10 APPENDICES

APPENDIX 1: SCOPE FOR THE DEVELOPMENT OF THE CLINICAL GUIDELINE

1. GUIDELINE TITLE

Autism: the management and support of autism in children and young people on the autism spectrum

1.1. Short title

Autism: management of autism in children and young people

2. THE REMIT

The Department of Health has asked NICE: 'To produce a clinical guideline in collaboration with the Social Care Institute for Excellence on the management of autism spectrum disorder in children and young people'[1].

3. CLINICAL NEED FOR THE GUIDELINE

3.1. Epidemiology

a) Autism is a spectrum of lifelong neurodevelopmental, biologically- based and genetically heritable conditions influenced significantly by environmental factors, diagnosed on the basis of a triad of behavioural impairments: impaired social interaction, impaired communication, and restricted and repetitive interests and activities.

b) In addition to these core features, children and young people with autism frequently experience a range of cognitive, learning, language, medical, mental, emotional and behavioural problems, including a need for routine; difficulty in understanding other people, including their intentions, feelings and perspectives; sleeping and eating disturbances; and mental health

[1] The scoping group recognises that different people and groups prefer a variety of terms, including 'autism spectrum disorder', 'autistic spectrum condition', 'autistic spectrum difference' and 'neurodiversity'. 'Autism' is used to cover all of these terms in recent Department of Health, National Audit Office and Public Accounts Committee documents. In this guideline 'autism' refers to all of these.

problems such as anxiety, depression, problems with attention, self-injurious behaviour and other challenging, sometimes aggressive behaviour. Some or all of these features substantially impact on the quality of life of the individual and lead to a social vulnerability especially in the most able group.

c) The clinical picture of autism is variable because of differences in autistic severity, coexisting conditions and levels of ability, from profound intellectual disability to an uneven cognitive profile with superior skills in some areas.

d) Diagnostic criteria are described and defined in the World Health Organization ICD-10 and the Diagnostic and Statistical Manual DSM-IV. Both the major diagnostic classification systems (DSM-IV and ICD-10) use the term 'pervasive developmental disorder', which encompasses autism, Asperger's syndrome and atypical autism (or 'pervasive developmental disorder not otherwise specified'). For a diagnosis to be made, there must be the presence of impairments and an impact on the person's adaptive function. Both classification systems are undergoing revision and have announced that the term 'autism spectrum disorder' will be used. For this guideline we will use the term 'autism' to include all autism spectrum disorders.

e) Although autism was once thought to be an uncommon developmental disorder, recent studies have reported prevalence rates of at least 1% of the child population. Autism is diagnosed more frequently in boys. As with many developmental and behavioural disorders, the diagnostic criteria applied substantially affect estimates of prevalence.

f) The core autism behaviours are typically present in early childhood, although some features may not manifest until a change of situation, for example, the start of nursery or school or, less commonly, the transition to secondary school. Regression or stasis of language and social behaviour is reported for 20 to 30% of children with autism. This usually, but not exclusively, occurs between the ages of 1 and 2 years, and the reasons for regression and stasis are unknown.

g) The way in which autism is expressed will differ across different ages and thus for any person may change over time as they mature, in response to environmental demands, in response to interventions, and in the context of coexisting conditions.

h) Around 70% of people with autism also meet diagnostic criteria for at least one other (often unrecognised) psychiatric disorder that further impairs psychosocial functioning, for example, ADHD, anxiety disorders. Intellectual

disability (IQ below 70) co-occurs in approximately 50% of children and young people with autism.

3.2. Current practice

a) Currently, autism is usually diagnosed within community health services although initial recognition may be made by parents or carers, teachers, health visitors or other members of the primary health care team. Different regions and areas have different referral policies, although in general young children will be referred to paediatricians at a child development centre or directly to speech and language therapy services, and older children to paediatricians or child and adolescent mental health services (CAMHS).

b) There is currently no cure for autism. However, there is general agreement that early diagnosis followed by appropriate therapeutic intervention can improve outcomes in later life for most people.

c) The heterogeneity of autism means that it is often difficult to be sure who will benefit from the many available therapies. The timing of the intervention and the age of onset of autism is also likely to affect outcomes.

d) A variety of therapeutic interventions have been proposed to improve symptoms associated with autism, including early intensive behavioural intervention, social skills training, sensory integration therapy, facilitated communication, music therapy, acupuncture, vitamins, and dietary supplements.

