National Institute for Health and Care Excellence

Draft for consultation

Cerebral palsy in adults

[B1] Assessing and monitoring complications and comorbidities: Disorders of bones and joints

NICE guideline tbc

Evidence reviews

July 2018

Draft for Consultation

These evidence reviews were developed by the National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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ISBN:

Contents

Monitoring protocol for disorders of bones and joints in adults with cerebral palsy

Review question

B1 What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

Introduction

Adults with cerebral palsy can experience more bone and joint problems due to the effects of the movement disorder (weakness, spasticity and dystonia) and some of the treatments they receive, for example those who are less mobile, or on anticonvulsants, may also have loss of bone mineral density. This review question aims to look at how these problems with joints and bone should be assessed and monitored in adults with cerebral palsy.

PICO / PIRO table

Please see

Table 1 for a summary of the Population, Intervention / Index test, Comparison / Reference Standard and Outcome (PICO/PIRO) characteristics of this review.

Table 1: Summary of the protocol (PICO / PIRO table)

Population	Adults aged 25 and over with cerebral palsy (study median age of at least 18 years)

Intervention / Index test	Monitoring protocol for disorders of bones and joints could include:
	• Clinical examination
	• Radiograph
	• Annual health check (learning disabilities)
	• Questionnaire:
	  ○ MCPHCS (Melbourne cerebral palsy hip classification system)
	  ○ CPUP (Swedish assessment questionnaire)
	• DEXA scanning

Comparison / Reference standard	• Each other • Any other monitoring protocol • No monitoring protocol

Outcomes	**Critical**
	• Incidence of bone or joint disorders
	• Severity of bone or joint disorders
	• Diagnostic accuracy (in the absence of test/treat studies)
	  ○ Sensitivity
	  ○ Specificity
	  ○ Negative/positive likelihood ratio

	• Validity and reliability **Important** • Patient satisfaction

CPUP: Cerebral Palsy Follow-Up Program: DEXA: dual energy X-ray absorptiometry; MCPHCS: The Melbourne cerebral palsy hip classification system;

For full details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual 2014. Methods specific to this review question are described in the review protocol in appendix A and for a full description of the methods see supplementary document C.

Declaration of interests were recorded according to NICE's 2014 conflicts of interest policy from May 2016 until April 2018. From April 2018 onwards they were recorded according to NICE's 2018 conflicts of interest policy. Those interests declared until April 2018 were reclassified according to NICE's 2018 conflicts of interest policy (see Interests Register).

Clinical evidence

Included studies

Two non-comparative observational studies (number of participants, N=82), including one longitudinal study (Grossberg 2015) and one retrospective follow-up study (Marciniak 2016) were included in the review. Both focused on the use of dual-energy X-ray absorptiometry (DEXA) to assess and monitor the bone mineral density in adults with cerebral palsy.

Although the Grossberg 2015 and Marciniak 2016 studies had no comparator group they provided information about the prevalence and severity of osteoporosis in adults with cerebral palsy as measured using the reference standard DEXA test. This information informs an estimate of how many cases would be missed if there was no monitoring for osteoporosis.

The clinical studies included in this evidence review are summarised in Table 2 and evidence from these are summarised in the clinical evidence profile below (

Table 3).

See also the literature search strategy in appendix B, study selection flow chart in appendix C, forest plots in appendix E and study evidence tables in appendix D.

Excluded studies

Studies excluded from this systematic review, with reasons for their exclusion, are provided in appendix K.

Summary of clinical studies included in the evidence review

Table 2 provides a brief summary of the included studies.

Table 2: Summary of included studies

Study	Design	Participants	Monitoring Protocol	Outcomes
Grossberg 2015	Longitudinal study	40 adults with cerebral palsy, residents of a specialized long term facility. United States	Dual energy X-Ray absorptiometry (DEXA)	Bone Mineral density : Mean and standard deviation of BMD scores, Median annualized BMD percentage change
Marciniak 2016	Retrospective follow-up study	42 adults with cerebral palsy with functional limitations, GMFCS III-V. United States	Dual energy X-Ray absorptiometry (DEXA)	Bone Mineral density: Mean and standard deviation of BMD scores, Number of subjects with Z score less than -2

BMD: Bone mineral density; CP: cerebral palsy; DEXA: dual energy X-Ray absorptiometry; GMFCS: Gross motor function classification system

See appendix D for full evidence tables.

Quality assessment of clinical studies included in the evidence review

The clinical evidence profile for this review question is presented in

Table 3.

Table 3: Summary clinical evidence profile: Comparison 1: DEXA versus any other monitoring protocol

Outcomes	Risk with other monitoring protocol	Illustrative Risk with DEXA	No of Participants (studies)	Quality of the evidence (GRADE)
Incidence of bone or joint disorders				
Osteoporosis incidence Bone mineral density (Lumbar spine)	NR	The percentage of subjects with bone mineral density Z score[1] less than -2 was 44.7%	38 (1 observational study)[2]	Very low[3]
Osteoporosis incidence Bone mineral density (Total hip right)	NR	The percentage of subjects with bone mineral density Z score[1] less than -2 was 31.3%	32 (1 observational study)[2]	Very low[3]
Osteoporosis incidence Bone mineral density (Total hip left)	NR	The percentage of subjects with bone mineral density Z score[1] less than -2 was 26.5%	34 (1 observational study)[2]	Very low[3]
Osteoporosis incidence Bone mineral density (Femoral neck right)	NR	The percentage of subjects with bone mineral density Z score[1] less than -2 was 48.5%	33 (1 observational study)[2]	Very low[3]

Outcomes	Risk with other monitoring protocol	Illustrative Risk with DEXA	No of Participants (studies)	Quality of the evidence (GRADE)
Osteoporosis incidence Bone mineral density (Femoral neck left)	NR	The percentage of subjects with bone mineral density Z score[1] less than -2 was 28.6%	35 (1 observational study)[2]	Very low[3]
Severity of bone or joint disorders				
Median annualized change in BMD (%) (Follow up: 5-6 years)	NR	The median annualized change in BMD was 0.7 to 1.0%	40 (1 observational study)[2]	Very low[3]
Bone mineral density (Region 1)[4]	NR	The mean (SD) bone mineral density for Region 1 was 0.54 (0.17)	40 (1 observational study)[2]	Very low[3]
Bone mineral density (Region 2)[5]	NR	The mean (SD) bone mineral density for Region 2 was 0.77 (0.16)	40 (1 observational study)[2]	Very low[3]
Bone mineral density (Region 3)[6]	NR	The mean (SD) bone mineral density for Region 3 was 0.87 (0.14)	40 (1 observational study)[2]	Very low[3]
Diagnostic accuracy				
Diagnostic accuracy-not reported	-	-	-	-
Validity and reliability				
Validity and reliability-not reported	-	-	-	-
Patient satisfaction				
Patient satisfaction-not reported	-	-	-	-

BMD: Bone mineral density; DEXA: dual energy X-Ray absorptiometry; NR: not reported; SD: standard deviation
1. Z score: Number of standard deviations compared to mean bone mineral density values in age-matched individuals.
2. The number of participants is not the same as the total number of participants in the Marciniak 2016 study, because z-scores related to the incidence of bone or joint disorders were not available for every patient for each bone density site. Data for all 40 participants in the Grossberg 2015 on severity of bone or joint disorders were available.
3. Downgraded for serious risk of bias Downgraded for serious risk of bias due to selection from a centre with severe cases which may inflate true overall incidence in adults with cerebral palsy.
4. Region 1: Cancellous bone
5. Region 2: Metaphyseal to diaphyseal region
6. Region 3: Cortical bone

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no studies were identified which were applicable to this review question.

Excluded studies

No studies were identified which were applicable to this review question.

Summary of studies included in the economic evidence review

No economic evaluations were included in this review.

