the evidence review protocol. The majority of themes listed in the protocol were identified in the studies, apart from the need for health care professional training in transition to improve practice. An additional theme: 'expectations around the timing', was identified in the literature and included.

A total of 5 studies were included in this review (Bjorquist 2015; Carroll 2015; Di Fazio 2014; Lariviere-Bastien 2013; Young 2009).

The following provides a brief description of the studies included:

One study (Bjorquist 2015) was conducted in Sweden and used a combination of focus groups and individual interviews, in a sample of 12 adolescents with cerebral palsy. The study reported on a number of themes, including data on information delivery, awareness of

services available, hopes and concerns for the future (independency), and need for a named point of contact throughout the process.

One study (Carroll 2015) was conducted in the US and used unstructured interviews in a sample of 9 young adults with cerebral palsy. The study reported in particular on the need for multidisciplinary team involvement and continuity in coordinated care, service configurations, expectations around the timing of transition, and on the patients' role during visits (self-advocacy).

One study (Di Fazio 2014) was conducted in the US and used semi-structured group interviews in a sample of 14 participants of which 5 were adults with cerebral palsy and 9 were parents of adults with cerebral palsy. The study reported in particular on transition planning, with regards to timing and readiness, accessibility of services, training of staff, need for continuity in coordinated care, and need for more information, for example in the form of a support group for parents.

One study (Lariviere-Bastien 2013) was conducted in Canada and used semi-structured, one-to-one qualitative interviews in a sample of 14 young adults with cerebral palsy. The study reported on several themes, including the loss of continuity with specialist paediatric services, reduction of time and resources from paediatric to adult services, different follow-up systems which is left to the family/carers and timing of information delivery.

Finally, 1 study (Young 2009), also conducted in Canada, used a semi-structured interviews format in a sample of 30 pairs of children and young people and their parents. The group included 14 individuals with cerebral palsy (5 mild cerebral palsy, 5 with moderate cerebral palsy and 4 with severe cerebral palsy), 9 participants with spina bifida and 7 with acquired brain injury. The study reported on the need for guidance and information during the process of transition, the importance of a coordinator figure and the lack of continuity of care from paediatric services.

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, study evidence tables in Appendix J and exclusion list in Appendix K.

29.2.1 Summary of included studies

A summary of the studies that were included in this review are presented in Table 132.

Table 132: Summary of included studies

Study	Study design/ methods	Population	Aims	Comments
Bjorquist 2015	A combination of focus group and individual interviews.	N = 12 adolescents with CP, aged between 17 and 18 years.	To gain a deeper understanding of how adolescents with CP experience their own health, well-being and needs of support during their transition to adulthood.	Overall quality based on limitations: moderate
Carroll 2015	Individual interviews	N = 9 young adults with cerebral palsy	To uncover the meaning of transition to adult-centred care as experiences by young adults with CP.	Overall quality based on limitations: moderate
Di Fazio 2014	Prior to	N=14 (5 adult	To describe and	Overall quality

Study	Study design/ methods	Population	Aims	Comments
	conducting the 2 focus groups, separate but parallel moderator guides were developed for the patients and carers to be used in facilitating group discussion as needed.	patients with CP and 9 parents of adults with CP).	define the experiences of adults with CP and parents of adults with CP who have been involved in a transfer of psychiatric care from paediatric to adult healthcare and to explore their experiences more generally in the transition from paediatric to adult services.	based on limitations: moderate
Lariviere-Bastien 2013	Participation included a semi-structured, one-to-one qualitative interview	N= 14 young adults with cerebral palsy aged 18-25 years.	To report data about the transition process gathered from young adults with cerebral palsy who have experienced various forms of transition.	Overall quality based on limitations: very low
Young 2009	Youths and parents were interviewed separately with in semi-structured interview format.	N=30 children and young people and their 30 parents (n=30 pairs). The youth sample ranged in age from 14.8 to 19.6 (mean 17.8) years and the adult sample from 24.8 to 32.8 (mean 28.0) years. In total, there were 14 individuals with CP (5 mild CP, 5 with moderate CP and 4 with severe CP), 9 participants with SB and 8 with ABI.	To examine the issue of clinical transition from the perspectives of individual patients with mild, moderate, and severe CP, spina bifida (SB) and acquired brain injury (ABI) and their parents, to better understand the scope of this issue and to assist with the development of evidence-based health care transition	Overall quality based on limitations: low/moderate

1 *CP cerebral palsy, SB spina bifida, ABI acquired brain injury.*

29.2.2 Clinical evidence profile

3 Individual studies were assessed for methodological limitations using an adapted Critical
4 Appraisal Skills Programme (CASP 2006) checklist for qualitative studies, where items in the

original CASP checklist were adapted and fitted into 5 main quality appraisal areas according to the following criteria:

- aim (description of aims and appropriateness of the study design)
- sample (clear description, role of the researcher, data saturation, critical review of the researchers' influence on the data collection)
- rigour of data selection (method of selection, independence of participants from the researchers, appropriateness of participants)
- data collection analysis (clear description, how are categories or themes derived, sufficiency of presented findings, saturation in terms of analysis, the role of the researcher in the analysis, validation)
- results / findings (clearly described, applicable and comprehensible, theory production)

An adapted GRADE approach was used to assess the evidence by themes. Similar to GRADE in effectiveness reviews this includes 4 domains of assessment and an overall rating:

- limitations across studies for a particular finding or theme (using the criteria described above)
- coherence of findings (equivalent to heterogeneity but related to unexplained differences or incoherence of descriptions)
- applicability of evidence (equivalent to directness, i.e. how much the finding applies to our review protocol)
- saturation or sufficiency (this related particularly to interview data and refers to whether all possible themes have been extracted or explored)

The clinical evidence profile for this review question (transition to adult services) is presented diagrammatically in a theme map Figure 6 in the adapted GRADE approach for qualitative findings in Table 133 and Table 134.

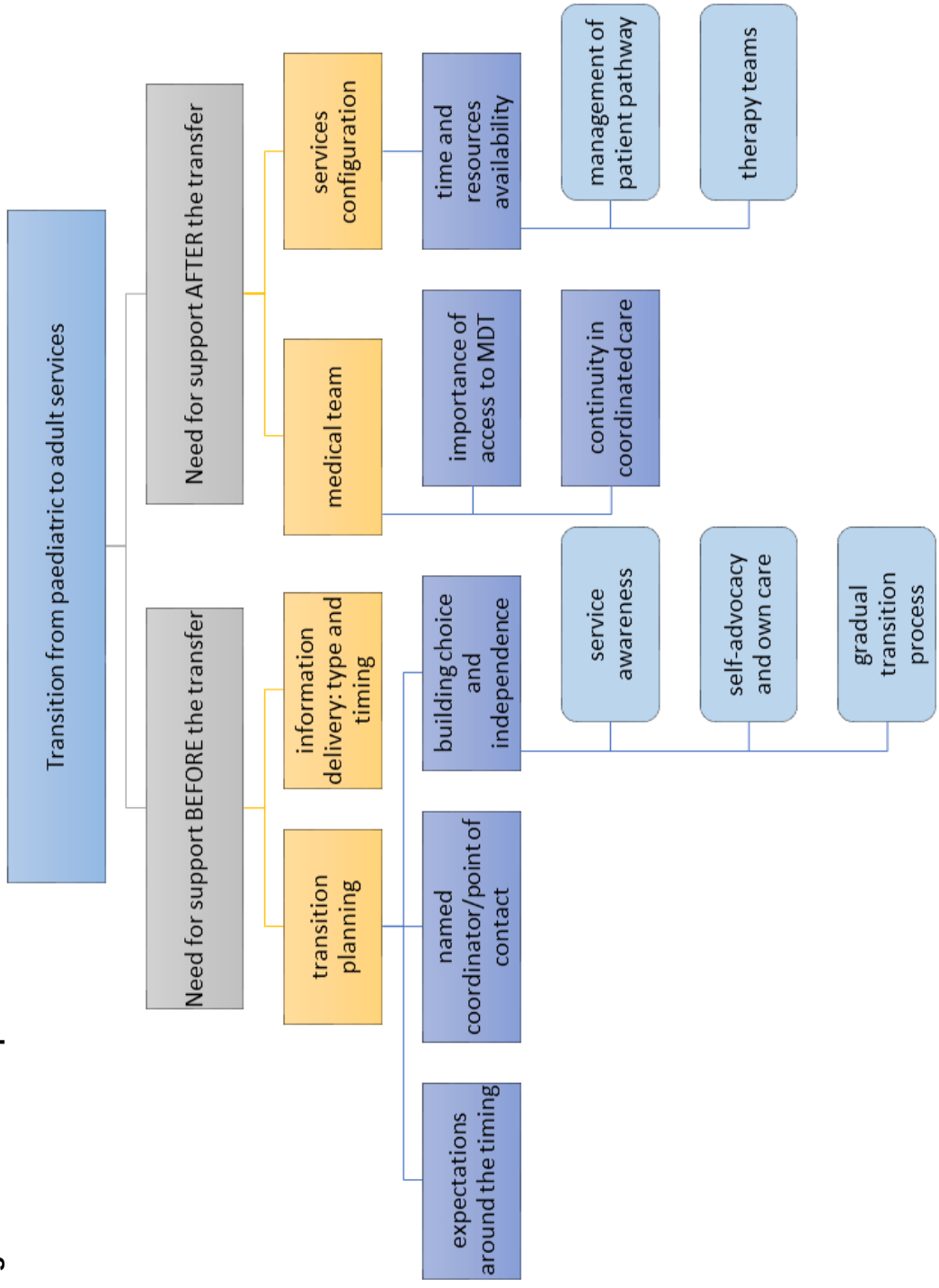


Figure 6: Theme map of the evidence

Table 133: Summary of clinical evidence (adapted GRADE approach for qualitative findings) – theme: need for support before the transfer to adult services

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
Sub-theme 1: transition planning					
4 studies	1 individual interview, 3 semi-structured group interviews	• Expectations around the timing • 4 studies (Carroll 2015; Di Fazio 2014; Lariviere-Bastien 2013; Young 2009) reported the need of careful transition planning, especially with regards to the timing involved: the topic of transition with CP to adulthood shouldn't be a new concept. Participants were unprepared and they felt that they were not active participants of the timing of the decision. • *: "(...) if you're seeing somebody every six months or every year until you're like seventeen, eighteen, there's some kind of connection there. So then they'd be like okay you are away now. It's kind of like wait, what are you doing with me?"* • Patients and their parents wanted the process to be transparent, specific and clear, with frank discussion around its trajectory • *: "I think a discussion needs to occur earlier (...) just need to bring this up with the two parents and adolescent at an earlier stage so that everybody, parent and child become comfortable with the fact that they are going to have a transition period (...)" (parent).* • Another parent recommended that the transition process started earlier: • *"I just would wish it would start early and get parents involved, to the point that we kind of know where we're going. I think the hardest part is we're scared, we're nervous".* • A Feeling of abandonment during the transition was also reported. • *"...when I moved from the paediatric system to the adult system, I felt really disoriented. Because I saw that we would*	Limitation of evidence Coherence of findings Applicability of evidence Sufficiency or saturation	Major limitations Coherent Applicable Saturated	Moderate

Study information			Quality assessment		
Number of studies	Design	Description of theme or finding	Criteria	Rating	Overall
		be less supported and that it would be more difficult". • Named coordinator/point of contact • 3 studies (Bjorquist 2015; Di Fazio 2014; Young 2009) reported on the need for a contact person or coordinator who would be able to give more individual support. • Parents identified the need for a social worker, nurse or care coordinator who could help to advocate on their behalf as needed, as well as support groups for parents designed for information sharing: • *"Support groups are great, but they take up your time. I'm too busy doing everything. I want to be knowledgeable and empowered. I want something where you can talk about your concerns, share ideas and have a nurse or a physician or something bring the information".* • A parent of a participant who had transitioned 2 years before: *"someone, on a one-on-one basis, who would walk through all the individuals that you are seeing and if not give you names [of new adult services providers], at least give you some specifics so you would go look for them. In other words, the best person to make recommendations might be the current caregiver, but again to have somebody help us to coordinate it so that we are not out there trying to do it ourselves".* • Building choice and independence • 3 studies (Carroll 2015; Bjorquist 2015; Di Fazio 2014) reported on the importance of being allowed to make choice and build independence gradually. • Self-advocacy and own care - There is an expectation that patients should be partners in the health visit. • Need of understanding what is different about adult care, thus allowing them to be more proactive, informed decisions about care requirements and preferences.			