e) In routine practice, specialist behavioural and educational interventions have become the predominant therapeutic approach for social, adaptive, and behavioural functions in children with autism.

f) Drugs have also been used as an adjunct to behavioural interventions because of their effect on coexisting conditions such as hyperactivity, aggression, obsessive-compulsive behaviours, sleep disturbance, mood disorder, poor attention or concentration, and self-injurious behaviour.

g) Many of the available therapies are invasive, time-consuming and costly, and there is a paucity of evidence about their efficacy or potential to do harm.

h) NICE and the National Collaborating Centre for Women's and Children's Health have developed a clinical guideline covering recognition, referral and diagnosis of children and young people with autism. This NICE-SCIE guideline will cover the second part of the care pathway. Together with the

one on recognition, referral and diagnosis, this will provide guidance to the NHS on the full range of care for children and young people with autism: case identification, assessment and diagnosis; management; and support for children and young people, their families and other carers.

4. THE GUIDELINE

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1. Population

4.1.1. Groups that will be covered

a) Children and young people (from birth until their 19th birthday) with autism (across the full range of intellectual ability) and their families and carers.

b) Consideration will be given to the particular management and support needs of:
- looked after children
- immigrant groups
- children with regression in skills

4.1.2. Groups that will not be covered.

a) Adults (19 years and older).

4.2. Setting

a) Primary, secondary and tertiary health and social care. This guideline will also be relevant to other health and social care settings (including forensic services and youth justice settings) although they are not explicitly covered.

b) The guideline will also address interventions relevant to early years services and educational setting

4.3. Management

4.3.1. Key issues that will be covered

a) Psychosocial interventions, including:
- behavioural therapies (for example, applied behavioural analysis, applied behaviour intervention)
- educational interventions, carer- and peer-delivered interventions
- arts-based therapies (for example, dramatherapy, art and music therapy)
- sensory interventions (for example, auditory integration therapy, sensory integration)
- interventions that address communication and social interaction.

b) Pharmacological interventions, including:
- anticonvulsants
- antidepressants
- antipsychotics
- stimulants
- hormones
- cognitive enhancers
- chelation therapy.

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

c) Physical interventions, including:
- acupuncture
- hyperbaric oxygen therapy
- exercise
- massage
- cranial osteopathy.

d) Nutritional interventions, including:
- diet
- vitamins
- supplements.

e) Modifications to the management of autism made necessary by the child or young person with autism having any of the following as a coexisting condition:

- mental and behaviour problems and disorders (including ADHD, anxiety disorders and phobias, mood disorders, oppositional defiant behaviour, tics or Tourette syndrome, OCD and self- injurious behaviour)
- neurodevelopmental problems and disorders (including global delay or intellectual disability, motor coordination problems or developmental coordination disorder, academic learning problems and speech and language disorder)
- medical or genetic problems and disorders (including epilepsy and epileptic encephalopathy, chromosome disorders, genetic abnormalities, tuberous sclerosis, muscular dystrophy and neurofibromatosis)
- functional problems and disorders (including feeding problems, urinary incontinence or enuresis, constipation, altered bowel habit, faecal incontinence or encopresis, sleep disturbances and vision or hearing impairment).

f) Anticipating, preventing and managing behaviour that challenges.

g) Alterations needed to routine and acute healthcare.

i) Information for children and young people, and their families (including siblings) and carers, throughout the care pathway.

i) Support needs of children and young people, their families and carers throughout the care pathway (for example, case management).

j) Interface with other services within healthcare and outside for the optimal organisation and delivery of care.

4.3.2. Clinical issues that will not be covered

a) Recognition, referral and diagnosis

b) Therapeutic intervention and management of the symptoms and behaviours associated with Rett syndrome

c) Management of coexisting conditions, unless these affect interventions, management or support for autism

4.4. Main outcomes

a) Quality of life.

b) Participation and functioning in social and educational settings.
c) Outcomes associated with core and non-core features of autism.

d) Effect on families including siblings.

e) Effective transition to adult services

f) Experience of care, including experience of services and transition.

4.5. Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), but a different unit of effectiveness may be used depending on the availability of appropriate clinical and utility data for children and young people with autism. Costs considered will be from an NHS and personal social services (PSS) perspective in the main analyses.