Economic model

This question was not prioritised for economic modelling although the committee noted there may be variation in practise across England and that imaging investigations are more expensive than clinical investigations. However, the committee considered that the comparative evidence identified was not strong enough to build an informative economic model.

Resource impact

No unit costs were presented to the committee as these were not prioritised for decision-making purposes.

Evidence statements

DEXA versus any other monitoring protocol

Critical outcomes

Incidence of bone or joint disorders

- Very low quality evidence from 1 observational study (n=38) found that 44.7% adults with cerebral palsy had low bone mineral density values compared to age matched individuals measured using DEXA scan at lumbar spine.
- Very low quality evidence from 1 observational study (n=32) found that 31.3% adults with cerebral palsy had low bone mineral density values compared to age matched individuals measured using DEXA scan at total hip (right).
- Very low quality evidence from 1 observational study (n=34) found that 26.5% adults with cerebral palsy had low bone mineral density values compared to age matched individuals measured using DEXA scan at total hip(left),.
- Very low quality evidence from 1 observational study (n=33) found 48.5% adults with cerebral palsy had low bone mineral density values compared to age matched individuals measured using DEXA scan at femoral neck(right)
- Very low quality evidence from 1 observational study (n=35) found 28.6% adults with cerebral palsy had low bone mineral density values compared to age matched individuals measured using DEXA scan at femoral neck(left).

Severity of bone or joint disorders

- Very low quality evidence from 1 observational study found that DEXA scan was able to capture change in bone mineral density in 40 adult patients with cerebral palsy at rate 0.7 to 1 % annually over 5-6 year follow-up period.
- Very low quality evidence from 1 observational study (n=40) found that the mean (standard deviation) bone mineral density scores using DEXA scan in adult patients with cerebral palsy at region 1 (cancellous bone) was 0.54 (0.17).
- Very low quality evidence from 1 observational study (n=40) found that the mean (standard deviation) bone mineral density scores using DEXA scan in adult patients with cerebral palsy at region 2 (metaphyseal to diaphyseal region) was 0.77(0.16).
- Very low quality evidence from 1 observational study (n=40) found that the mean (standard deviation) bone mineral density scores using DEXA scan in adult patients with cerebral palsy at region 3 (cortical bone) was 0.87 (0.14).

Diagnostic accuracy

- No evidence was found for this outcome.

Validity and reliability

- No evidence was found for this outcome.

Important outcomes

Patient satisfaction

- No evidence was found for this outcome.

Recommendations

B1.1 Discuss with adults with cerebral palsy (and their families or carers, if appropriate) that:

- musculoskeletal function may deteriorate gradually, and any changes should be investigated to identify treatable causes
- early recognition of bone and joint disorders enables early treatment, which may improve outcomes.

B1.2 Be aware that low bone mineral density is common in adults with cerebral palsy, particularly in people:

- with reduced mobility or reduced weight bearing
- taking anticonvulsants or proton pump inhibitors
- who have had a previous low-impact fracture.

B1.3 Consider assessing for risk of fractures secondary to osteoporosis in adults with cerebral palsy. Risk factors to assess include:

- needing help with moving or having to be moved, for example hoisting
- history of falls
- low BMI
- history of low-impact fractures
- other medical factors, for example steroid use, that may adversely affect bone health.

For more information about assessment of fracture risk, see NICE's guideline on osteoporosis: assessing the risk of fragility fracture.

B1.4 Consider a dual-energy X-ray absorptiometry (DXA) assessment in adults with cerebral palsy who have 2 or more risk factors (see recommendation B1.3), particularly if they have had a previous low-impact fracture.

B1.5 Consider referring adults with cerebral palsy for specialist assessment and management, for example, to a rheumatology, endocrinology or bone health service, if they have:

- a high fracture risk or
- a positive DXA result.

B1.6 Be aware that, because of abnormal musculoskeletal development, adults with cerebral palsy are more likely to have bone and joint disorders.

B1.7 Refer adults with cerebral palsy to a specialist orthopaedic or musculoskeletal service if a bone or joint disorder is suspected and causing pain or affecting posture or function. These may include:

- osteoarthritis
- cervical instability or spondylosis
- spinal deformity (including scoliosis, kyphosis and lordosis
- subluxation of the hips, wrist and shoulders
- biomechanical knee problems
- abnormalities of the foot structure.

B1.8 Do not offer an X-ray to assess for hip subluxation or curvature of the spine in adults with cerebral palsy, unless the person is in pain or their posture or function is affected.

Rationale and impact

Why the committee made the recommendations

Based on their experience, the committee noted that there is a lack of awareness, both among adults with cerebral palsy and healthcare professionals, that people with cerebral palsy are at increased risk of bone and joint complications, and that musculoskeletal function may worsen over time. Common complications include osteoporosis and conditions caused by abnormal musculoskeletal development, such as scoliosis and subluxation of joints. Increasing awareness and discussing this with adults with cerebral palsy will enable early identification and management of these conditions.

Osteoporosis and fracture risk

The committee agreed that assessing fracture risk is important for adults with cerebral palsy who are at increased risk of osteoporosis to enable action to be taken to manage osteoporosis and prevent fractures. Based on their experience and knowledge the committee identified factors that are associated with increased risk and agreed that fracture risk assessment should be considered for adults with cerebral palsy with these factors. In addition to the risk factors related to cerebral palsy (such as reduced weight bearing), risk factors for the general population also apply. These are described in NICE's guideline on osteoporosis: assessing the risk of fragility fracture along with information about assessing fracture risk.

There was some evidence that dual-energy X-ray absorptiometry (DXA) scanning can be effective in identifying reduced bone density in adults with cerebral palsy. However, the committee noted that these scans can often be uncomfortable and the results difficult to interpret in people with cerebral palsy. The risks of treatment may also outweigh the benefits

in people without symptoms. For these reasons they agreed that it should only be considered for people with more than 1 risk factor, suggesting a high risk of fractures and osteoporosis.

Based on their experience, the committee agreed that assessment and management of osteoporosis in adults with cerebral palsy is highly complex, and that referral to a specialist service is often necessary. For some people this may be to a rheumatology or bone health service, for others referral to endocrinology may be considered to explore whether a hormonal condition could be affecting their bones.

Disorders caused by abnormal musculoskeletal development

Adults with cerebral palsy may develop joint abnormalities due to problems of tone, movement and posture. No evidence was identified on monitoring for these disorders. However, the committee agreed that specialist referral is needed for assessment and management if these conditions are suspected and causing problematic symptoms. They highlighted some of the more common disorders to help increase awareness and improve recognition.

The committee were aware that hip and spine X-rays may be offered routinely to children and young people in paediatric services. However, ongoing surveillance is not necessary for adults once growth is complete, and X-rays should not be offered unless there are new problems of pain, posture or difficulties with care.

Impact of the recommendations on practice

The recommendations for risk assessment and DXA scanning are unlikely to change current practice. DXA scans should already be considered under NICE's guideline on assessing the risk of fragility fracture.

The recommendations could increase referrals to specialist services. However, the impact of this is likely to be balanced by better treatment and prevention of hospital stays.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Since this review question focused on the monitoring protocols for disorders of bones and joints, incidence and severity of bone and joint disorders were considered the critical outcomes. The diagnostic accuracy of monitoring protocols, their validity and reliability were also critical because accurate identification of bone or joint disorders is likely to improve outcomes. The impact of repeated and potentially uncomfortable monitoring tests meant patient satisfaction was included as an important outcomes.

The quality of the evidence

The quality of the evidence for this review was assessed using a modified GRADE approach (see the methods in supplementary document C). Only outcomes related to incidence and severity of bone and joint disorders were reported. Evidence about incidence of bone and joint disorders identified by monitoring tools was rated as very low quality due to risk of bias. There was serious risk of bias due to the non-comparative study design. The evidence regarding severity of bone and joint disorders was also downgraded for risk of bias due to the non-comparative study design.