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		• *"They don't put him under anaesthesia, they just kind of tranquilize him... my son doesn't speak so he has no real way of communicating, but when he feels strongly about something, he sticks his tongue out and the whole time we were there, he had his tongue out" (Mother of a young man with significant global impairment reflected on the differing approaches to Botox injections".* • Patients indicated they needed more formal preparation in self-advocacy and needed to learn how to become self-sufficient in managing their own care (i.e. how to manage appointments, maintain personal healthcare records...). • *"As kids I mean we just see like pieces of paper being handed off to people and assuming it goes off to some magical land where it gets taken care of when that's not the case at all and then when it gets handed over to us, you kind of don't know what to do with it".* • However, patients expressed some ambivalence when it comes to handling bureaucratic issues: *"I don't know if it was my parents doing it and I just thought that the office staff did it. I really don't know, but I'm doing more work that leads me to advocate for myself, but I feel like you have assistants, you have secretaries: can't somebody else send a letter or make a phone call?"* • Gradual process - Participants looked forward to being independent and being treated with respect as adults, but at the same time they thought it was too early to think about the future and they lacked readiness and willingness to move away from home. They were concerned about the future and unsure about what kind of support they would need. Moving away from home step-by-step was considered an option to facilitate the first time in adult life just as settling down near the parents or moving to a college or a group home with staff and friends nearby, like a stepping-stone.:			

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		• *"...excuse me, but do I really have to think about the future right now?"* • Service awareness - Participants had little awareness about adult services and they only had a vague idea about the type of support that was available there. One participant described his experience from an information meeting about becoming an adult: • *"...It was one of those big meetings. It was about if you're moving away from home and you need help with the economy and things like that if you have like more severe disabilities. But... there wasn't really much that concerned me, just that I'll transfer to the Adult Rehabilitation services when I turn 20..."*			
Sub-theme 2: information delivery: type and timing					
4 studies	1 combination of focus group and individual interviews, 3 semi-structured group interviews	4 studies (Bjorquist 2015; Di Fazio 2014; Lariviere-Bastien 2013; Young 2009) reported on the need for more information throughout the process of transition • Patients wished for support in the process of transition and individualised information about what kind of support would they be able to get. Verbal information was preferred to information booklets which were difficult to read. • Parents also identified the need of a social worker, nurse or care coordinator who could help to advocate on their behalf as needed, as well as support groups for parents designed for information sharing: • *"Support groups are great, but they take up your time. I'm too busy doing everything. I want to be knowledgeable and empowered. I want something where you can talk about your concerns, share ideas and have a nurse or a physician or something bring the information".* • Participants would have liked more information about the characteristics, better support during the transition period	Limitation of evidence	Moderate limitations	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Saturated	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		and having been introduced earlier to the healthcare professionals. • *"(...) at least to be told "OK, you are now 18, so you will go there, and it is so-and-so physician who will take care of you"* • Many participants thought it was necessary having more information before the process of transition, and not solely directed to parents, but also to patients: • *"I think they've told my mom the different services. They don't really inform me. They seem to have my mom still more involved than me, I'd like to know".*			

Table 134: Summary of clinical evidence (adapted GRADE approach for qualitative findings) – theme: need for support after the transfer to adult services

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
Sub-theme 1: the medical team					
2 studies	1 interviews, 1 interviews and focus groups	• Importance of access to MDT • 1 study (Di Fazio 2014) reported on the lack of access to appropriately trained/experienced adult providers as the most significant challenge that parents and patients identified. • *"It was like he had no clue of my non-verbal child and I was totally put off by his suggestions. He has lost 12 pounds. This is a three year transition. He has contractures... I know he needs care and it's very frustrating" (Parent).* • The lack of specialty providers comfortable with dealing the underlying developmental issues and the lack of multidisciplinary teams was also acknowledged: • *"(...) like he (his son) has GI problems also. If I just went to my local hospital for convenience and went to a GI doctor, they'd look at him like oh my God, I don't know what to do.*	Limitation of evidence	Major limitations	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	
			Sufficiency or saturation	Saturated	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		Like they can do the GI part, but they don't know the other part and that's what is nice about coming here (referring to the paediatric setting) (...)". • Parents and patients found inconvenient the shift from multi-disciplinary care in paediatric services to brief specialty visits focusing in a single complaint in the adult setting. • Continuity in coordinated care • 2 studies (Carroll 2015; Di Fazio 2014) reported on patients and parents/carers experiencing unfamiliar and more fragmented adult health care models. • No bridge to care from one to another: patients often were placed in limbo, often resulting in delaying necessary care: • *"My knee has been hurting for years...They're kind of okay go see Dr... and I'm like Dr... is awesome, but he doesn't deal with knees, he in turn refers me to somebody else and that person does not get back to me and I still haven't done this (...)"* • Participants were also dissatisfied with the lack of coordinated care covering the gamut of preventive, corrective, and restorative services: • *"(...) There's so many more comprehensive interdisciplinary paediatric services period for any illness than there are for adults... so there isn't a continuity for this" (Parent).*			
Sub-theme 2: services configuration					
2 studies	1 interviews, 1 interviews and focus groups	Time and resources availability 2 studies (Carroll 2015; Di Fazio 2014) reported that participants felt they have lost the resources available to them in the paediatric system. It is the abruptness of the transition that was most disruptive to participants, and lack of time and resources in the adult healthcare system.	Limitation of evidence	Moderate limitations	Moderate
			Coherence of findings	Coherent	
			Applicability of evidence	Applicable	

Study information			Quality assessment		
Number of studies	**Design**	**Description of theme or finding**	**Criteria**	**Rating**	**Overall**
		• Several participants missed the lengthy medical visits they had received in the paediatric system • *"When I was at [name of the paediatric hospital] for the same surgery I would stay for 12 hours and sleep overnight, whereas in the adult system, after the same surgery they ship you home after an hour (...)"* • *"And they give you 15 minutes. So like they're trying to figure out, trying to figure it out in 15 minutes. When a normal person goes in for their 15 minutes, forget about all the other stuff and I don't know about you guys but I always leave feeling like I didn't get results".* • Management of patient pathway - Better support and more follow-up in the paediatric system • Participants valued the follow-up and support received in paediatric healthcare, especially the fact that they took the time to communicate with them, reminding them to attend appointments. • *"(...) if you don't run after them [occupational therapists, physicians], if you don't remember you need to see a physician, they won't call you".* • Difficulty accessing physicians and healthcare professionals in the adult healthcare system was also reported • *"That, I will admit that, I had forgotten that but I really struggle to find a physiatrist (doctor). And I don't feel my request was taken seriously (...)"* • Therapy teams – patients and parents reported that primary care and specialty physicians willing to care for adults with CP were either unavailable or unexperienced. Additionally, the lack of specialists made the transition more challenging. For example, adults with CP usually require less orthopaedic surgical interventions than children, but they still need ongoing support:	Sufficiency or saturation	saturated	

Study information			Quality assessment		
Number of studies	Design	Description of theme or finding	Criteria	Rating	Overall
		• *"Again in the orthopaedic end, I asked my doctor if there was anybody he would recommend to transfer my care over, he did not know. So I was left in limbo and still to this day I'm looking for a surgeon that will take a look at me and my care".* • *"With the CP stuff it's a whole different level of complicated. How frustrating it is to be, to having an acute need and to have the doctor say I don't know what the effects would be because I don't know enough about CP and you ask him well where should I go and they don't have an answer for you"* • Patients reported that often professionals are less familiar with characteristics of CP • *"(...) physicians do not know what to do (...) when they say "Oh, well you can go do your exercises, and workout, and you'll be OK, you'll be better". This is what I have done all my life. They do not have any other solutions than this for me"*			

29.3 Economic evidence

This review question is not relevant for economic analysis because this area is about identifying particular needs associated with transition rather than alternative approaches to providing transition.

One study protocol (Colver 2013) related to the process of transition from paediatric to adult services was identified in the literature search conducted for this guideline, but the results from this cost-consequence analysis are yet to be published. No further economic evaluations were identified for this review question. Full details of the search and economic article selection flow chart can be found in Appendix E and Appendix F, respectively.

29.4 Evidence statements

A number of themes emerged from the evidence provided from interviews, focus groups and discussion groups with both young people with cerebral palsy and their parents or carers.

The themes developed around an a-priori division between support needed before the transfer to the new health care services and the support needed after the transfer has happened. Specific themes were: transition planning, information delivery, set up of clinical teams, and service configuration.

29.4.1 Transition planning

Four studies of overall moderate evidence reported on the theme of transition planning.

Four studies reported evidence from both young people with cerebral palsy and their parents on expectations around the timing of transition, which showed how patients and their families felt unprepared to deal with the change. The evidence also showed that patients and their parents wanted the process to be transparent, specific and clear, with frank discussion around its trajectory from the very beginning of the process.

Three studies reported on the subtheme of “named coordinator/point of contact”, demonstrating the importance of a contact person or coordinator who would be able to give more individual support to patients and families.

Three studies reported on a third subtheme, “building choice and independence”: the evidence showed that the patients would like a care system that allows them to be more proactive, and make informed decisions about care requirements. The studies showed that the patients indicated they needed more formal preparation in self-advocacy and needed to learn how to become self-sufficient in managing their own care. Participants had little awareness about adult services and they only had a vague idea about the type of support that was available there.

29.4.2 Information delivery

Four studies of overall moderate evidence reported on the theme of information delivery.

The evidence showed that patients wished for support in the process of transition and individualised information about what kind of support they would be able to get. It was reported that verbal information was preferred to information booklets which may be difficult to read. The studies also showed that participants wished that the information was available not solely to parents, but to patients as well.

29.4.3 The medical/clinical team

Two studies of overall moderate quality reported on the theme of the medical/clinical team.

One study reported on the importance of having access to a multidisciplinary team of health care professionals, showing that the lack of access to appropriately trained/experienced adult providers is the most significant challenge that both young people with cerebral palsy and their parents identified. In addition, participants reported that there is a lack of specialty providers comfortable with dealing the underlying developmental issues.

Two studies reported on the importance of having continuity of coordinated care from the paediatric to adult services.

29.4.4 Service configuration

Two studies of overall moderate quality reported on the theme of service configuration.