Further analyses may be conducted to consider wider social costs associated with the care of children and young people with autism. Such costs may include, for example, cost of special education and training, voluntary sector respite care, and housing services. Economic analyses will ideally attempt to consider long-term outcomes and related financial implications of interventions for the management and support of children and young people with autism through adulthood. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.6. Status

4.6.1. Scope

This is the final scope.

4.6.2. Timing

The development of the guideline recommendations will begin in December 2011.

5. RELATED NICE GUIDANCE

NICE is currently developing the following related guidance (details available from the NICE website:

- Autism: recognition, referral and diagnosis of children and young people on the autism spectrum. NICE clinical guideline 128. September 2011.

- Autism: recognition, referral, diagnosis and management of adults on the autism spectrum. NICE clinical guideline. Publication expected June 2012.

- Looked after children and young people. NICE public health guidance 28. October 2010.

6. FURTHER INFORMATION

Information on the guideline development process is provided in: 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'

- 'The guidelines manual'.

These are available from the NICE website (www.nice.org.uk/GuidelinesManual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk).

APPENDIX 2: DECLARATIONS OF INTERESTS BY GUIDELINE DEVELOPMENT GROUP MEMBERS

With a range of practical experience relevant to autism in children and young people in the GDG, members were appointed because of their understanding and expertise in healthcare for children and young people with autism and support for their families/carers, including: scientific issues; health research; the delivery and receipt of healthcare, along with the work of the healthcare industry; and the role of professional organisations and organisations for children and young people with autism and their families/carers.

To minimise and manage any potential conflicts of interest, and to avoid any public concern that commercial or other financial interests have affected the work of the GDG and influenced guidance, members of the GDG must declare as a matter of public record any interests held by themselves or their families which fall under specified categories (see below). These categories include any relationships they have with the healthcare industries, professional organisations and organisations for children and young people with autism and their families/carers.

Individuals invited to join the GDG were asked to declare their interests before being appointed. To allow the management of any potential conflicts of interest that might arise during the development of the guideline, GDG members were also asked to declare their interests at each GDG meeting throughout the guideline development process. The interests of all the members of the GDG are listed below, including interests declared prior to appointment and during the guideline development process.

Categories of interest to be written in third person

Paid employment

Personal pecuniary interest: financial payments or other benefits from either the manufacturer or the owner of the product or service under consideration in this guideline, or the industry or sector from which the product or service comes. This includes holding a directorship or other paid position; carrying out consultancy or fee paid work; having shareholdings or other beneficial interests; receiving expenses and hospitality over and above what would be reasonably expected to attend meetings and conferences.

Personal family interest: financial payments or other benefits from the healthcare industry that were received by a member of your family.

Non-personal pecuniary interest: financial payments or other benefits received by the GDG member's organisation or department, but where the GDG member has not

personally received payment, including fellowships and other support provided by the healthcare industry. This includes a grant or fellowship or other payment to sponsor a post, or contribute to the running costs of the department; commissioning of research or other work; contracts with, or grants from, NICE.

Personal non-pecuniary interest: these include, but are not limited to, clear opinions or public statements you have made about children and young people with autism, holding office in a professional organisation or advocacy group with a direct interest in autism in children and young people, other reputational risks relevant to autism in children and young people.

Guideline Development Group –declarations of interest	
Professor Gillian Baird	
Employment	Consultant Paediatrician and Professor of Paediatric Neurodisability, Guy's and St Thomas' NHS Foundation trust and King's Health partners, London
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	Chair of NICE children's & young people's autism guideline Member of DSM V working party Member of ICD 11 working party Author or co-author of several papers relevant to recognition, diagnosis, co-existing conditions and management of children and young people with autism Member of the Futures Forum for children and young people
Non-personal non-pecuniary interest	None
Action taken	None
Ms Virginia Bovell	
Employment	Service user and carer representative
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	Has chosen Applied Behaviour Analysis as an underpinning principle and / or approach in relation to son's learning and behaviour
Non-personal non-pecuniary interest	None
Action taken	None
Dr Carole Buckley	
Employment	General Practitioner, Bristol
Personal pecuniary interest	Executive director GP Care (UK) Ltd
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action taken	None