Although this evidence was rated as very low quality, the findings were consistent with the committee's clinical practice and the available evidence contributed at least in part to the recommendations.

There was no evidence about the diagnostic accuracy, reliability or validity of monitoring protocols or about patient satisfaction.

With the lack of high quality evidence, these recommendations were largely based on the experience and expertise of the committee. The committee were aware of NICE guideline CG146 Osteoporosis: assessing the risk of fragility fracture and cross-referenced to it. Due to lack of evidence on annual health check-ups, radiographs and questionnaires, recommendations regarding these monitoring protocols could not be made.

Benefits and harms

The committee agreed that it was good practice to discuss disorders of bones and joints with the adult with cerebral palsy. It was noted based on the committee's experience that adults with cerebral palsy may not realise or recognise that they are at a higher risk of having musculoskeletal disorders because they may attribute bone pain to cerebral palsy rather than a specific bone or joint condition. Spotting signs early would lead to targeted treatment and consequently improvements in outcomes. This should also be highlighted in the discussion with the adult with cerebral palsy.

The committee noted, based on their knowledge and experience that low bone mineral density can be particularly common in people with cerebral palsy, because there are specific risks which make this more likely to occur. The committee were aware that there was an Medicines & Healthcare products Regulatory Agency (MHRA) drug safety update on anticonvulsants: adverse effects on bone issued in April 2009 and an MHRA drug safety update on proton pump inhibitors in long-term use: increased risk of fracture issued in April 2012.Therefore the committee highlighted these drug groups. The committee noted that being aware of those at risk can help in early detection and effective management of low bone mineral density in these people. Early identification and management reduces the likelihood of fractures. Complications of low bone mineral density can be associated with severe pain and worsened spasticity, permanent deterioration of function, and also long hospital stays. The end result is that the person is less able to participate in usual activities.

The committee discussed that the risk of fractures secondary to osteoporosis is more likely in certain situations and medical conditions and hence there is need to assess the risk of fractures in these groups. Assessing the risk of fracture and identifying those at most risk can help take steps for prevention of fractures. The committee made this recommendation based on their experience and expertise, as there was lack of evidence on risk factors.

The committee were aware of NICE guideline CG146 Osteoporosis: assessing the risk of fragility fracture and agreed that risk factors for fractures in the general population would also apply to adults with cerebral palsy. They therefore cross-referred to this guideline to make sure that risks are identified early so that fractures can be prevented.

The committee noted that there is evidence that Dual-energy X-Ray absorptiometry (DXA) scans can capture changes in bone mineral density in people with cerebral palsy. The committee believed that referral for assessment of osteoporosis should be determined by the presence of symptoms or strong risk factors. The procedure may be uncomfortable for the adult with cerebral palsy and results may be difficult to interpret and therefore the committee would not recommend routine DXA scan for all adults with cerebral palsy. Also, the committee were aware that the risks of treatment of osteoporosis may outweigh the benefits in the absence of symptoms. They therefore only made a weak recommendation for DXA scans for adults with cerebral palsy who have 2 or more risk factors.

The committee discussed, based on their expertise, that referral may be necessary for further specialist assessment. They discussed that there are, for example, endocrine conditions like hypothyroidism which could also be one of the contributors to low bone mineral density and repeated fractures in people with cerebral palsy. Hence, they made the recommendation regarding referral to endocrinology and other specialties for adults with

cerebral palsy with a high fracture risk or a positive DXA result. They made a weak recommendation for this since it was based on the committee's expertise and experience.

Early identification and management of orthopaedic problems helps prevent dislocation and degenerative changes which may further impair activity and participation. For example, the committee particularly wanted to highlight the risk of cervical spondylosis because it causes cervical myelopathy in dyskinetic cerebral palsy. Being aware of a high risk for this and other conditions could help detection. This recommendation was based on the experience and expertise of the committee. Due to lack of evidence on this topic, the committee did not make a strong recommendation.

The committee discussed not only low bone mineral density and fracture risk secondary to osteoporosis, but also talked about other conditions bone or joint disorders caused by abnormal musculoskeletal development (as specified in the review protocol). The committee, from experience, were aware that adults with cerebral palsy may potentially develop abnormalities of all joints due to problems of tone, movement and posture. The committee believed that there is inadequate awareness about this. Knowledge of this would lead to earlier identification of bone and joint disorder. Based on their knowledge the committee decided that any such condition could cause pain and affect posture or function which would limit the adult with cerebral palsy's quality of life. Targeted referral of people most affected by conditions would improve outcomes. Based on their expertise the committee listed those bone and joint disorders that can be experienced by adults with cerebral palsy (e.g. scoliosis, cervical spondylosis, biomechanical knee problems, subluxation of the hips, wrists and shoulders and abnormalities of the foot structure) and if these are suspected and impact on pain or function, referral should be made for specialist assessment.

The committee is aware that hip and spine X-rays may have been offered routinely by paediatric services, but ongoing surveillance was not necessary in adults once growth is complete, unless there were new problems of pain, posture or difficulties in care. This is why the committee did not recommend X-ray to assess for hip subluxation or curvature of the spine in adults with cerebral palsy, unless the person is in pain or their posture or function is affected.

Cost effectiveness and resource use

No economic evaluations were identified for this review question.

As the population group is already covered under previous NICE guidelines and the recommendations made here largely reiterate these, the committee considered there would little impact on practice and consequently minimal impact upon resource use.

The recommendations could potentially lead to an increase in referral to endocrinologists although with limited evidence it was difficult to establish if this would be true. Any increase in resource use though would be offset by better management and subsequent reduction in hospital visits and stays as a result of bone fractures.

Other factors the committee took into account

The only evidence identified related to DXA scanning. Given that a high proportion of people with cerebral palsy have low bone mineral density, the committee considered that the recommendations in the NICE guideline CG146 Osteoporosis: assessing the risk of fragility fracture would also apply to this patient group. They therefore agreed to cross-reference these recommendations.

References

Grossberg 2015

Grossberg, R., Blackford, M. G., Kecskemethy, H. H., Henderson, R., Reed, M. D., Longitudinal assessment of bone growth and development in a facility-based population of young adults with cerebral palsy, Developmental Medicine & Child Neurology, 57, 1064-9, 2015

Marciniak 2016

Marciniak, C., Gabet, J., Lee, J., Ma, M., Brander, K., Wysocki, N., Osteoporosis in adults with cerebral palsy: feasibility of DEXA screening and risk factors for low bone density, Osteoporosis International, 27, 1477-84, 2016

Appendices

Appendix A – Review protocols

Review protocol for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

Table 4: Review protocol for disorders of the bones and joints

Field (based on PRISMA-P)	Content
Review question	B.1 What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy: • osteoarthritis • osteoporosis (including osteopenia and osteomalacia) • hip displacement • spinal deformity, including scoliosis, kyphosis and lordosis • cervical instability leading to cervical myelopathy?
Type of review question	Intervention and diagnostic test accuracy review
Objective of the review	The aim of this review is to determine the most effective protocol for monitoring the disorders of bones and joints in adults with cerebral palsy.
Eligibility criteria – population/disease/condition/issue/domain	Adults aged 25 and over with cerebral palsy (Study median of age 18 years or older)

Field (based on PRISMA-P)	Content
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	Monitoring protocol for disorders or bones and joints could include: • Clinical examination • Radiograph • Annual health check (learning disabilities) • Questionnaire: o MCPHCS (Melbourne cerebral palsy hip classification system) o CPUP (Swedish assessment questionnaire) • DEXA scanning
Eligibility criteria – comparator(s)/control or reference (gold) standard	• Each other • Any other monitoring protocol • No monitoring protocol
Outcomes and prioritisation	**Critical outcomes** • Incidence of bone or joint disorders • Severity of bone or joint disorders • Diagnostic accuracy (in the absence of test/treat studies) o Sensitivity o Specificity o Negative /positive likelihood ratio o Validity and reliability **Important outcomes** o Patient satisfaction Minimally important differences • dichotomous outcomes will use default MIDs [RR thresholds of 0.80 and 1.2] • continuous outcomes will use default MIDs [0.5 times the SD of the control group] The thresholds for clinical usefulness of tests:

Field (based on PRISMA-P)	Content
	Sensitivity and specificity (sensitivity will be prioritised): • High >90% • Moderate 75-90% • Low <75% Positive likelihood ratio: • Very useful test >10 • Moderately useful test 5-10 • Not a useful test <5 Negative likelihood ratio: • Very useful test <0.1 • Moderately useful test 0.1 to 0.2 • Not a useful test>0.2 Reliability, validity, or internal consistency • Poor < 0.4 • Moderate reliability ≥0.4 to 0.6 • Good >0.6 to 0.8 • Excellent > 0.8
Eligibility criteria – study design	Only published full text papers – For interventional studies (comparing the impact of monitoring protocols on patient outcomes) • Systematic reviews of RCTs • RCTs • Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making) For diagnostic studies (evaluating diagnostic accuracy of monitoring protocols) • Comparative cohort studies
Other inclusion exclusion criteria	Community, residential, primary and secondary care. UK and non-UK studies from other high income countries (WHO classification)

Field (based on PRISMA-P)	Content

Proposed sensitivity/sub-group analysis, or meta-regression	Groups that will be reviewed and analysed separately:
	• Functional level of disability
	• Ambulant versus non-ambulant
	• People with hips in joint versus people with hips out of joint (dislocation)
	
	In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis:
	• Population subgroups:
	  ○ Those taking anti-convulsant medication
	
	• Important confounders
	  ○ Ambulant vs. non-ambulant,
	  ○ hips in/out of joint,
	  ○ anti-convulsant medication

Selection process – duplicate screening/selection/analysis	A random sample of the references identified in the search will be sifted by a second reviewer. This sample size will be 10% of the total, or 100 studies if the search identifies fewer than 1000 studies. All disagreements in study inclusion will be discussed and resolved between the two reviewers. The senior systematic reviewer or guideline lead will be involved if discrepancies cannot be resolved between the two reviewers.
Data management (software)	STAR was used to sift through the references identified by the search, and for data extraction.
Information sources – databases and dates	For details please see appendix B.
Identify if an update	Not an update
Author contacts	For details please see the guideline in development web site.
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual 2014
Search strategy – for one database	For details please see appendix B.

Field (based on PRISMA-P)	Content
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).
Methods for assessing bias at outcome/study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual 2014
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual 2014
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the methods in supplementary document C.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual 2014
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual 2014
Rationale/context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Alliance (NGA) and chaired by Dr Paul Eunson in line with section 3 of Developing NICE guidelines: the manual 2014. Staff from the NGA undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods in supplementary document C.
Sources of funding/support	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Name of sponsor	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Roles of sponsor	NICE funds NGA to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not applicable

CPUP: Cerebral Palsy Follow-Up Program; DEXA: dual energy X-ray absorptiometry; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MCPHCS: The Melbourne cerebral palsy hip classification system; MID: minimally important difference; NGA: National Guideline Alliance; NHS: National Health Service; NICE: National Institute for Health and Care Excellence; QUADAS: quality assessment of diagnostic accuracy studies; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; WHO: World Health Organization

Appendix B – Literature search strategies

Literature search strategies for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

Database: Medline & Embase (Multifile)

Database(s): Embase 1974 to 2018 March 22, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present

Table 5: Last searched on 22 March 2018

#	Searches
1	exp Cerebral Palsy/ use prmz
2	exp cerebral palsy/ use oemezd
3	((cerebral or brain or central) adj2 (pal* or paralys#s or pares#s)).tw.
4	cerebral palsy.ti,ab.
5	little? disease.tw.
6	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) adj5 spastic*).tw.
7	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) adj3 ataxi*).tw.
8	or/1-6
9	limit 8 to english language
10	limit 9 to (adult <18 to 64 years> or aged <65+ years>) use oemezd [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process; records were retained]
11	limit 9 to "all adult (19 plus years)" [Limit not valid in Embase; records were retained]
12	11 use prmz
13	or/10,12
14	exp Osteoarthritis/ or exp Osteoporosis/ or exp Bone Diseases, Metabolic/ or exp Osteomalacia/ or exp Hip Dislocation/ or exp Hip Joint/ or exp Femur Neck/ or exp Lumbar Vertebrae/ or exp Scoliosis/ or exp Kyphosis/ or exp Lordosis/ or exp Spinal Curvatures/ or exp Nerve Compression Syndromes/ or exp Joint Instability/ or exp Posture/ or exp Locomotion/ or exp Bone Density/ or exp Arthroplasty, Replacement/ or exp Hip Prosthesis/
15	14 use prmz
16	exp osteoarthritis/ or exp osteoporosis/ or exp metabolic bone disease/ or exp osteomalacia/ or exp hip dislocation/ or exp hip/ or exp femur neck/ or exp lumbar vertebra/ or exp scoliosis/ or exp kyphosis/ or exp lordosis/ or exp spine disease/ or exp nerve compression/ or exp joint instability/ or exp body posture/ or exp locomotion/ or exp bone density/ or exp replacement arthroplasty/ or Hip Prosthesis/ or exp hip prosthesis/
17	16 use oemezd
18	(osteopenia or scoliosis or kyphosis or lordosis or (hip adj (displace* or dislocat*)) or (cervical adj (instabilit* or myelopathy)) or ((curvature* or deterioat* or alter* or deform* or abnormal* or instab*) adj5 (spine or skelet* or bone* or hip* or joint*))).ti,ab.
19	(osteo* or ostheo*).tw.
20	15 or 17 or 18 or 19

#	Searches
21	13 and 20
22	exp Patient Care Planning/ or exp Managed Care Programs/ or exp "Standard of Care"/ or exp Needs Assessment/ or exp Physical Examination/ or exp Health Status/ or exp Long-Term Care/ or exp Algorithms/ or exp Disability Evaluation/ or exp Disease Progression/ or exp Monitoring, Ambulatory/ or exp Monitoring, Physiologic/ or exp Follow-Up Studies/ or exp Aging/ or exp Salvage Therapy/ or exp "Continuity of Patient Care"/ or exp Transition to Adult Care/ or exp Equipment Failure Analysis/ or exp Radiotherapy Planning, Computer-Assisted/ or exp Tomography, X-Ray Computed/ or exp Absorptiometry, Photon/ or exp Radiography/
23	22 use prmz
24	((exp patient care planning/ or exp health care quality/ or exp needs assessment/ or exp physical examination/ or exp health status/ or exp long term care/ or exp algorithm/ or exp disease course/ or disability/ or exp "Hip Disability and Osteoarthritis Outcome Score"/ or exp ambulatory monitoring/ or exp physiologic monitoring/ or exp follow up/ or exp aging/ or exp salvage therapy/ or exp patient care/ or exp transition to adult care/ or exp device failure analysis/ or planning/) and radiotherapy/) or exp computer assisted tomography/ or exp photon absorptiometry/ or exp radiography/
25	24 use oemezd
26	(radiography or annual or regular or (every adj1 year*) or follow up or follow?up or (multidisciplin* adj (clinic* or team*)) or monitor* or assess* or review* or observ* or routine* or protocol* or exam* or test* or surveill* or managment or red flag or pathway or revision or x-ray or (health adj check) or (hip adj2 surveillance*)).ti,ab.
27	"treatment planning".mp.
28	("Melbourne cerebral palsy hip classification system" or MCPHCS).tw.
29	23 or 25 or 26 or 27 or 28
30	21 and 29
31	conference abstract.pt. use oemezd
32	letter.pt. or LETTER/ use oemezd
33	Letter/ use prmz
34	EDITORIAL/ use prmz
35	editorial.pt. use oemezd
36	NEWS/ use prmz
37	exp HISTORICAL ARTICLE/ use prmz
38	note.pt. use oemezd
39	ANECDOTES AS TOPIC/ use prmz
40	COMMENT/ use prmz
41	CASE REPORT/ use prmz
42	CASE REPORT/ use oemezd
43	CASE STUDY/ use oemezd
44	(letter or comment* or abstracts).ti.
45	or/31-44
46	RANDOMIZED CONTROLLED TRIAL/ use prmz
47	RANDOMIZED CONTROLLED TRIAL/ use oemezd
48	random*.ti,ab.
49	or/46-48
50	45 not 49
51	ANIMALS/ not HUMANS/ use prmz
52	ANIMAL/ not HUMAN/ use oemezd