The evidence showed that participants felt as though they have lost the resources available to them in the paediatric system, as they valued the follow-up and support received in paediatric healthcare. Additionally, patients and parents reported the lack of experienced primary care and specialty physicians willing to care for adults with cerebral palsy, and that this made the transition more challenging.

29.5 Evidence to recommendations

29.5.1 Relative value placed on the outcomes considered

The aim of this review was to identify elements of the transition process (for example, transition planning involvement) from paediatric to adult services from perspectives of young people with cerebral palsy and their family and carers. Evidence on all of the themes relevant to the evidence review question were considered important by the Committee but it was recognised that many of these are covered in the NICE guidance on transition which is duly referenced.

29.5.2 Consideration of clinical benefits and harms

The Committee acknowledged the evidence presented and was not aware of important studies that have been missed in the review.

An overarching recommendation pointed to the NICE guideline on transition from children's to adult services for young people using health or social care services. Although a personal 'folder' was recommended in the NICE guideline on transition from children's to adult services, the Committee agreed that it was important to emphasise the value of this by including consideration of the development of a personal folder to contain relevant information for the transition in this guidance.

The Committee recognised that during and following periods of transition, there was on-going developmental, social and medical change in children and young people with cerebral palsy, therefore services needed should be optimised and individualised. In addition, it was highlighted that because of the range of comorbidities encountered and associated problems, often there were multiple sub-transitions within 1 overall transition frame (for example, transition in speech and language therapy or from school to College). This is most commonly encountered in the change from children's health to adult health services.

In paediatrics there is a focus on holistic management of the individual, however in many adult healthcare services often a single system approach is encountered, with specialists in a particular aspect such as epilepsy, gastroenterology or rheumatology. This change to a wider

variety of health resources can be particularly challenging. The need to develop a more wide spread professional expertise in managing adults with cerebral palsy was highlighted. The Committee were aware of the huge variability in providing transition services in the UK, and also about the resource impact that the recommendations in this guideline might have.

The Committee highlighted how social care aspects of transition to adult services seem to be missing from the evidence despite their crucial role during this process, and therefore tried to incorporate both health and social care when making recommendations.

The Committee discussed the evidence and agreed that readiness to transition was key for the whole process, so it is important to start the conversation about transition with both the patient and families at an early stage. Involvement of a key worker / coordinator or named GP to facilitate this process is crucial for success.

When reviewing the evidence, the Committee recognised the importance of strengthening the links between adult and paediatric services. By ensuring this link, the transition planning for the person would be more effective. A recommendation was made to this effect which also reflects that both health and social care systems should be developed at a local and regional level. The Committee also agreed on the importance of ensuring that pathways and protocols for transition to adults' services were implemented from an early stage across health, social care and education settings at both local and regional levels ensuring a transparent and gradual trajectory of care and providing clear knowledge of what services are available.

The Committee agreed that it was important to establish connections before the transfer begun by identifying the key worker/ named GP and at an early stage named individuals who would be involved in the adult services at a local and regional level. The Committee underlined the importance of accessing professionals with an understanding of managing cerebral palsy. Once again, this was particularly important as there are often a variety of service providers in adult care, in contrast with coordination of care by a multidisciplinary team within paediatrics, particularly in a child development service.

The need for training in awareness of the needs of young people with cerebral palsy for all service providers in adults' services was discussed for example by utilising the 'Engagement with The Disability Matters' e-learning programme. This is a learning programme targeted at all those who work, volunteer or engage with children and young people with disability. (https://www.disabilitymatters.org.uk/) Service providers for children and young people with cerebral palsy were also expected to maintain competencies through the normal channels of continued professional development through their relevant specialist bodies.

The Committee also wanted to highlight the theme in the evidence in terms of the need of people with cerebral palsy to feel able to be more pro-active and to self-advocate during the transition process.

The Committee discussed the fact that in the studies analysed, people with cerebral palsy and families reported that they preferred verbal communication to written and thought this may reflect the need for adequate verbal information to be given before presenting children and young people and their families with written information. The Committee recognised that ultimately the goal was to provide individualised information, in the form most suited to the young adult, their families and carers. in particular, when it comes to delivering and making available information, the Committee agreed that this should be a 2 way process – individualised and personalised in a format preferred and directed to the young person's needs.

Moreover, the Committee acknowledged the importance of maintaining the information and patient pathway through life. They noted that it was crucial to capture the paediatric history, for example birth history or the timing and outcome of any intervention. It is important that

this information is available for the person with cerebral palsy journey into and throughout adult care, the personal folder is one such way to ensure this.

29.5.3 Consideration of economic benefits and harms

This review question was not relevant for economic analysis because it does not involve a decision between alternative courses of action. Even so, there may be resource implications arising from the provision of any services that facilitate the transition from paediatric to adult services.

From their experience, the Committee believed that there were not enough resources devoted to the transition from paediatric to adult services in children and young people with cerebral palsy. Consequently they wanted to make recommendations that identified the minimum level of support children and young people with cerebral palsy, their families and carers should expect to receive to prevent geographical variation.

Identifying accountable health care professionals prior to the transition from paediatric to adult services would promote a transparent and efficient transition at a negligible administration cost. Following this, the Committee considered a role for pathway/medical co-ordinators to identify and contact health care professionals on behalf of patients; however, this would have a substantial implementation cost as administrators do not regularly take on this role in UK clinical practice. Despite this, the Committee agreed this would promote timely access to the appropriate healthcare professional, leading to better identification and thus more timely management, therefore, some of the investment may produce offsetting downstream costs.

The Committee noted that cerebral palsy is a trained and compulsory speciality in paediatrics that provides patients with a specialist MDT. Conversely cerebral palsy is managed as a health care professional's normal case load in adult services. Ideally the Committee wanted adult patients to have access to health care professionals with a specialist interest in cerebral palsy. This would have a significant cost implication as training would need to increase as the number of health care professionals with the necessary competencies to manage adult patients with cerebral palsy are thought to be insufficient.

The Committee advised reengagement with the General Practitioner (a named contact) prior to the transition from paediatric to adult services, as this is where specific medical needs are likely to be identified in adulthood. This may increase the workload of General Practitioners as it is thought their advice is not regularly sought. The Committee advised that General Practitioners often have a long standing relationship with children and young people with cerebral palsy and possess the data and knowledge to piece together all of their history and treatment (history and treatment related to, and not limited to cerebral palsy) to deliver timely and appropriate management. Additional training costs are not expected to be substantial as General Practitioners should already know when to identify the complications of cerebral palsy in the general population. Training may be needed to increase General Practitioners awareness of the prevalence of those complications, but this guideline can provide a basis for this.

Overall, providing the identified needs of the process of transition could incur large staff training costs and potentially stretch the workload of administrators and General Practitioners; however, early and ongoing support would increase patient satisfaction and potentially, their health-related quality of life.

29.5.4 Quality of evidence

The quality of the evidence ranged from moderate to very low. The main reasons for downgrading the evidence was data collection and/or analysis was not reported clearly and the roles and potential influences of researchers described.

29.5.5 Other considerations

The recommendations related to this evidence review were based on the evidence and the Committee's clinical experience.

29.5.6 Key conclusions

The Committee concluded that whilst effective transition is important for all young people with health needs, young people with cerebral palsy and their families and carers have additional challenges which make it even more difficult. Lifelong care has to date been provided by multidisciplinary paediatric teams with little or no contact with their GP. It is recognised that adult care is more fragmented and health care professionals do not universally have skills in managing young people with cerebral palsy and the associated comorbidities. However with early planning, named individuals with appropriate training and full involvement of the young person with cerebral palsy and their families and carers this can be achieved.

29.6 Recommendations

145. Follow the NICE guideline on transition from children's to adults' services for young people using health or social care services.

Overarching principles

146. Recognise that challenges for young people with cerebral palsy continue into adulthood, and ensure that their individual developmental, social and health needs, particularly those relating to learning and communication, are addressed when planning and delivering transition.

147. Recognise that for young people with cerebral palsy there may be more than one transition period in health and social care settings; for example, college, resident educational and adult home settings.

Transition planning

148. Develop clear pathways for transition that involve:

- the young person's GPs **and**
- named paediatricians and named clinicians in adults' services, both locally and regionally, who have an interest in the management of cerebral palsy.

149. Ensure that professionals involved in providing future care for young people with cerebral palsy have sufficient training in order to address all their health and social care needs.

150. As a minimum standard of care, ensure that the young person has access to adults' services both locally and regionally that include healthcare professionals with an understanding of managing cerebral palsy.

151. Ensure that all relevant information is communicated at each point of transition; for example, using a personal 'folder' containing relevant information as described in recommendation 36 (see also recommendations about support before transfer in the NICE guideline on transition from children's to adults' services).

152. Recognise that functional challenges (including those involving eating, drinking and swallowing, communication and mobility) and physical problems (including pain and discomfort) may change over time for people with cerebral palsy, and take this into account in transition planning.

153. Provide a named worker to facilitate timely and effective transition, and recognise the importance of continuity of care (see also recommendations about transition planning in the NICE guideline on transition from children's to adults' services) and about continuity of care and relationships in the NICE guideline on patient experience in adult NHS services).

29.7 Research recommendations

None identified for this topic.

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31 Acronyms and abbreviations

Table 135: Acronyms and abbreviations

Abbreviation	Definition
AAC	Alternative augmentative communication
ABI	Acquired brain injury
ACA	Available case analysis
ACPR	Australian Cerebral Palsy register
ACT	Acceptance and Commitment Therapy
ADD	Attention deficit disorder
ADHD	Attention deficit hyperactivity disorder
AGA	Appropriate birthweight for gestational age
aHR	Adjusted hazard ratio
AMED	Allied and complementary medicine database
aOR	Adjusted odds ratio
Apgar (score)	Appearance, Pulse, Grimace, Activity, and Respiration
ASD	Autistic spectrum disorder
ARD	Absolute risk difference
aRRs	Adjusted risk ratios
ATN	Asymmetric tonic neck posture
AUC	Area under the curve
Bayley-III	The Bayley Scales of Infant and Toddler Development – Third edition
BMAD	Bone mineral apparent density
BMC	Bone mineral composition
BMD	Bone mineral density
BMI	Body mass index
BMI	Body mass index
BNF	British National Formulary
BP	Twice daily
BPD	Bronchopulmonary dysplasia
BSID	Bayley Scale of Infant Development
BW	Birth weight
BOTOX	Botulinum toxin type
CASP	Critical appraisal skills programme
CBA	Cost-benefit analysis
CBCL	Child Behavioural Checklist
CBT	Cognitive Behavioural Therapy
CC	Complications and comorbidities
CCA	Cost-consequence analysis
CCTR	Cochrane Controlled Trials Register
CDIIT	Comprehensive Development Inventory for Infants and Toddlers
CEA	Cost-effectiveness analyses
CEACS	Cost-effectiveness acceptability curve
CFC	Chlorofluorocarbon
CHQ	Child Health Questionnaire
CI	Confidence interval