Professor Tony Charman	
Employment	Chair in Clinical Child Psychology, Institute of Psychiatry King's College London
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	The following grants involving autism interventions (past and present): *Innovative Medicines Initiative* "European Autism Interventions – A Multicentre Study for Developing New Medications (EU-AIMS)" Co-Investigator with Declan Murphy, Will Spooren (Principal Investigators) + 24 others €19 million (April 2012 – March 2017) The research of EU-AIMS receives support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n° 115300, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013), from the EFPIA companies' in kind contribution and from the Autism Speaks resulting in a total of €29.6 million. EFPIA companies: Roche, Eli Lilly, Servier, Janssen Pharmaceutica, Pfizer and Vifor Pharma *NIHR Health Technology Assessment* "MeASURe: Measurement in autism spectrum disorder" Co-Investigator with Helen McConachie (Principal Investigator) + 16 others £240,000 (April 2012 – March 2014) *Autism Education Trust (DfE funded)* "AET programme evaluation" Co-Investigator with Geoff Lindsay (Principal Investigator), Julie Dockrell, Mairi Ann Cullen, Steve Strand, Liz Pellicano £40,000 (October 2011 – March 2013) *Autistica* "Intervention within the British Autism Study of Infant Siblings (iBASIS)". Co-Investigator with Jonathan Green (Principal Investigator), Mark Johnson, Vicky Slonims, Andrew Pickles £279,776 (February 2011 – January 2013) *European Science Foundation (COST Action).* "Enhancing the scientific study of early autism (ESSEA): A network to improve research, services and outcomes" Principal Investigator. 48 Co-Investigators from 20 European countries €400,000 (January 2011 – December 2014)

	Department for Children Schools and Families "Speech, Language and Communication Needs (SLCN) Cost-Effectiveness Research Programme" Co-Investigator with Geoff Lindsay (Principal Investigator), Julie Dockrell, James Law, Sue Roulstone, Anna Vignoles, Jennifer Beecham, Steve Strand £1.2 million (September 2009 – March 2012) *Training and Development Agency* "The production of web-based training materials to enable teachers to gain advanced and specialist skills in relation to the most prevalent types of SEN" Co-Investigator with John Brown (Principal Investigator), Nick Peacey, Philippa Stobbs, Julie Dockrell, Jackie Masterson, Gill Brackenbury, Nicola Joffe, Brahm Norwich £221,120 (April 2011 – September 2011) *Autism Education Trust (DfE funded)* "Outcomes Research" Co-Investigator with Kerstin Wittemeyer (Principal Investigator). Other investigators: James Cusack, Karen Guldberg, Richard Hastings, Patricia Howlin, Natasha Macnab, Sarah Parson, Liz Pellicano, Vicky Slonims £80,000 (January 2011 – May 2011) *Autism Education Trust (DfE funded)* "What is Good Practice Research in Autism Education?" Principal Investigator. Co-Investigators: Liz Pellicano, Julie Dockrell £20,000 (January 2011 – May 2011) *Medical Research Council/Department of Health* "The Preschool Autism Communication Trial (PACT)" Co-Principal Investigator with Jonathan Green (Chief Investigator), Helen McConachie. Other Investigators: Catherine Aldred, Sarah Byford, Patricia Howlin, Ann Le Couteur, Wendy Macdonald, Andrew Pickles, Vicky Slonims £1,318,908 plus £647,129 subvented excessive treatment costs from the Department of Health (February 2006 – March 2010) *Autism Speaks (USA)* "Further development of the COSMIC as a measure of the generalisation of treatment efficacy in the PACT study" Principal Investigator $82,000 (January 2007 – December 2008)

	The Three Guineas Trust "The effectiveness of PECS communication training for non-verbal children with autism" Co-Principal Investigator with Patricia Howlin £124,164 (July 2002 – March 2006) *Cure Autism Now (USA)* "The Pre-school Social Communication Assessment Measure (PSCAM): Sensitivity to developmental change and early intervention effects" Principal Investigator. Co-Investigators: Gillian Baird, Simon Baron-Cohen $39,018 (May 2002 – December 2003) *Guy's & St Thomas' Charitable Foundation* "Follow-up evaluation of a social-communication parent-training intervention for pre-school children with autism" Co-Investigator with Gillian Baird (Principal Investigator), Samantha Peacock £28,096 (May 2002 – December 2003) *The Wellcome Trust* "An award towards meeting expenses for a study of early intervention programmes for preschool children with autism" Principal Investigator. Co-Investigator: Patricia Howlin £3,800 (November 2001)
Personal non-pecuniary interest	None
Action taken	None
Professor Nick Gould	
Employment	Emeritus Professor of Social Work, University of Bath
Personal pecuniary interest	Specialist member, Mental Health Tribunal Consultant, Social Care Institute for Excellence Adviser, Griffiths University, Brisbane, Australia Adviser, Chinese University of Hong Kong, Hong Kong Consultant, University of East London
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action taken	None
Professor Jonathan Green	
Employment	Professor of Child and Adolescent Psychiatry, King's College London Honorary consultant, Royal Manchester Children's Hospital
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	Member of the MeASURE study investigating measurement in autism
Personal non-pecuniary interest	None