#	Searches
53	exp ANIMALS, LABORATORY/ use prmz
54	exp ANIMAL EXPERIMENTATION/ use prmz
55	exp MODELS, ANIMAL/ use prmz
56	exp RODENTIA/ use prmz
57	NONHUMAN/ use oemezd
58	exp ANIMAL EXPERIMENT/ use oemezd
59	exp EXPERIMENTAL ANIMAL/ use oemezd
60	ANIMAL MODEL/ use oemezd
61	exp RODENT/ use oemezd
62	(rat or rats or mouse or mice).ti.
63	or/50-62
64	30 not 63

Database: Cochrane Library

Table 6: Last searched on 22 March 2018

#1	MeSH descriptor: [Cerebral Palsy] explode all trees
#2	((cerebral or brain or central) N2 (pal* or paralys?s or pare?s))
#3	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) N5 spastic*)
#4	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) N3 ataxi*)
#5	#1 or #2 or #3 or #4
#6	MeSH descriptor: [Osteoarthritis] explode all trees
#7	MeSH descriptor: [Osteoporosis] explode all trees
#8	MeSH descriptor: [Bone Diseases, Metabolic] explode all trees
#9	MeSH descriptor: [Osteomalacia] explode all trees
#10	MeSH descriptor: [Hip Dislocation] explode all trees
#11	MeSH descriptor: [Hip Joint] explode all trees
#12	MeSH descriptor: [Femur Neck] explode all trees
#13	MeSH descriptor: [Lumbar Vertebrae] explode all trees
#14	MeSH descriptor: [Scoliosis] explode all trees
#15	MeSH descriptor: [Kyphosis] explode all trees
#16	MeSH descriptor: [Lordosis] explode all trees
#17	MeSH descriptor: [Spinal Curvatures] explode all trees
#18	MeSH descriptor: [Nerve Compression Syndromes] explode all trees
#19	MeSH descriptor: [Joint Instability] explode all trees
#20	MeSH descriptor: [Posture] explode all trees
#21	MeSH descriptor: [Locomotion] explode all trees
#22	MeSH descriptor: [Bone Density] explode all trees
#23	MeSH descriptor: [Arthroplasty, Replacement] explode all trees
#24	MeSH descriptor: [Hip Prosthesis] explode all trees
#25	osteo* or ostheo* or Scoliosis or Kyphosis or Lordosis or hip near (displace* or dislocat*) or cervical near (instabilit* or myelopathy)
#26	(curvature* or deterioat* or alter* or deform* or abnormal* or instab*) near (spine or skelet* or bone* or hip* or joint*)
#27	{or #6-#26}

#1	MeSH descriptor: [Cerebral Palsy] explode all trees
#28	#5 and #27
#29	MeSH descriptor: [Patient Care Planning] explode all trees
#30	MeSH descriptor: [Managed Care Programs] explode all trees
#31	MeSH descriptor: [Standard of Care] explode all trees
#32	MeSH descriptor: [Needs Assessment] explode all trees
#33	MeSH descriptor: [Physical Examination] explode all trees
#34	MeSH descriptor: [Health Status] explode all trees
#35	MeSH descriptor: [Long-Term Care] explode all trees
#36	MeSH descriptor: [Algorithms] explode all trees
#37	MeSH descriptor: [Disability Evaluation] explode all trees
#38	MeSH descriptor: [Disease Progression] explode all trees
#39	MeSH descriptor: [Monitoring, Ambulatory] explode all trees
#40	MeSH descriptor: [Monitoring, Physiologic] explode all trees
#41	MeSH descriptor: [Follow-Up Studies] explode all trees
#42	MeSH descriptor: [Aging] explode all trees
#43	MeSH descriptor: [Salvage Therapy] explode all trees
#44	MeSH descriptor: [Continuity of Patient Care] explode all trees
#45	MeSH descriptor: [Transition to Adult Care] explode all trees
#46	MeSH descriptor: [Equipment Failure Analysis] explode all trees
#47	MeSH descriptor: [Radiotherapy Planning, Computer-Assisted] explode all trees
#48	MeSH descriptor: [Tomography, X-Ray Computed] explode all trees
#49	MeSH descriptor: [Absorptiometry, Photon] explode all trees
#50	MeSH descriptor: [Radiography] explode all trees
#51	Radiography or annual or regular or (every N1 year*) or follow up or follow-up or multidisciplin* or monitor* or assess* or review* or observ* or routine* or protocol* or exam* or test* or surveill* or management or red flag or pathway or revision or x-ray or treatment plan* or health near check
#52	{or #29-#51}
#53	#28 and #52

Database: Web of Science

Table 7: Last searched on 22 March 2018

# 5	#4 AND LANGUAGE: (English)
#4	#3 AND #2 AND #1
# 3	ts=Patient Care Planning or ts=Managed Care Programs or ts="Standard of Care" or ts=Needs Assessment or ts=Physical Examination or ts=Health Status or ts=Long-Term Care or ts=Algorithms or ts=Disability Evaluation or ts=Disease Progression or ts=Ambulatory Monitoring or ts=Physiologic Monitoring or ts=Follow-Up or ts=follow up or ts=Aging or ts=Salvage Therapy or ts="Continuity of Patient Care" or ts=Transition to Adult Care or ts=Failure Analysis or ts=Radiotherapy Planning or ts=X-Ray or ts=Absorptiometry or ts=Radiography or ts=annual or ts=regular or ts=every year* or ts=assess* or ts=review* or ts=observ* or ts=routine* or ts=protocol* or ts=exam* or ts=test* or ts=surveill* or ts=management or ts=red flag or ts=pathway or ts=revision or ts=treatment planning or ts=health check
# 2	ts=Osteoarthritis or ts=Osteoporosis or ts=Bone Disease* or ts=Osteomalacia or ts=Hip Dislocation or ts= Joint* or ts=Femur Neck or ts=Lumbar Vertebrae or ts=Scoliosis or