Abbreviation	Definition
CIMT	Constraint-induced movement therapy program
CINAHL	Cumulative index of nursing and allied health literature
CMV	Cytomegalovirus infection
CNS	Central nervous system
CoNS	Coagulase-negative staphylococcus
CP	Cerebral palsy
CP-QOL	Cerebral palsy quality of life
CrI	Credible interval
CSDI	Composite sleep disturbance index
CSF	Cerebro-spinal fluid
CUA	Cost-utility analysis
CVD	Cardiovascular disease
CVI	Cortical visual impairment
DA	Definitely abnormal
DALYs	Disability-adjusted life years
dB	Decibel
DEXA	Dual-energy X-ray absorptiometry
DGM	Deep grey matter lesion
ECBI	Eyberg Child Behaviour Inventory
EBD	Emotional Behavioural Difficulties
EDS	Emotional difficulties score
EMPP	Early Motor Pattern Profile
ENT	Ear, nose and throat
EOS	Early onset sepsis
EPIPAGE (study)	Etude Epidémiologique sur les Petits Ages Gestationnels
EQ-5D	EuroQol five dimensions questionnaire
FEES	Fiberoptic endoscopic evaluation of swallowing
FFAm	Functional Feeding Assessment
FLACC	Face Legs Activity Cry and Consolability
FMs	fidgety movements
FRAX	Fracture risk assessment tool
GA	Gestational age
GHQ	General Health Questionnaire
GMA	General Movement Assessment
GMFCS	Gross motor function classification system
GMFM	Gross Motor Function Measure
GORD	Gastro-oesophageal reflux disease
GOT	Grating Orientation Task
GP	General practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GRRBAS	Grade, Roughness, Breathiness, Asthenia, Strain scale
HABIT	Hand-arm intensive manual therapy
HADs	Hospital anxiety and depression scale
HCHS	Hospital and community services
HCP	Healthcare professional

Abbreviation	Definition
HEED	Health economic evaluations database
HIE	Hypoxic ischaemic event
HR	Hazard ratio
HRG	Healthcare resource group
HRQoL	Health related quality of life
HTH	Health technology assessment
HYEs	Healthy year equivalents
ICD	International classification of diseases
ICER	Incremental cost-effectiveness ratios
ICF	International Classification of disability and health
IMP	Infant motor profile
INB	Incremental net benefit
INRS	Individualized Numeric Rating Scale
IQ	Intellectual quotient
IS	Impact score
ISMAR	Innsbruck Sensorimotor Activator and Regulator
ITT	Intention-to-treat analysis
IUGR	Intrauterine growth restriction
IVH	Intra-ventricular haemorrhage
KG	Kilogram
LAQ-CP	Lifestyle assessment questionnaire- Cerebral palsy
LETR	Linking evidence to recommendations
LL	Lower limbs
LOS	Late onset sepsis
LSVT LOUD	Intensive voice treatment
MABC-2	Movement Assessment Battery for children – second edition
MFQ	Mood and Feelings Questionnaire
MG	Multiple gestation
MID	Minimally important difference
MR	Means ratio
MRI	Magnetic resonance imaging
MSMP	Motor-speech movement pattern
MV	Mechanical ventilation
N/A	Not applicable
N/R	Non reported
NC	Not calculable
NCCPC-PV	Non-communicating Children's Pain Checklist – Postoperative Version
NE	North-east
NECCPS	North of England Collaborative Cerebral Palsy Survey
NG	Nasogastric
NGA	National Guideline Alliance
NHAMES	National health and nutrition examination survey
NHS	National health service
NHS EED	NHS economic evaluation database
NICE	National Institute for Health and Care Excellence

Abbreviation	Definition
NICPR	Northern Ireland Cerebral Palsy Register
NICU	Neonatal intensive care unit
NIHR	National Institute for Health Research
NMB	Net monetary benefit
NNE	Neonatal neurological examination
NNT	Number needed to treat
NPV	Negative predictive value
OMAS	Oral Motor Assessment Scale
ONS	Office of National Statistics
OR	Odds ratio
OT	Occupational therapist
OTseeker	Occupational therapy systematic evaluation of evidence
P	P-value
PA	Perinatal asphyxia
PA	Perceptual accuracy
PAT	Physical Activity Test
PDA	Patent ductus arteriosus
PDT	Palatal training aid/device
PEDI	Paediatric Evaluation of Disability Inventory
PEDro	Physiotherapy evidence database
PedsQL	Pediatric Quality of Life Inventory
PEDS-QL	Pediatric quality of life inventory
PEG	Percutaneous endoscopic gastrostomy
PhS	Physical health (subscale)
PICO	Population, intervention, comparison, outcome
PPP	Pediatric Pain Profile
PPV	Positive predictive value
PRISMA	Preferred reporting items for systematic reviews and metal-analyses
PROM	Premature rupture of membranes
PROMPT	Prompts for Restructuring Oral Muscular Phonetic Targets
PSA	Probabilistic sensitivity analysis
PsS	Psychosocial (subscale)
PSSRU	Personal social services research unit
PsycINFO	Psychological information database
PTA	Palatal training aid
PVL	Peri-ventricular haemorrhage
QALY	Quality adjusted life year
QOL-CP	Cerebral Palsy Quality of Life Questionnaire
QUADAS	Quality Assessment tool of Diagnostic Accuracy Studies
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomised control trial
RDS	Respiratory distress syndrome
RR	Risk ratio/relative risk
SALT	Speech and Language Therapy
SB	Spina bifida

Abbreviation	Definition
SCBU	Special baby care unit
sCP	Spastic cerebral palsy
SCPE	Study of Participation of Children with Cerebral Palsy Living in Europe
SD	Standard deviation
SDCS	Sleep disturbance checklist score
SDQ	Strengths and difficulties questionnaire
SDSC	Sleep Disturbance Scale for Children
SE	Standard error
SES	Socioeconomic status
SGA	small for gestational age
SGD	Speech generating device
SLT	Speech and language therapist
SMA	Spinal muscular atrophy
SMD	Standardised mean differences
SPARCLE	Study of Participation of Children with Cerebral Palsy Living in Europe
speechBITE	Speech pathology database for best interventions and treatment efficacy
SRs	Systematic reviews
SSRI	Selective serotonin reuptake inhibitors
SSTP	Stepping Stones Triple P
SW	South-west
SWM	Semmes-Weinstein
TDS	Teacher Drooling scale
TDS	Total difficulties score
TDS	Three times daily
TIS	Total impairment score
TSG	Thomas-Stonell and Greenberg scale
UK	United Kingdom
UL	Upper limbs
US	Ultrasound
US	United States
USA	United states of America
USCP	Unilateral spastic cerebral palsy
UTI	Urinary tract infection
VAS	Visual analogue scale
VF	Videofluoroscopic swallow studies
VFSE	Videofluroscopic swallowing exam
VLBW	Very low birth weight
WHO	World Health Organization
Wk	Week
WL	Waiting list
WM	White Matter
WTP	Willingness to pay
CFCS	Communication Function Classification System
MACS	Manual Ability Classification System

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32 Glossary

Table 136: Glossary

Term	Definition
Abstract	Summary of a study, which may be published alone or as an introduction to a full scientific paper.
Acetylcholine	A chemical produced by the nervous system to send messages from one nerve to another or from nerve to muscle. One of the neurotransmitters.
Acquired	A disease or condition that is a result of an illness that is not genetic
Acquired brain injury	A brain injury that occurs after the neonatal period (more than 28 days after birth).
Actigraphy	A non-invasive way of measuring activity and rest. Sleep actigraphy is monitored using a watch-type device worn on the wrist which monitors movements later downloaded onto a computer.
Adolescence	Period from around the onset of puberty to adulthood (different legal definitions in different countries – usually 16-18).
Age appropriate sleep routine / sleep hygiene programme	Advice given to parents, carers and children and young people about habits and practices for getting the child or young person ready for sleep that is appropriate for age. It would include advice about decreasing stimulation in the hour before bedtime and avoidance of stimulating drinks in the evening.
Analgesics	Medicines given to reduce pain.
Antenatal	The period of time before birth when the foetus is in utero.
Anthropometry	Measurements of body size, such as height, weight, head circumference and skin fold thickness. Used to assess normal patterns of growth.
Anticholinergic drugs	Medicines that block action of Acetycholine. In children and young people with cerebral palsy, most often used to reduce production of saliva or reduce dystonic movements.
Anticonvulsant therapy	Treatment to manage and minimise the risk of seizures usually epileptic seizures. This is usually a medicine but there are other ways of preventing epileptic seizures such as diet therapy inducing ketones and epilepsy surgery.
Anticonvulsants	Medicines used to prevent or treat seizures.
Antidepressants & anxiolytics	Medicines used to prevent or treat depression or anxiety.
Antiemetics	Medicines used to prevent or treat vomiting.
Anxiety	An emotional state where the person may have physical symptoms such as sweating or fast heart rate as well as a feeling of fear that something bad is going to happen.
Apgar score	A rapid measure of a baby's physical condition in the first few minutes of life. APGAR rates Airways, Pulse, Grimace, Activity and Respiration, scoring heart rate, breathing effort, colour, cry and activity level, each between 0-2. The maximum score, indicating a baby in very good condition is 10. The baby is scored usually at 1 minute, 5 minutes, and occasionally 10 minutes following delivery.
Arm (of a clinical study)	Subsection of individuals within a study who receive one particular intervention, for example placebo arm.
Aspiration or risk of aspiration	Aspiration occurs when food, fluid or other material passes through the vocal cords and into the airways. People may be considered at risk of aspiration if they have poor swallowing skills, poor cough reflex or have had previous episodes of aspiration.
Assistive technology	Technology used to improve a person's ability to carry out a task of daily

Term	Definition
	living. This may be a communication device or equipment that helps with feeding, care, environmental management or mobility.
Association	Statistical relationship between 2 or more events, characteristics or other variables. The relationship may or may not be causal.
Attention Deficit Hyperactivity Disorder (ADHD)	A behavioural disorder where a person is both inattentive with poor concentration span and poor attention skills, and is also impulsive and overactive. It may occur in isolation but may accompany other neurodevelopmental problems.
Attrition bias	Systematic differences between comparison groups for withdrawal or exclusion of participants from a study.
Augmentative and Alternative Communication (AAC) Intervention / System	A communication system to help a person with poor or no speech. These can take a variety of different forms such as no-tech gestures, low-tech picture cards though to high-tech sophisticated computer generated speech.
Autism / Autistic Spectrum Disorder (ASD)	ASD is a neurodevelopmental disorder affecting social interaction, communication, interests and behaviour. It is characterised by a limited range of repetitive activities, poor verbal and non-verbal communication and poor social interaction with other people. Some children and young people have some but not all of the features of autism and may be described as having an autistic spectrum disorder
Available case analysis (ACA)	Analysis of data that is available for participants at the end of follow-up.
Basal ganglia	Collection of grey matter structures deep in the brain involved in control of movement and some aspects of learning. Damage to the basal ganglia may be a cause of dystonic or dyskinetic cerebral palsy.
Baseline	The initial set of measurements at the beginning of a study (after run-in period where applicable) with which subsequent results are compared.
Before-and-after study	A study that investigates the effects of an intervention by measuring particular characteristics of a population both before and after taking the intervention, and assessing any change that occurs.
Behavioural difficulties	Or Emotional Behavioural Difficulties (EBD). Behaviour or Emotional responses that are so inappropriate for a child's age that they adversely affect their function and performance.
Benzodiazepines	A group of psycho-active medicines used for a variety of medical problems. In children and young people with cerebral palsy, they would most often be used to reduce muscle spasticity (increased tone), to treat or prevent seizures or reduce anxiety.
Bias	Influences on a study that can make the results look better or worse than they really are. Bias can occur by chance, deliberately or as a result of systematic errors in the design and execution of a study. It can also occur at different stages in the research process, for example during the collection, analysis, interpretation, publication or review of research data. For examples see confounding factor, performance bias, publication bias or Selection bias.
Bilirubin	A yellow pigment form when haemoglobin is broken down in the body. Excess amounts of bilirubin will a cause a person to appear yellow (jaundice). Very high levels in a baby can cause brain damage
Bisphosphonate	Medicines used to prevent the loss of bone mass in osteoporosis. Their use maintains or increases bone density and strength.
Blissymbols and Makaton	See Augmentative and Alternative Communication Systems. Bliss symbols are low-tech meaning based symbols that can be used by people with severe communication difficulties. Makaton programme is a no-tech and low-tech system using speech, hand signs and symbols to support language in people who cannot communicate effectively with speech alone.