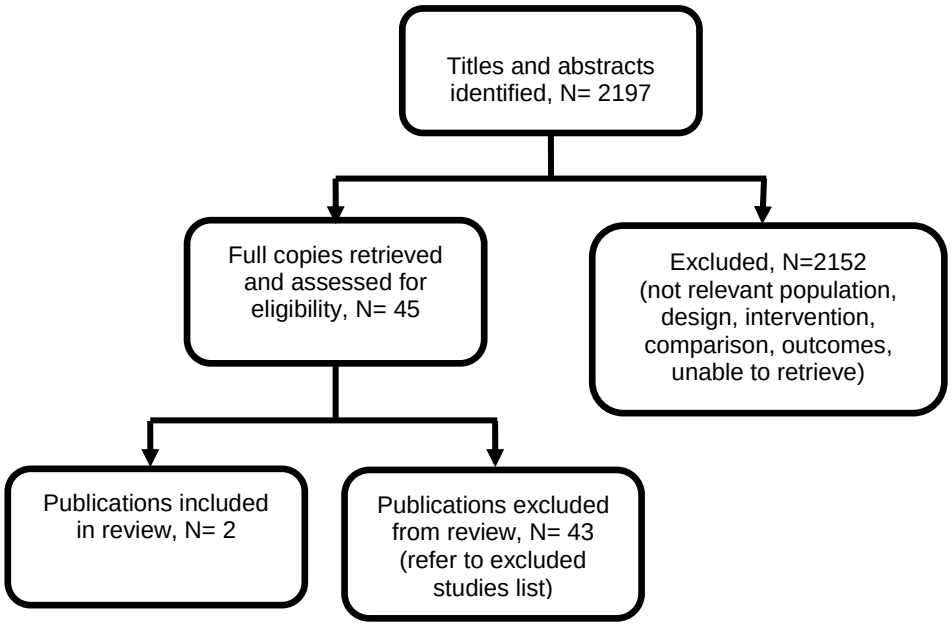
# 5	#4 AND LANGUAGE: (English)
	ts=Kyphosis or ts=Lordosis or ts=Spinal Curvatures or ts=Nerve Compression Syndromes or ts=Joint Instability or ts=Posture or ts=Locomotion or ts=Bone Density or ts= Replacement Arthroplasty or ts=Hip Prosthesis or ts=osteopenia or ts=osteo* or ts=ostheo* or ts= deterioat* or ts=alter* or ts=deform* or ts=abnormal*
# 1	ts=Cerebral Palsy

Appendix C – Clinical evidence study selection

Clinical evidence study selection for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

Figure 1: Flow diagram of clinical article selection for monitoring protocol for disorders of bones and joints review



Appendix D – Clinical evidence tables

Clinical evidence tables for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

Table 8: Studies included in the evidence review for disorders of bone and joint disorders

Study details	Participants	Monitoring Protocol	Methods	Outcomes and Results	Comments
Full citation Grossberg, R., Blackford, M. G., Kecskemethy, H. H., Henderson, R., Reed, M. D., Longitudinal assessment of bone growth and development in a facility-based population of young adults with cerebral palsy, Developmental Medicine & Child Neurology, 57, 1064-9, 2015 **Ref Id** 443712 **Country/ies where the study was carried out**	**Sample size** N=40 **Characteristics** Mean age: 23.10 (4.95) Male 52.5% GMFCS level V, n (%) 38 (95) **Inclusion criteria** Residents of specialized long-term care facility for paediatric and young adult residents with	**Interventions** Bone mineral density (BMD) using DEXA	**Details** BMD was assessed at the right and left distal femurs for three distinct regions of interest	**Results** Five subjects had a fracture that occurred during the study period; this represented a fracture rate of 2.1% per year in the study group. Longitudinally, annualized change in the median BMD was 0.7% to 1.0% per year in the different regions of the distal femur, but ranged widely among the study group, with both increases and decreases in BMD. Increase in BMD over time was negatively correlated with age and	**Limitations** Risk of bias: 1) Selection bias: High risk, due to selection from a centre with severe cases 2) Comparability: Follow up study 3) Outcomes & Follow Up : Adequate **Other information**

Study details	Participants	Monitoring Protocol	Methods	Outcomes and Results	Comments
United States **Study type** Prospective cohort study **Aim of the study** To assess changes in bone mineral density (BMD) over 5 to 6 years in a group, including adults with CP, **Study dates** Not mentioned **Source of funding** Akron Children's Hospital Foundation.	substantial neuromuscular and intellectual impairments in the severe to profound range **Exclusion criteria** Not described			positively correlated with weight.	
Full citation Marciniak, C., Gabet, J., Lee, J., Ma, M., Brander, K., Wysocki, N., Osteoporosis in adults with cerebral palsy: feasibility of DEXA screening and risk factors for low bone density, Osteoporosis International, 27, 1477-84, 2016	**Sample size** N=42 **Characteristics** **Inclusion criteria** 1) Adults with CP seen in clinic over a 2.5 period who underwent	**Interventions** Dual energy X-Ray absorptiometry (DEXA)	**Details** BMD and Z-scores for the lumbar (L), spine (total), and hip (right (R) or left (L) femoral neck and total hip sites) were recorded. BMD and Z-	**Results** 13 fractures in 8 subjects were noted, most often lower limb. 50% of spine studies in individuals under 50 had a Z-score of less than −2, while 25 and 30.8 % of these individuals had such scores at	**Limitations** Risk of bias: 1) Selection bias: High risk. (Mostly severely limited ambulatory population)

Study details	Participants	Monitoring Protocol	Methods	Outcomes and Results	Comments
Ref Id 443723 **Country/ies where the study was carried out** United States **Study type** Retrospective chart review study **Aim of the study** This study aims to describe osteoporosis screening in adults with cerebral palsy (CP) and identify any associated factors. **Study dates** Not described **Source of funding** Not mentioned	DXA scan(s) to assess bone health status 2) GMFCS III-V **Exclusion criteria** 1) Those who got DEXA scans at other centres		scores from baseline to follow-up DEXA for those with more than a single DEXA was also noted.	the right and left total hip sites, respectively. Need for transfer assistance was associated with lower BMD and Z-scores at all hip sites, but not the lumbar spine. Progressive abnormalities were seen at follow-up DEXAs at some sites, however these were not statistically significant.	2) Comparison: Follow up study 3) Outcomes & follow-up- Adequate **Other information**

BMD: Bone mineral density; CP: Cerebral palsy; DEXA: dual energy X-Ray absorptiometry; GMFCS: Gross Motor Function Classification System

Appendix E – Forest plots

Forest plots for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

No forest plots were included in this review.

Appendix F – GRADE tables

GRADE tables for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

Table 9: Clinical evidence profile: Comparison 1: DEXA versus any other monitoring protocol

Quality assessment							No of participants	Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	DXA scan	Relative (95% CI)	Absolute	Quality	Importance
Incidence of bone or joint disorders (Osteoporosis incidence : Subjects with BMD Z score[1] less than -2, lumbar spine)											
1	observational studies	Serious[2]	No serious inconsistency	No serious indirectness	Not applicable	None	38[3]	-	44.7%	VERY LOW	CRITICAL
Incidence of bone or joint disorders (Osteoporosis incidence : Subjects with BMD Z score[1] less than -2, total hip right)											
1	observational studies	Serious[2]	No serious inconsistency	No serious indirectness	Not applicable	None	32[3]	-	31.3%	VERY LOW	CRITICAL
Incidence of bone or joint disorders (Osteoporosis incidence : Subjects with BMD Z score[2] less than -2, total hip left)											
1	observational studies	Serious[2]	No serious inconsistency	No serious indirectness	Not applicable	None	34[3]	-	26.5%	VERY LOW	CRITICAL
Incidence of bone or joint disorders (Osteoporosis incidence : Subjects with BMD Z score[1] less than -2, femoral neck right)											
1	observational studies	Serious[3]	No serious inconsistency	No serious indirectness	Not applicable	None	33[3]	-	48.5%	VERY LOW	CRITICAL
Incidence of bone or joint disorders (Osteoporosis incidence : Subjects with BMD Z score[1] less than -2, femoral neck left)											
1	observational studies	Serious[2]	No serious inconsistency	No serious indirectness	Not applicable	None	35[3]	-	28.6%	VERY LOW	CRITICAL
Severity of bone or joint disorders: The median annualized change in BMD, Follow up: 5-6 years											
1	observational studies	Serious[2]	No serious inconsistency	No serious indirectness	Not applicable	None	40[3]	-	0.7 to1%	VERY LOW	CRITICAL
Severity of bone or joint disorders: Bone mineral density (Region 1)[4]											
1	observational studies	Serious[2]	No serious inconsistency	No serious indirectness	Not applicable	None	40[3]	-	Mean(SD) BMD was 0.54 (0.17)	VERY LOW	CRITICAL
Severity of bone or joint disorders: Bone mineral density (Region 2)[5]											

Quality assessment							No of participants	Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**DXA scan**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	observational studies	Serious[2]	No serious inconsistency	No serious indirectness	Not applicable	None	40[3]	-	Mean(SD) BMD was 0.77 (0.16)	VERY LOW	CRITICAL
Severity of bone or joint disorders: Bone mineral density (Region 3)[6]											
1	observational studies	Serious[2]	No serious inconsistency	No serious indirectness	Not applicable	None	40[3]	-	Mean(SD) BMD was 0.87(0.14)	VERY LOW	CRITICAL
Diagnostic accuracy-not reported											
-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Validity and reliability-not reported											
-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Patient satisfaction-not reported											
--	-	-	-	-	-	-	-	-	-	-	IMPORTANT

BMD: Bone mineral density; DEXA: dual energy X-Ray absorptiometry; SD: standard deviation
1. Z score: Number of standard deviations compared to mean bone mineral density values in age-matched individuals
2. Downgraded for serious risk of bias due to selection from a centre with severe cases which may inflate true overall incidence in adults with cerebral palsy
3. The number of participants is not the same as the total number of participants in the Marciniak 2016 study, because z-scores related to the incidence of bone or joint disorders were not available for every patient for each bone density site. Data for all 40 participants in the Grossberg 2015 on severity of bone or joint disorders were available.
4. Region 1: Cancellous bone
5. Region 2: Metaphyseal to diaphyseal region
6. Region 3: Cortical bone

Appendix G – Economic evidence study selection

Economic evidence study selection for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

No economic evidence was identified for this review.

Appendix H – Economic evidence tables

Economic evidence tables for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

No economic evidence was identified for this review.

Appendix I – Health economic evidence profiles

Health economic evidence profiles for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

No economic evidence was identified for this review.

Appendix J – Health economic analysis

Health economic analysis for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

No economic analysis was included in this review.

Appendix K – Excluded studies

Clinical and economic lists of excluded studies for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

Clinical studies

Table 10: Clinical studies for disorders of bones and joints

Excluded studies - B.1 What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?	
Study	**Reason for Exclusion**
Abel, M. F., Wenger, D. R., Mubarak, S. J., Sutherland, D. H., Quantitative-Analysis of Hip-Dysplasia in Cerebral-Palsy - a Study of Radiographs and 3-D Reformatted Images, Journal of Pediatric Orthopaedics, 14, 283-289, 1994	Does not include monitoring protocol
Andersson,C., Asztalos,L., Mattsson,E., Six-minute walk test in adults with cerebral palsy. A study of reliability, Clinical Rehabilitation, 20, 488-495, 2006	Intervention not related to monitoring protocol for orthopaedic disorders
Ando,N., Ueda,S., Functional deterioration in adults with cerebral palsy, Clinical Rehabilitation, 14, 300-306, 2000	Intervention not related to monitoring protocol for orthopaedic disorders
Bahrami, F., Noorizadeh Dehkordi, S., Dadgoo, M., Inter and intra rater reliability of the 10 meter walk test in the community dweller adults with spastic cerebral palsy, Iranian Journal of Child Neurology, 11, 57-64, 2017	Intervention not related to monitoring protocol for orthopaedic disorders
Boldingh, E. J. K., Jacobs-Van Der Bruggen, M. A. M., Bos, C. F. A., Lankhorst, G. J., Bouter, L. M., Determinants of hip pain in adult patients with severe cerebral palsy, Journal of Pediatric Orthopaedics Part B, 14, 120-125, 2005	Study not related to monitoring protocol for orthopaedic disorders
Boldingh, E. J. K., Jacobs-Van Der Bruggen, M. A. M., Bos, C. F. A., Lankhorst, G. J., Bouter, L. M., Radiographic hip disorders and associated complications in severe cerebral palsy, Journal of Pediatric Orthopaedics Part B, 16, 31-34, 2007	Does not include intervention related to monitoring protocol for orthopaedic disorders
Brantmark, A., Westbom, L., Nordmark, E., Mobility and joint range of motion in adults with cerebral palsy: A population-based study, European Journal of Physiotherapy, 17, 192-199, 2015	Study not related to monitoring protocol
Cohran,V., Cassedy,A., Hawkins,A., Bean,J., Heubi,J., Oral risedronate sodium improves bone mineral density in non-ambulatory patients: a randomized, double-blind, placebo controlled trial, Journal of Pediatric Rehabilitation Medicine, 6, 85-93, 2013	Intervention not related to monitoring protocol for orthopaedic disorders
Cooke, P. H., Cole, W. G., Carey, R. P. L., Dislocation of the hip in cerebral palsy. Natural history and predictability, Journal of Bone and Joint Surgery - Series B, 71, 441-446, 1989	Age group is less than 18 years
Dhawlikar,S.H., Root,L., Mann,R.L., Distal lengthening of the hamstrings in patients who have cerebral palsy. Long-term retrospective analysis, Journal of Bone and Joint Surgery - American Volume, 74, 1385-1391, 1992	Intervention not related to monitoring protocol for orthopaedic disorders
Dreher,T., Wolf,S.I., Maier,M., Hagmann,S., Vegvari,D., Gantz,S., Heitzmann,D., Wenz,W., Braatz,F., Long-term results after distal rectus femoris transfer as a part of multilevel surgery for the correction of stiff-	Intervention not related to monitoring protocol for orthopaedic disorders

Excluded studies - B.1 What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?	
knee gait in spastic diplegic cerebral palsy, Journal of Bone and Joint Surgery - American Volume, 94, e142-10, 2012	
Dyball,K.M., Taylor,N.F., Dodd,K.J., Retest reliability of measuring hip extensor muscle strength in different testing positions in young people with cerebral palsy, BMC Pediatrics, 11, 42-, 2011	Intervention not related to monitoring protocol for orthopaedic disorders
Fowler, E. G., Rao, S., Nattiv, A., Heberer, K., Oppenheim, W. L., Bone density in premenopausal women and men under 50 years of age with cerebral palsy, Archives of Physical Medicine & Rehabilitation, 96, 1304-9, 2015	No comparison
Gorski, M., Scroggie, G., Haines, T., Validity and reliability of the 20-m run, horizontal leap, and four-bound tests measuring high-level mobility in neurologically impaired patients, Hong Kong Physiotherapy Journal, 33, 59-66, 2015	CP population is only a small subgroup
Henderson, R. C., Henderson, B. A., Kecskemethy, H. H., Hidalgo, S. T., Nikolova, B. A., Sheridan, K., Harcke, H. T., Thorpe, D. E., Adaptation of the lateral distal femur DXA scan technique to adults with disabilities, Journal of Clinical Densitometry, 18, 102-108, 2015	Diagnostic accuracy outcomes not reported.
Hilberink, S. R., Roebroeck, M. E., Nieuwstraten, W., Jalink, L., Verheijden, J. M. A., Stam, H. J., Health issues in young adults with cerebral palsy: Towards a life-span perspective, Journal of Rehabilitation Medicine, 39, 605-611, 2007	Intervention not related to monitoring protocol for orthopaedic disorders
Hodgkinson,I., Jindrich,M.L., Duhaut,P., Vadot,J.P., Metton,G., Berard,C., Hip pain in 234 non-ambulatory adolescents and young adults with cerebral palsy: a cross-sectional multicentre study, Developmental Medicine and Child Neurology, 43, 806-808, 2001	Intervention not related to monitoring protocol for orthopaedic disorders
Jaffe,J.S., Timell,A.M., Gulanski,B.I., Prevalence of low bone density in women with developmental disabilities, Journal of Clinical Densitometry, 4, 25-29, 2001	CP is a small subgroup
Jasien, J., Daimon, C. M., Maudsley, S., Shapiro, B. K., Martin, B., Aging and bone health in individuals with developmental disabilities, International Journal of Endocrinology, 2012, 2012	CP is a small subgroup
Kim, W., Lee, S. J., Yoon, Y. K., Shin, Y. K., Cho, S. R., Rhee, Y., Adults with spastic cerebral palsy have lower bone mass than those with dyskinetic cerebral palsy, Bone, 71, 89-93, 2015	Does not include intervention related to monitoring protocol for orthopaedic disorders
Kitsios, A., Tsaklis, P., Koronas, K., Varsamis, P., Abatzides, G., Agelopoulou, N., The effects of a physiotherapeutic programme on bone mineral density, in individuals of postpuberty age (18-30 years), with cerebral palsy, Journal of Back and Musculoskeletal Rehabilitation, 15, 41-45, 2000	Does not include intervention related to monitoring protocol for orthopaedic disorders
Lee, S. Y., Chung, C. Y., Lee, K. M., Kwon, S. S., Cho, K. J., Park, M. S., Annual changes in radiographic indices of the spine in cerebral palsy patients.[Erratum appears in Eur Spine J. 2016 May;25(5):1641; PMID: 26980602], European Spine Journal, 25, 679-86, 2016	Mean age: 10 years
Lee, S. Y., Sung, K. H., Chung, C. Y., Lee, K. M., Kwon, S. S., Kim, T. G., Lee, S. H., Lee, I. H., Park, M. S., Reliability and validity of the Duncan-Ely test for assessing rectus femoris spasticity in patients with cerebral palsy, Developmental Medicine and Child Neurology, 57, 963-968, 2015	Not related to bone and joint disorders
Lohiya,G.S., Tan-Figueroa,L., Iannucci,A., Identification of low bone mass in a developmental center: finger bone mineral density measurement in 562 residents, Journal of the American Medical Directors Association, 5, 371-376, 2004	Does not include intervention related to monitoring protocol for orthopaedic disorders
Maanum, G., Jahnsen, R., Fr, OSlie K. F., Larsen, K. L., Keller, A., Walking ability and predictors of performance on the 6-minute walk test in adults with spastic cerebral palsy, Developmental Medicine and Child Neurology, 52, e126-e132, 2010	Does not include intervention related to monitoring protocol for orthopaedic disorders