Term	Definition
BMI z score	See BMI. BMI z score is a measure of how many standard deviations a child or young person's BMI is above or below the average BMI for their age and gender. (This is based on a reference population known as a child growth reference).
Body mass index (BMI)	Person's weight in kilograms divided by the square of their height in metres and is reported in units of kg/m2.
Bone Mineral Density (BMD)	A measure of the amount of calcium and other minerals in bone. It is measured through use of X-rays (usually dual energy X-Rays – DEXA, or CT scans). This helps predict the strength of bone and the risk of minimally or a-traumatic fractures.
Botulinum toxin type A	This is a neurotoxin produced by the bacterium Clostridium Botulinum that blocks the release of the neurotransmitter Acetylcholine from nerve terminals. Type A is 1 of 7 serologically distinct toxin types. It is manufactured by laboratory fermentation of C Bot cultures. Therapeutically it can be injected into muscle to reduce over-activation and tone or salivary glands to reduce production and release of Saliva.
Carer (caregiver)	Someone who looks after family, partners or friends in need of help because they are ill, frail or have a disability.
Case series	Report of a number of cases of a given disease, usually covering the course of the disease and the response to treatment. There is no comparison (control) group of patients.
Case-control study	A study to find out the cause(s) of a disease or condition. This is done by comparing a group of patients who have the disease or condition (cases) with a group of people who do not have it (controls) but who are otherwise as similar as possible (in characteristics thought to be unrelated to the causes of the disease or condition). This means the researcher can look for aspects of their lives that differ to see if they may cause the condition. Such studies are retrospective because they look back in time from the outcome to the possible causes of a disease or condition.
Cerebro-spinal fluid (CSF) investigations	Measurement of protein, glucose, blood cells and testing for infection in CSF. This is usually done in testing for meningitis but other conditions can be diagnosed in this way, including progressive movement disorders where levels of certain neurotransmitter levels are altered.
Challenging behaviour	Behaviours that affect the quality of life, participation or threaten the safety of the individual or others.
Child	A person aged 1 year to 11 years.
Childhood	From birth through to around the onset of puberty.
Cholinergic	Relating to nerve cells where acetylcholine is a neurotransmitter.
Chorioamnionitis	Inflammation of the membranes surrounding the foetus (chorion and amnion), usually caused by infection.
Clinical audit	A systematic process for setting and monitoring standards of clinical care. Whereas ‘guidelines’ define what the best clinical practice should be, ‘audit’ investigates whether best practice is being carried out. Clinical audit can be described as a cycle or spiral. Within the cycle there are stages that follow a systematic process of establishing best practice, measuring care against specific criteria, taking action to improve care and monitoring to sustain improvement. The spiral suggests that as the process continues, each cycle aspires to a higher level of quality.
Clinical effectiveness	How well a specific test or treatment works when used in the 'real world' (for example when used by a doctor with a patient at home), rather than in a carefully controlled clinical trial. Trials that assess clinical effectiveness are sometimes called management trials. Clinical effectiveness is not the same as efficacy.
Clinical efficacy	The extent to which an intervention is active when studied under

Term	Definition
	controlled research conditions.
Clinician	A healthcare professional who provides patient care. For example a doctor, nurse or physiotherapist.
Clotting disorders /hyper coagulation in mother	Conditions where a mother has a disorder where her blood clots easily stick together. This may affect the blood supply in the placenta and is thought to be a risk factor for cerebral palsy.
Cochrane Review	The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of RCTs prepared by the Cochrane Collaboration).
Cohort study	A study with 2 or more groups of people – cohorts – with similar characteristics. One group receives a treatment, is exposed to a risk factor or has a particular symptom and the other group does not. The study follows their progress over time and records what happens.
Communication difficulties	This describes the range of problems that a child may have with expression and understanding. This includes problems with speech and non-verbal forms of expression, understanding what is being said to them, understanding emotions, using words and grammar and speaking fluently.
Comorbidity	A clinical or developmental condition occurring with a primary disease. It may be caused by this disease of be co-incidental.
Concealment of allocation	The process used to ensure that the person deciding to enter a participant into an RCT does not know the comparison group into which that individual will be allocated. This is distinct from blinding and is aimed at preventing selection bias. Some attempts at concealing allocation are more prone to manipulation than others and the method of allocation concealment is used as an assessment of the quality of a trial.
Conduct disorder	Repetitive and persistent behaviours which are often disruptive and violent – also termed anti-social behaviour.
Confidence interval (CI)	There is always some uncertainty in research. This is because a small group of patients is studied to predict the effects of a treatment on the wider population. The confidence interval is a way of expressing how certain we are about the findings from a study, using statistics. It gives a range of results that is likely to include the 'true' value for the population. The CI is usually stated as '95% CI', which means that the range of values has a 95 in 100 chance of including the 'true' value. For example, a study may state that “based on our sample findings, we are 95% certain that the 'true' population blood pressure is not higher than 150 and not lower than 110”. In such a case the 95% CI would be 110 to 150. A wide confidence interval indicates a lack of certainty about the true effect of the test or treatment – often because a small group of patients has been studied. A narrow confidence interval indicates a more precise estimate (for example if a large number of patients have been studied).
Confounding factor	Something that influences a study and can result in misleading findings if it is not understood or appropriately dealt with. For example, a study of heart disease may look at a group of people who exercise regularly and a group who do not exercise. If the ages of the people in the 2 groups are different, then any difference in heart disease rates between the 2 groups could be because of age rather than exercise. Therefore age is a confounding factor.
Congenital Infection	Infection acquired before a baby is born.
Constipation	Bowel movements which are infrequent and hard to pass.
Construct validity	This assesses how well a test measures what it claims to test.
Continuous outcome	Data with a potentially infinite number of possible values within a given

Term	Definition
	range. Height, weight and blood pressure are examples of continuous variables.
Control group	A group of people in a study who do not receive the treatment or test being studied. Instead, they may receive the standard treatment (sometimes called 'usual care') or a dummy treatment (placebo). The results for the control group are compared with those for a group receiving the treatment being tested. The aim is to check for any differences. Ideally, the people in the control group should be as similar as possible to those in the treatment group, to make it as easy as possible to detect any effects due to the treatment.
Cortical visual impairment / Cortical blindness (CVI)	Problem with seeing objects caused by damage to the parts of the brain that control vision, rather than diseases of the eyes. This may range from difficulties with judging distances or shapes to complete blindness.
Cost–benefit analysis (CBA)	Cost-benefit analysis is one of the tools used to carry out an economic evaluation. The costs and benefits are measured using the same monetary units (for example UK pounds) to see whether the benefits exceed the costs.
Cost–consequence analysis (CCA)	Cost-consequence analysis is one of the tools used to carry out an economic evaluation. This compares the costs (such as treatment and hospital care) with the consequences (such as health outcomes) of a test or treatment with a suitable alternative. Unlike cost–benefit analysis or cost-effectiveness analysis, it does not attempt to summarise outcomes in a single measure (such as the quality adjusted life year) or in financial terms. Instead, outcomes are shown in their natural units (some of which may be monetary) and it is left to decision-makers to determine whether, overall, the treatment is worth carrying out.
Cost-effectiveness analysis (CEA)	Cost-effectiveness analysis is one of the tools used to carry out an economic evaluation. The benefits are expressed in non-monetary terms related to health, such as symptom-free days, heart attacks avoided, deaths avoided or life years gained (that is, the number of years by which life is extended as a result of the intervention).
Cost-effectiveness model	An explicit mathematical framework which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes.
Cost–utility analysis (CUA)	Cost–utility analysis is one of the tools used to carry out an economic evaluation. The benefits are assessed in terms of both quality and duration of life, and expressed as quality adjusted life years (QALYs). See also Utility.
COX proportional hazard model	In survival analysis, a statistical model that asserts that the effect of the study factors (for example the intervention of interest) on the hazard rate (the risk of occurrence of an event) in the study population is multiplicative and does not change over time.
Credible interval (CrI)	The Bayesian equivalent of a confidence interval.
Criterion-related/concurrent validity	This compares measuring something in a test with an outcome at the same time. Used to assess psychological tests e.g. does a psychology assessment in school compare well with what the teacher's assessment of the child's performance.
Cytomegalovirus	A virus that can infect the developing foetus and cause a variety of neurological problems including cerebral palsy, deafness, visual problems and epilepsy.
Decision analysis	An explicit quantitative approach to decision-making under uncertainty, based on evidence from research. This evidence is translated into probabilities, and then into diagrams or decision trees which direct the clinician through a succession of possible scenarios, actions and outcomes.
Deep grey matter	Basal ganglia – see above

Term	Definition
Depression	A state where a person has a low mood, loss of motivation and unwillingness to participate in usually enjoyed activities.
Developmental delay	A child not meeting the developmental milestones at an appropriate age
Developmental neurodisability	Impaired function due to a disorder affecting the developing brain that affects a child's quality of life, activity and participation.
DEXA scan	A scan that measures bone density – Dual Energy X-Ray Absorptiometry. It estimates BMD against population standards and as such it is important in practise to compare with age appropriate comparative groups.
Dichotomous outcomes	Outcome that can take 1 of 2 possible values, such as dead/alive, smoker/non-smoker, present/not present (also called binary data).
Discounting	Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present.
Dominance	A health economics term. When comparing tests or treatments, an option that is both less effective and costs more is said to be 'dominated' by the alternative.
Drop-out	A participant who withdraws from a trial before the end.
Dysarthria	Dysarthria is the difficulty a person has due to problems with the muscles involved in speaking.
Dysmenorrhea	Painful menstruation / period pain.
Dysphagia	Difficulty in swallowing.
Dyspraxia	Dyspraxia is the difficulty a person has with planning and carrying out a task in a smooth, efficient and coordinated manner.
Economic evaluation	An economic evaluation is used to assess the cost effectiveness of healthcare interventions (that is, to compare the costs and benefits of a healthcare intervention to assess whether it is worth doing). The aim of an economic evaluation is to maximise the level of benefits – health effects – relative to the resources available. It should be used to inform and support the decision-making process; it is not supposed to replace the judgement of healthcare professionals. There are several types of economic evaluation: cost–benefit analysis, cost–consequence analysis, cost-effectiveness analysis, cost-minimisation analysis and cost–utility analysis. They use similar methods to define and evaluate costs, but differ in the way they estimate the benefits of a particular drug, programme or intervention.
Effect (as in effect measure, treatment effect, estimate of effect, effect size)	A measure that shows the magnitude of the outcome in 1 group compared with that in a control group. For example, if the absolute risk reduction is shown to be 5% and it is the outcome of interest, the effect size is 5%. The effect size is usually tested, using statistics, to find out how likely it is that the effect is a result of the treatment and has not just happened by chance.
Effectiveness	How beneficial a test or treatment is under usual or everyday conditions.
Efficacy	How beneficial a test, treatment or public health intervention is under ideal conditions (for example in a laboratory).
Enteral tube feeding	Feeding through a naso-gastric tube, gastrostomy tube or jejunostomy tube.
Epidemiological study	The study of a disease within a population, defining its incidence and prevalence and examining the roles of external influences (for example infection, diet) and interventions.
Epilepsy	Abnormal electrical activity in the brain leading to recurrent episodes of