Excluded studies - B.1 What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?	
Madigan,R.R., Wallace,S.L., Scoliosis in the institutionalized cerebral palsy population, Spine, 6, 583-590, 1981	Does not include intervention related to monitoring protocol for orthopaedic disorders
Majd,M.E., Muldowny,D.S., Holt,R.T., Natural history of scoliosis in the institutionalized adult cerebral palsy population, Spine, 22, 1461-1466, 1997	Does not include intervention related to monitoring protocol for orthopaedic disorders
Marks,M.C., Alexander,J., Sutherland,D.H., Chambers,H.G., Clinical utility of the Duncan-Ely test for rectus femoris dysfunction during the swing phase of gait, Developmental Medicine and Child Neurology, 45, 763-768, 2003	Not related to bones and joint disorders
Moreau, M., Drummond, D. S., Rogala, E., Ashworth, A., Porter, T., Natural history of the dislocated hip in spastic cerebral palsy, Developmental Medicine & Child Neurology, 21, 749-53, 1979	Does not include intervention related to monitoring protocol for orthopaedic disorders
Murnaghan, M. L., Simpson, P., Robin, J. G., Shore, B. J., Selber, P., Graham, H. K., The cerebral palsy hip classification is reliable AN INTER- AND INTRA-OBSERVER RELIABILITY STUDY, Journal of Bone and Joint Surgery-British Volume, 92B, 436-441, 2010	Age range: 14-19 years
Nakano, H., Aovagi, K., Ohgi, S., Akiyama, T., Factors influencing metacarpal bone mineral density in adults with cerebral palsy, Journal of Bone and Mineral Metabolism, 21, 409-414, 2003	Does not include intervention related to monitoring protocol for orthopaedic disorders
Nishioka, E., Yoshida, K., Yamanaka, K., Inoue, A., Radiographic studies of the wrist and elbow in cerebral palsy, Journal of Orthopaedic Science, 5, 268-274, 2000	Does not include intervention related to monitoring protocol for orthopaedic disorders
Noonan, K. J., Jones, J., Pierson, J., Honkamp, N. J., Leverson, G., Hip function in adults with severe cerebral palsy, Journal of Bone and Joint Surgery - Series A, 86, 2607-2613, 2004	Does not include intervention related to monitoring protocol for orthopaedic disorders
Park, J. Y., Choi, Y., Cho, B. C., Moon, S. Y., Chung, C. Y., Lee, K. M., Sung, K. H., Kwon, S. S., Park, M. S., Progression of Hip Displacement during Radiographic Surveillance in Patients with Cerebral Palsy, Journal of Korean Medical Science, 31, 1143-1149, 2016	Age <20 years. Mean age 8.3 years
Raphael,B.S., Dines,J.S., Akerman,M., Root,L., Long-term followup of total hip arthroplasty in patients with cerebral palsy, Clinical Orthopaedics and Related Research, 468, 1845-1854, 2010	Does not include intervention related to monitoring protocol for orthopaedic disorders
Riquelme, I., Cifre, I., Montoya, P., Are physiotherapists reliable proxies for the recognition of pain in individuals with cerebral palsy? A cross sectional study, Disability & Health Journal, 8, 264-70, 2015	Does not include intervention related to monitoring protocol for orthopaedic disorders
Robin, J., Graham, H. K., Baker, R., Selber, P., Simpson, P., Symons, S., Thomason, P., A classification system for hip disease in cerebral palsy, Developmental Medicine & Child Neurology, 51, 183-92, 2009	Mean age 16 years
Shrader, M. W., Andrisevic, E. M., Belthur, M. V., White, G. R., Boan, C., Wood, W., Inter- and Intraobserver Reliability of Pelvic Obliquity Measurement Methods in Patients With Cerebral Palsy, Spine Deformity., 2017	Conference abstract
Smeltzer,S.C., Zimmerman,V.L., Usefulness of the SCORE index as a predictor of osteoporosis in women with disabilities, Orthopaedic Nursing, 24, 33-39, 2005	CP population is a small subgroup
Srikanth, R., Cassidy, G., Joiner, C., Teeluckdharry, S., Osteoporosis in people with intellectual disabilities: a review and a brief study of risk factors for osteoporosis in a community sample of people with	Does not include intervention related to

Excluded studies - B.1 What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?	
intellectual disabilities, Journal of Intellectual Disability Research, 55, 53-62, 2011	monitoring protocol for orthopaedic disorders
Thometz, J. G., Simon, S. R., Progression of scoliosis after skeletal maturity in institutionalized adults who have cerebral palsy, Journal of Bone & Joint Surgery - American Volume, 70, 1290-6, 1988	Mean age 16.3 years
Willoughby, K. L., Kerr, H., Early radiographic surveillance is needed to prevent sequelae of neglected hip displacement in cerebral palsy, British Medical Journal, 345, 2012	Exclusion by population age group
Zylstra, R. G., Porter, L. L., Shapiro, J. L., Prater, C. D., Prevalence of Osteoporosis in Community-Dwelling Individuals with Intellectual and/or Developmental Disabilities, Journal of the American Medical Directors Association, 9, 109-113, 2008	CP population is a small subgroup

CP: Cerebral palsy

Economic studies

No economic evidence was identified for this review.

Appendix L – Research recommendations

Research recommendation for review question B1: What is the most effective protocol for monitoring the following disorders of bones and joints in adults with cerebral palsy?

- osteoarthritis
- osteoporosis (including osteopenia and osteomalacia)
- hip displacement
- spinal deformity, including scoliosis, kyphosis and lordosis
- cervical instability leading to cervical myelopathy

No research recommendation was made for this review.