Term	Definition
	sensory disturbance, loss of consciousness or convulsions. Two or more of these seizures should occur more than 24 hours apart and not be triggered by a rise in temperature or inter-current illness.
EQ-5D (EuroQol 5 dimensions)	A standardised instrument used to measure health-related quality of life. It provides a single index value for health status.
Equivalence study	A trial designed to determine whether the response to 2 or more treatments differs by an amount that is clinically unimportant. This is usually demonstrated by showing that the true treatment difference is likely to lie between a lower and an upper equivalence level of clinically acceptable differences.
Evidence	Information on which a decision or guidance is based. Evidence is obtained from a range of sources including RCTs, observational studies, expert opinion (of clinical professionals or patients).
Exclusion criteria (clinical study)	Criteria that define who is not eligible to participate in a clinical study.
Exclusion criteria (literature review)	Explicit standards used to decide which studies should be excluded from consideration as potential sources of evidence.
Extended dominance	If Option A is both more clinically effective than Option B and has a lower cost per unit of effect when both are compared with a do-nothing alternative, then Option A is said to have extended dominance over Option B. Option A is therefore more cost effective and should be preferred, other things remaining equal.
Extrapolation	An assumption that the results of studies of a specific population will also hold true for another population with similar characteristics.
Face and content validity	Content validity is an assessment of how well a measure looks at all aspects of a situation - an assessment of pain should look at all aspects, not only whether a child is crying. Face validity is a subjective assessment of whether a test does what it says it does – does everyone agree that it is doing what it is supposed to do.
False negative	A diagnostic test result that incorrectly indicates that an individual does not have the disease of interest, when they do actually have it.
False positive	A diagnostic test result that incorrectly indicates that an individual has the disease of interest, when they actually do not have it.
Feeding positioning	Feeding the child in a position that encourages safe and effective feeding, reducing the risk of aspiration and vomiting and is comfortable and enjoyable for child and person feeding the child.
Fibroscopic endoscopy	A procedure where a flexible tube with a camera is passed into the bowel enabling pictures of the inside of the bowel and biopsies to be taken.
Fixed-effect model	In meta-analysis, a model that calculates a pooled effect estimate using the assumption that all observed variation between studies is caused by random sample variability. Studies are assumed to estimating the same overall effect.
Focal ischaemic infarct or haemorrhagic lesions	Damage to specific parts of the brain caused by lack of blood supply or bleeding in that area.
Follow-up	Observation over a period of time of an individual, group or initially defined population whose appropriate characteristics have been assessed in order to observe changes in health status or health-related variables.
Fore gut dysmotility	Problems of muscle activity or co-ordination in the upper / small bowel causing lack of movement of food / fluids through the upper gut leading to increased vomiting, abdominal pain and bloating after a meal.
Forest plot	A graphical representation of the individual results of each study

Term	Definition
	included in a meta-analysis together with the combined meta-analysis result. The plot also allows readers to see the heterogeneity among the results of the studies. The results of individual studies are shown as squares centred on each study's point estimate. A horizontal line runs through each square to show each study's confidence interval. The overall estimate from the meta-analysis and its confidence interval are shown at the bottom, represented as a diamond. The centre of the diamond represents the pooled point estimate, and its horizontal tips represent the confidence interval.
Function	The ability to perform normal activities or actions.
Functional Classification Systems	Standardised ways of describing specific areas of function of a child with cerebral palsy. There are currently 3 commonly in use – Gross Motor Functional Classification System (see below), Manual Ability Classification System (MACS) and Communication Function Classification System (CFCS). These are a variety of others developed that also look at other developmental areas.
Fundoplication	Surgical tightening of the junction between the oesophagus and stomach to reduce the risk of reflux and vomiting.
Gastrointestinal pain/discomfort	Pain arising from the gastro-intestinal tract including oesophagus, stomach, small and large bowel.
Gastro-Oesophageal Reflux Disease (GORD)	Symptoms arising from food and stomach acid passing back up into the oesophagus and commonly causing pain, vomiting, poor feeding, loss of weight and anaemia.
Gastrostomy tube feeding	Feeing the child through a tube that passes through the skin of the tummy straight into the stomach.
General Movement assessment (GMA)	A standardised system of close observation of a baby's spontaneous movements when awake to help predict future developmental problems
Generalisability	The extent to which the results of a study hold true for groups that did not participate in the research.
Genetic disorders (eg hereditary spastic paraparesis, progressive Dopa responsive dystonia, Retts syndrome, Pelizaeus Merzbacher syndrome)	Disorders caused by faults in a child's genes that can present with problems with movement initially presenting in a similar way to cerebral palsy.
Glycopyrrolate	An anticholinergic medicine used to reduce and thicken the amount of saliva a child produces.
Gold standard	A method, procedure or measurement that is widely accepted as being the best available to test for or treat a disease.
GRADE, GRADE profile	A system developed by the GRADE Working Group to address the short-comings of present grading systems in healthcare. The GRADE system uses a common, sensible and transparent approach to grading the quality of evidence. The results of applying the GRADE system to clinical trial data are displayed in a table known as a GRADE profile.
Gross Motor Function Classification System (GMFCS).	A 5-point classification system that describes the gross motor skills of a child with CP. In summary: Level I, walks without restrictions Level II, walks without assistive devices Level III, walks with assistive devices Level IV, has limited self-mobility Level V, dependent on others for Developed by the Canchild centre at McMaster University in Canada.
Group B Streptococcus	A bacteria that can cause meningitis and septicaemia in new born

Term	Definition
	babies. Prolonged rupture of membranes is a risk factor for infection.
Haemorrhagic events, neonatal and perinatal stroke	Bleeding into the brain can occur in the foetus and in the new born baby and is a potential cause of cerebral palsy.
Harms	Adverse effects of an intervention.
Hazard ratio	A hazard is the rate at which events happen, so that the probability of an event happening in a short time interval is the length of time multiplied by the hazard. Although the hazard may vary with time, the assumption in proportional hazard models for survival analysis is that the hazard in 1 group is a constant proportion of the hazard in the other group. This proportion is the hazard ratio.
Health economics	Study or analysis of the cost of using and distributing healthcare resources.
Health-related quality of life (HRQoL)	A measure of the effects of an illness to see how it affects someone's day-to-day life.
Hearing impairment / difficulties	Loss of hearing that can be due to problems at any point of the hearing system from the ear cochlea, nerves going from the ear to the brain, or in the auditory part of the brain.
Heterogeneity	The term is used in meta-analyses and systematic reviews to describe when the results of a test or treatment (or estimates of its effect) differ.
Hind Gut dysmotility	Problems of muscle activity or co-ordination in the lower bowel / Colon causing lack of movement of stool through the lower gut, leading to abdominal pain, constipation and bloating.
Hydrotherapy	Physical therapy delivered in a warm swimming pool/therapy pool.
Hypertonia, hypotonia, dystonia and mixed.	Hypertonia: increased muscle resistance to externally imposed movement. Hypotonia: decreased muscle resistance to externally imposed movement. Dystonia: involuntary, sustained or intermittent muscle contractions that cause twitching and repetitive movements, abnormal postures or both. It can be precipitated by attempts to move or change position and by emotions. Mixed: combination of the above, particularly experienced at different body levels.
Hypoxic Ischaemic Encephalopathy (HIE).	A clinical state caused by a lack of oxygen or reduced blood supply to the brain, characterised by seizures, altered conscious level and abnormal neurological examination.
Hypoxic ischaemic events / injury	Damage to the brain caused by lack of oxygen delivery to the brain or poor blood supply to the brain.
Imprecision	Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of effect.
Incidence	The incidence of a disease is the rate at which new cases occur in a population during a specified period.
Inclusion criteria (clinical study)	Specific criteria that define who is eligible to participate in a clinical study.
Inclusion criteria (literature review)	Explicit criteria used to decide which studies should be considered as potential sources of evidence.
Incremental cost	The extra cost linked to using 1 test or treatment rather than another. Or the additional cost of doing a test or providing a treatment more frequently.
Incremental cost effectiveness ratio (ICER)	The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest for 1 treatment compared with another.

Term	Definition
Incremental net benefit (INB)	The value (usually in monetary terms) of an intervention net of its cost compared with a comparator intervention. The INB can be calculated for a given cost-effectiveness (willingness to pay) threshold. If the threshold is £20,000 per QALY gained then the INB is calculated as: (£20,000×QALYs gained) minus incremental cost.
Indirectness	The available evidence is different to the review question being addressed, in terms of population, intervention, comparison and outcome (PICO).
Infant	A person older than 28 days but younger than 1 year.
Infections: meningitis and encephalitis	Meningitis refers to an acute inflammation of the membranes lining the brain and spinal cord (meninges), generally caused by a viral or bacterial infection. Encephalitis refers to a direct inflammation of the brain, caused by infection, usually viral, or allergy.
Intellectual / Learning / cognitive disability	IQ<70
Intellectual / Learning / difficulty	Difficulties in intellectual functioning such as reasoning, problem solving and learning.
Intention-to-treat analysis (ITT)	An assessment of the people taking part in a clinical trial, based on the group they were initially (and randomly) allocated to. This is regardless of whether or not they dropped out, fully complied with the treatment or switched to an alternative treatment. Intention-to-treat analyses are often used to assess clinical effectiveness because they mirror actual practice: that is, not everyone complies with treatment and the treatment people receive may be changed according to how they respond to it.
Intervention	In medical terms this could be a drug treatment, surgical procedure, diagnostic or psychological therapy. Examples of public health interventions could include action to help someone to be physically active or to eat a more healthy diet.
Intrauterine growth retardation (IUGR)	A foetus or baby who has not grown well during pregnancy and is underweight for gestation at birth.
Intraventricular Haemorrhage (IVH)	Bleeding into the chambers in the brain which contain cerebro-spinal fluid. Premature babies are particularly at risk from this.
Jejunostomy tube feeding	Feeding through a tube passed through the tummy wall and passed into the jejunum (upper small intestine)
Kappa statistic	A statistical measure of inter-rater agreement that takes into account the agreement occurring by chance
Kernicterus	Brain dysfunction caused by very high levels of bilirubin. This can cause cerebral palsy, deafness, and severe learning problems.
Length of stay	The total number of days a patient stays in hospital.
Licence	See Product licence.
Life expectancy	How many years a person can expect to live.
Life years gained	Mean average years of life gained per person as a result of the intervention compared with an alternative intervention.
Lifestyle changes	Changing some aspect of daily life – diet, exercise, sleeping – with a view to promoting health and wellbeing.
Likelihood ratio	The likelihood ratio combines information about the sensitivity and specificity. It tells you how much a positive or negative result changes the likelihood that a patient would have the disease. The likelihood ratio of a positive test result (LR+) is sensitivity divided by (1 minus specificity).
Loss to follow-up	Patients who have withdrawn from the clinical trial at the point of follow-up.
MACS levels	Manual Ability Classification System – a standardised way of describing

Term	Definition
	a child's fine motor abilities. Developed by teams across universities in Sweden.
Magnetic Resonance Imaging (MRI)	A scan used for obtaining detailed images of internal organs.
Markov model	A method for estimating long-term costs and effects for recurrent or chronic conditions, based on health states and the probability of transition between them within a given time period (cycle).
Maternal-Foetal infection	Infection that is passed form the mother across the placenta to the foetus during pregnancy.
Mean	An average value, calculated by adding all the observations and dividing by the number of observations.
Mean difference	In meta-analysis, a method used to combine measures on continuous scales (such as weight), where the mean, standard deviation and sample size in each group are known. The weight given to the difference in means from each study (for example how much influence each study has on the overall results of the meta-analysis) is determined by the precision of its estimate of effect.
Median	The value of the observation that comes half-way when the observations are ranked in order.
Melatonin	A medicine used to encourage sleep onset. Melatonin is normally produced by the brain in response to falling light levels in the evening.
Mental health problems	Mental health problems can affect the way you think, feel and behave. More common ones include depression, generalised anxiety disorder and obsessive compulsive disorder.
Meta-analysis	A method often used in systematic reviews. Results from several studies of the same test or treatment are combined to estimate the overall effect of the treatment.
Metabolic bone disease	A disorder of bone strength caused by deficiencies in calcium, phosphate, magnesium, or vitamin D.
Minimal important difference (MID)	Threshold for clinical importance which represents the minimal important difference for benefit or for harm; for example the threshold at which drug A is less effective than drug B by an amount that is clinically important to patients.
Monte Carlo	A technique used to approximate the probability of certain outcomes by running multiple simulations using random variables.
Multilevel surgery	Single orthopaedic intervention to improve function, such as walking by addressing many joint levels at the same time, involving soft tissue (muscle and tendon) surgery plus or minus bony procedures at more than 1 level of the body. For example Gastrocnemius slide, Medial Hamstring lengthening plus Iliopsoas tenotomy (Calf, Hamstring and hip flexor surgery).
Multivariate model	A statistical model for analysis of the relationship between 2 or more predictors, (independent) variables and the outcome (dependent) variable.
Muscle tone	The normal state of continuous passive partial contraction in a resting muscle. Muscle tone is important in maintaining posture. Increased muscle tone (hypertonia) is associated with an abnormal resistance to passive stretch, while reduced muscle tone (hypotonia) is associated with floppiness of the limbs or trunk and poor posture.
Musculo-skeletal pain/discomfort	Pain coming from muscles, bones, joints and ligaments.
Myelination	A process where a myelin sheath is laid down around a nerve to allow it to send messages quicker. Myelination continues well into childhood.
Nasogastric tube	Feeding through a tube passed through the nose into the stomach.

Term	Definition
feeding	
Nasopharyngeal reflux/regurgitation	Fluids and food entering the nose when a baby swallows due to failure to close off the nasopharynx. The baby will pass milk through the nose and is often associated with other feeding difficulties.
Neonatal	Birth to 1 month of age.
Neonatal cranial ultrasound	Imaging of the brain through the fontanelle (soft spot) using an ultrasound probe. This gives good pictures of the middle structures of the brain and should not cause the baby any discomfort.
Neonatal encephalopathy	A clinical state characterised by neonatal seizures, altered conscious level and abnormal neurological examination. Severe neonatal encephalopathy is a strong risk factor for cerebral palsy.
Neonatal Hypoglycaemia	Low blood sugar levels in a neonate
Neonatal Intensive Care Unit (NICU)	A unit where there is a high staff-patient ratio and full supportive care can be given to very ill babies as well as very premature babies.
Neonatal sepsis	Infection in the first month of life that causes signs and symptoms and bacteria are found in the bloodstream.
Net monetary benefit (NMB)	The value (usually in monetary terms) of an intervention net of its cost. The NMB can be calculated for a given cost-effectiveness (willingness to pay) threshold. If the threshold is £20,000 per QALY gained then the NMB is calculated as: (£20,000×QALYs gained) minus cost.
Network meta-analysis	Meta-analysis in which multiple treatments (that is, 3 or more) are being compared using both direct comparisons of interventions within RCTs and indirect comparisons across trials based on a common comparator.
Network of Care	Linked groups of healthcare professionals and organisations working in an agreed and co-ordinated manner to deliver a clinical service. A network is not constrained by existing professional, organisational or institutional boundaries.
Network team	A multidisciplinary group of healthcare and other professionals working in a network of care to deliver a clinical service.
Neurodevelopmental disorder	A disorder causing impaired function due to a disorder affecting the developing brain that affects a child's quality of life, activity and participation.
Neurometabolic disorders: leukodystrophy, mitochondrial disorder	Diseases (usually genetic) where disturbances of production or breakdown of body chemicals cause neurological symptoms.
Neuromuscular disorders (SMA, muscular dystrophy),	Disorders of the peripheral nervous system – anterior horn cells, nerves, or muscles producing progressive problems of motor control or function.
Non-Communicating Children's Pain Checklist	Pain assessment tool for children ages 3-18 without clear communication. It is aimed at parents and carers and does not require the user to be trained.
Non-inferiority trial	A trial designed to determine whether the effect of a new treatment is not worse than a standard treatment by more than a pre-specified amount. A 1-sided version of an equivalence trial.
Non-progressive neurological disorder	A condition caused by an injury to or abnormal development of the brain that is not degenerative.
Number needed to treat (NNT)	The average number of patients who need to be treated to get a positive outcome. For example, if the NNT is 4, then 4 patients would have to be treated to ensure 1 of them gets better. The closer the NNT is to 1, the better the treatment. For example, if you give a stroke prevention drug to 20 people before 1 stroke is prevented, the number needed to treat is

Term	Definition
	20.
Numeric Pain Rating Scale	A scale of 0-10. Patients are asked to rate their pain with 0 being no pain at all and 10 being the worst pain they have ever experienced.
Nutritional inadequacy	Insufficient nutrition to maintain growth, body weight, or maintain a state of health.
Observational study	Individuals or groups are observed or certain factors are measured. No attempt is made to affect the outcome. For example, an observational study of a disease or treatment would allow 'nature' or usual medical care to take its course. Changes or differences in 1 characteristic (for example whether or not people received a specific treatment or intervention) are studied without intervening. There is a greater risk of selection bias than in experimental studies.
Obsessive Compulsive Disorder (OCD)	A disorder where people have to check things repeatedly, perform certain routines or have repeated thoughts.
Obstructive sleep apnoea and sleep apnoea	Pauses in breathing during sleep that may be due to the airway becoming blocked – for example from floppy larynx, large tonsils – or disordered neurological control of breathing (respiratory drive).
Odds ratio (OR)	Odds are a way to represent how likely it is that something will happen (the probability). An odds ratio compares the probability of something in 1 group with the probability of the same thing in another. An odds ratio of 1 between 2 groups would show that the probability of the event (for example a person developing a disease, or a treatment working) is the same for both. An odds ratio greater than 1 means the event is more likely in the first group. An odds ratio less than 1 means that the event is less likely in the first group. Sometimes probability can be compared across more than 2 groups – in this case, 1 of the groups is chosen as the 'reference category' and the odds ratio is calculated for each group compared with the reference category. For example, to compare the risk of dying from lung cancer for non-smokers, occasional smokers and regular smokers, non-smokers could be used as the reference category. Odds ratios would be worked out for occasional smokers compared with non-smokers and for regular smokers compared with non-smokers. See also Confidence interval, Relative risk.
Oesophageal obstruction/ dysmotility	Difficulty in swallowing or pain on swallowing because of a blockage of the oesophagus or poor muscle function in the oesophagus.
Opioids	Family of drugs used to control moderate to severe pain. These drugs are also strongly sedative.
Opportunity cost	The loss of other healthcare programmes displaced by investment in or introduction of another intervention. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.
Oro-motor control	The ability to move the muscle of the face, lips tongue and palate to feed and speak in a safe and effective manner.
Osteopaenia / Osteopenia	A condition where the mineral and protein content of the bone is reduced.
Osteoporosis	A severe form of osteopenia where the bones are now brittle and at risk of fractures and deformation.
Outcome	The impact that a test, treatment, policy, programme or other intervention has on a person, group or population. Outcomes from interventions to improve the public's health could include changes in knowledge and behaviour related to health, societal changes (for example a reduction in crime rates) and a change in people's health and wellbeing or health status. In clinical terms, outcomes could include the number of patients who fully recover from an illness or the number of

Term	Definition
	hospital admissions, and an improvement or deterioration in someone's health, functional ability, symptoms or situation. Researchers should decide what outcomes to measure before a study begins.
p value	The p value is a statistical measure that indicates whether or not an effect is statistically significant. For example, if a study comparing 2 treatments found that one seems more effective than the other, the p value is the probability of obtaining these results by chance. By convention, if the p value is below 0.05 (that is, there is less than a 5% probability that the results occurred by chance) it is considered that there probably is a real difference between treatments. If the p value is 0.001 or less (less than a 1% probability that the results occurred by chance), the result is seen as highly significant. If the p value shows that there is likely to be a difference between treatments, the confidence interval describes how big the difference in effect might be.
Paediatric Pain Profile (PPP)	Pain assessment tool for a child, aged 1-18 with severe learning and communication difficulties. It consist of 20 items looking at a child's behaviour.
Performance bias	Systematic differences between intervention groups in care provided apart from the intervention being evaluated. Blinding of study participants (both the recipients and providers of care) is used to protect against performance bias.
Perinatal	Birth to 7 days of age.
Periventricular Leukomalacia (PVL)	Damage to the white matter surrounding the lateral ventricles in the brain – "softening of the white matter". A common finding in children born prematurely who develop cerebral palsy.
Placebo	A fake (or dummy) treatment given to participants in the control group of a clinical trial. It is indistinguishable from the actual treatment (which is given to participants in the experimental group). The aim is to determine what effect the experimental treatment has had over and above any placebo effect caused because someone has received (or thinks they have received) care or attention.
Placebo effect	A beneficial (or adverse) effect produced by a placebo and not due to any property of the placebo itself.
Polysomnography	A test carried out during sleep, which measures oxygen levels, breathing and heart rate, brain wave activity and body movements. It is used to diagnose sleep disorders.
Post-hoc analysis	Statistical analyses that are not specified in the trial protocol and are generally suggested by the data.
Postnatal	Following birth.
Post-swallow pooling/residue	Feed that persist around the vocal cords after swallowing has swallowed. There is risk of aspirating this fluid with the next breath. It is a particular problem in babies and children with disordered oro-motor control.
Postural management	A planned programme of activity using equipment to help a child or young person's posture - lying, sitting and standing. Its use should help function and comfort and reduce unwanted positioning.
Power (statistical)	The ability to demonstrate an association when one exists. Power is related to sample size; the larger the sample size, the greater the power and the lower the risk that a possible association could be missed.
Premature rupture of membranes	Rupture of membranes before the onset of labour.
Prematurity / premature delivery / gestational age	Prematurity – born before 37 weeks of gestational age – the time period that has lapsed since the first day of the mother's last menstrual cycle. A normal gestation in humans is 40 weeks.
Prevalence	The prevalence of a disease is the proportion of a population that are

Term	Definition
	cases at a point in time.
Primary care	Healthcare delivered outside hospitals. It includes a range of services provided by GPs, nurses, health visitors, midwives and other healthcare professionals and allied health professionals such as dentists, pharmacists and opticians.
Primary outcome	The outcome of greatest importance, usually the one in a study that the power calculation is based on.
Product licence	An authorisation from the Medicines and Healthcare Products Regulatory Agency (MHRA) to market a medicinal product.
Prognosis	A probable course or outcome of a disease. Prognostic factors are patient or disease characteristics that influence the course. Good prognosis is associated with low rate of undesirable outcomes; poor prognosis is associated with a high rate of undesirable outcomes.
Prospective study	A research study in which the health or other characteristic of participants is monitored (or 'followed up') for a period of time, with events recorded as they happen. This contrasts with retrospective studies.
Protocol (review)	A document written prior to commencing a review that details exactly how evidence to answer a review question will be obtained and synthesised. It defines in detail the population of interest, the interventions, the comparators/controls and the outcomes of interest (PICO).
Publication bias	Publication bias occurs when researchers publish the results of studies showing that a treatment works well and don't publish those showing it did not have any effect. If this happens, analysis of the published results will not give an accurate idea of how well the treatment works. This type of bias can be assessed by a funnel plot.
Quadriplegia, diplegia, hemiplegia, monoplegia, triplegia,	Terms used to describe pattern of limb involvement in children with different patterns of cerebral palsy: • Quadriplegia – all 4 limbs affected • Diplegia – legs predominantly affected although there can also be milder involvement of the arms • Hemiplegia – arm and leg on 1 side of the body affected. Arm usually more than leg • Monoplegia – only 1 limb affected • Triplegia – 3 limbs affected – usually a combination of diplegia and triplegia The use of these terms have been superseded by the concept of unilateral vs bilateral involvement with focus on different functional levels of involvement as outlined by the Study of Cerebral Palsy in Europe team (SCPE).
Quality adjusted life year (QALY)	A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality-of-life. One QALY is equal to 1 year of life in perfect health. QALYS are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a quality-of-life score (on a scale of 0 to 1). It is often measured in terms of the person's ability to perform the activities of daily life, and freedom from pain and mental disturbance.
Quality of life	See Health-related quality of life.
Random effect model	In meta-analysis, a model that calculates a pooled effect estimate using the assumption that each study is estimating a different true treatment effect due to real differences between studies. Observed variation in effects are therefore caused by a combination of random sample variability (within-study variation) and heterogeneity between studies

Term	Definition
	(between-study variation). The overall effects is an average of the estimated true study effects.
Randomisation	Assigning participants in a research study to different groups without taking any similarities or differences between them into account. For example, it could involve using a random numbers table or a computer-generated random sequence. It means that each individual (or each group in the case of cluster randomisation) has the same chance of receiving each intervention.
Randomised controlled trial (RCT)	A study in which a number of similar people are randomly assigned to 2 (or more) groups to test a specific drug or treatment. One group (the experimental group) receives the treatment being tested, the other (the comparison or control group) receives an alternative treatment, a dummy treatment (placebo) or no treatment at all. The groups are followed up to see how effective the experimental treatment was. Outcomes are measured at specific times and any difference in response between the groups is assessed statistically. This method is also used to reduce bias.
Reduced bone mineral density and low-impact fractures	The concept that if the bones have less mineral and protein, they will appear to have reduced density on DEXA scan and so will be more likely to fracture with minimal trauma.
Reference standard	The test that is considered to be the best available method to establish the presence or absence of the outcome – this may not be the one that is routinely used in practice.
Relative risk (RR)	The ratio of the risk of disease or death among those exposed to certain conditions compared with the risk for those who are not exposed to the same conditions (for example the risk of people who smoke getting lung cancer compared with the risk for people who do not smoke). If both groups face the same level of risk, the relative risk is 1. If the first group had a relative risk of 2, subjects in that group would be twice as likely to have the event happen. A relative risk of less than 1 means the outcome is less likely in the first group. Relative risk is sometimes referred to as risk ratio.
Reliability	The extent to which a test will give the same result if repeated a number of times.
Reporting bias	See Publication bias.
Resource implication	The likely impact in terms of finance, workforce or other NHS resources.
Retrospective study	A research study that focuses on the past and present. The study examines past exposure to suspected risk factors for the disease or condition. Unlike prospective studies, it does not cover events that occur after the study group is selected.
Review question	The plan or set of steps to be followed in a study. A protocol for a systematic review describes the rationale for the review, the objectives and the methods that will be used to locate, select and critically appraise studies, and to collect and analyse data from the included studies.
Saliva Control Management	Measures to reduce the problems of drooling and choking caused by saliva. This may involve training the child to control saliva, and/or use of drugs, Botulinum Toxin A injections or surgery.
Scopolamine / Hyoscine	Anticholinergic drug used to reduce amount of saliva produced.
Screening	A method of identifying healthy people who may be at higher risk of developing a particular disease.
Secondary care	Care provided in hospitals.
Secondary outcome	An outcome used to evaluate additional effects of the intervention deemed a priori as being less important than the primary outcomes.
Sedatives: Alimemazine, Vallergan, Chloral	Sedatives are drugs used to sedate or help with sleep onset.

Term	Definition
hydrate, Clonidine	
Selection bias	Selection bias occurs if: • The characteristics of the people selected for a study differ from the wider population from which they have been drawn; or • There are differences between groups of participants in a study in terms of how likely they are to get better.
Sensitivity	How well a test detects the thing it is testing for. If a diagnostic test for a disease has high sensitivity, it is likely to pick up all cases of the disease in people who have it (that is, give a 'true positive' result). But if a test is too sensitive it will sometimes also give a positive result in people who don't have the disease (that is, give a 'false positive'). For example, if a test was developed to detect if a woman is 6 months pregnant, a very sensitive test would detect everyone who was 6 months pregnant but would probably also include those who are 5 and 7 months pregnant. If the same test were more specific (sometimes referred to as having higher specificity), it would detect only those who are 6 months pregnant and someone who was 5 months pregnant would get a negative result (a 'true negative'). But it would probably also miss some people who were 6 months pregnant (that is, give a 'false negative'). Breast screening is a 'real-life' example. The number of women who are recalled for a second breast screening test is relatively high because the test is very sensitive. If it was made more specific, people who don't have the disease would be less likely to be called back for a second test but more women who have the disease would be missed.
Sensitivity analysis	A means of representing uncertainty in the results of an analysis. Uncertainty may arise from missing data, imprecise estimates or methodological controversy. Sensitivity analysis also allows for exploring the generalisability of results to other settings. The analysis is repeated using different assumptions to examine the effect on the results. One-way simple sensitivity analysis (univariate analysis) – each parameter is varied individually in order to isolate the consequences of each parameter on the results of the study. Multi-way simple sensitivity analysis (scenario analysis) – 2 or more parameters are varied at the same time and the overall effect on the results is evaluated. Threshold sensitivity analysis – the critical value of parameters above or below which the conclusions of the study will change are identified. Probabilistic sensitivity analysis – probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (for example Monte Carlo simulation).
Sialorrhoea	Drooling or anterior saliva loss.
Significance (statistical)	See p-value. A result is deemed statistically significant if the probability of the result occurring by chance is less than 1 in 20 ($p<0.05$).
Sleep diaries	A diary that a person, parent or carer keeps of their sleep pattern on a daily basis allowing analysis of sleep habits.
Sleep disordered breathing	A general term for all breathing problems during sleep. Includes sleep apnoea, and snoring.
Sleep efficiency	The proportion of a sleep that is not restless sleep or being awake in the night.
Sleep initiation	The process of falling asleep.
Sleep latency	The time it takes to go from full wakefulness to sleep, often light sleep.
Sleep Questionnaire	A questionnaire designed to look at a person's sleep pattern and the impact it has on their daily life including day-time sleepiness.

Term	Definition
Sleep systems/ sleep positioning (postural devices, wedges and supports)	Devices used to keep a child in an advantageous position during sleep. Used to assist with prevention of muscle contractures.
Spasticity, ataxia, dyskinesia	Spasticity – a specific form of increased muscle tone (hypertonia) here one or more of the following are present: • the resistance to externally imposed movement increases with increasing speed of stretch and varies with the direction of joint movement. • the resistance to externally imposed movement increases rapidly beyond a threshold speed or joint angle. Ataxia – a disorder of control of movement that impairs balance. It may involve the trunk (truncal ataxia) or the limbs. In some children and young people it may result from sensory deficits. Dyskinesia – A term used to include movement disorders such as athetosis, chorea, dystonia and tics.
Special Care Baby Unit (SCBU)	A unit with a high staff-patient ratio where babies can be observed and treated but not usually to the same level as a neonatal intensive care unit. For example, a SCBU might stabilise a premature bay before transferring to an NICU.
Specificity	The proportion of true negatives that are correctly identified as such. For example, in diagnostic testing the specificity is the proportion of non-cases correctly diagnosed as non-cases. In terms of literature searching a highly specific search is generally narrow and aimed at picking up the key papers in a field and avoiding a wide range of papers. See also Sensitivity.
Spinal cord disorders	Problems of movement, feeling or bowel and bladder control caused by problems of the spinal cord, such as Spina Bifida.
Stakeholder	An organisation with an interest in a topic on which NICE is developing a clinical guideline or piece of public health guidance. Organisations that register as stakeholders can comment on the draft scope and the draft guidance. Stakeholders may be: - manufacturers of drugs or equipment - national patient and carer organisations - NHS organisations - organisations representing healthcare professionals.
Standard deviation (SD)	A measure of the spread or dispersion of a set of observations, calculated as the average difference from the mean value in the sample.
Structural / Congenital Brain Malformations	Malformation of the brain during its development. Usually genetic but can be the result of infection in utero or antenatal stroke.
Subgroup analysis	An analysis in which the intervention effect is evaluated in a defined subset of the participants in a trial, or in complementary subsets.
Surgical pain/discomfort	Pain as a result of an operation.
Systematic review	A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to predetermined criteria. It may include a meta-analysis.
Time horizon	The time span over which costs and health outcomes are considered in a decision analysis or economic evaluation.
Transdermal scopolamine/hyoscine hydrobromide (hyoscine patches)	A topical form of application of Hyoscine hydrobromide. It is licensed for use in travel sickness, nausea and vomiting but is also used to reduce saliva production and thicken secretions.
Treatment allocation	Assigning a participant to a particular arm of a trial.

Term	Definition
True negative	A diagnostic test result that correctly indicates that an individual does not have the disease of interest when they actually do not have it.
True positive	A diagnostic test result that correctly indicates that an individual has the disease of interest when they do actually have it.
Univariate	Analysis which separately explores each variable in a data set.
Utility	In health economics, a utility is the measure of the preference or value that an individual or society places upon a particular health state. It is generally a number between 0 (representing death) and 1 (perfect health). The most widely used measure of benefit in cost-utility analysis is the quality-adjusted life year, but other measures include disability-adjusted life years (DALYs) and healthy year equivalents (HYEs).
White matter injury	Similar meaning to PVL but also includes babies where the white matter damage or loss is not in the area around the lateral ventricles.
Young adult	A person aged 19 years to 25 years.
Young person	A person aged 12 years to 19 years.

1

33 Appendices

The appendices are contained in separate documents:

Appendix A: Scope

Appendix B: Stakeholders

Appendix C: Declarations of interest

Appendix D: Review protocols

Appendix E: Search strategies

Appendix F: Summary of identified studies

Appendix G: Excluded studies

Appendix H: Health Economics

Appendix I: Forest plots

Appendix J: Evidence tables

Appendix K: Excluded Studies

1