Action taken	None
Professor Patricia Howlin	
Employment	Emeritus Professor of Clinical Child Psychology, Institute of Psychiatry, King's College, London
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	Chair of Scientific committee for Autistica Co- PI with Jonathan Green et al; MRC funded PACT follow up study (2012-2014)
Personal non-pecuniary interest	None
Action taken	None
Professor Ann Le Couteur	
Employment	Professor of Child and Adolescent Psychiatry, Newcastle University Honorary Child and Adolescent Consultant Psychiatrist, Northumberland Tyne & Wear NHS Foundation Trust
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	The following research projects include the evaluation of interventions for Children and Young People with autism. Either PI or one of series Co-applicant on all these grants: RfPB – Managing Repetitive Behaviours FSF – Managing Repetitive Behaviours extension BAT (Beating Anxiety Together) completed RfPB PACT2 follow up (Pre-School Autism Communication Trial) – MRC funded. DIADS – (Diagnostic Instruments for Autism in Deaf Children Study – MRC funded
Personal non-pecuniary interest	None
Action taken	None
Dr Robin Mackenzie	
Employment	Service user and carer representative
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action taken	None
Ms Barbara Parker	
Employment	Service user and carer representative
Personal pecuniary interest	Working with Dorset County Council and the following universities: Southampton Solent, Portsmouth, Winchester, Chichester & the Open University
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	Unpaid work with some voluntary agencies, none of them with a specific role in supporting ASC children or their families.
Action taken	None

Professor Emily Simonoff	
Employment	Academic Lead, Child and Adolescent Mental Health, Institute of Psychiatry
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action taken	None
Mr Stephen Simpson	
Employment	Community Learning Disability Nurse, South West Yorkshire Partnership NHS Foundation Trust
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action taken	None
Dr Vicky Slonims	
Employment	Clinical Lead Speech and Language Therapist, Guy's and St Thomas' NHS Foundation Trust Honorary Senior Lecturer, Kings College London
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	Co-principal investigator on the Intervention within the British Autism Study of Infant Siblings (i-BASIS) funded by Autistica with Lead Researcher Prof Jonathan Green in Manchester. Committee member of Scientific and Advisory Committee of Research Autism and also Strategic Research Group of the British Academy of Childhood Disability (part of RCPCH). An international trainer for the Autism Diagnostic Observation Schedule (Lord et al). Co- Principal Investigator - Pre-school autism intervention and autism development: a longitudinal follow up of the Preschool Autism Communication Trial (PACT) MRC funded – amount £840,251 co- investigators: Jonathan Green, Helen McConachie; Sarah Byford); Tony Charman; A S Le-Couteur; Patricia Howlin; Andrew Pickles, Kathy Leadbitter; Catherine Aldred
Personal non-pecuniary interest	None
Action taken	None
Action Taken	None
Ms Alison Stewart	
Employment	Manager, Speech and Language Therapy Service to Education Central London Community Healthcare Trust Honorary Lecturer City University
Personal pecuniary interest	None

Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action taken	None
Ms Katy Strudwick	
Employment	Clinical Specialist Paediatric Occupational Therapist, St Thomas' Hospital
Personal pecuniary interest	Work as part of a private multi-disciplinary Autism Assessment Team, diagnostics only, not intervention.
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action taken	None
Dr Gabriel Whitlingum	
Employment	Consultant Paediatrician, Hampshire Hospitals Foundation trust
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action taken	None
Dr Glenys Jones	
Employment	Lecturer in Autism, University of Birmingham
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action taken	None

NCCMH staff

Professor Tim Kendall	
Employment	Director, NCCMH Medical Director, Sheffield Health and Social Care Trust Consultant Adult Psychiatrist
Personal pecuniary interest	None.
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action taken	None
Dr Odette Megnin-Viggars	
Employment	Senior Systematic Reviewer, NCCMH
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Dr Ifigeneia Mavranezouli	
Employment	Health Economist, NCCMH
Personal pecuniary interest	None

Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Ms Sarah Stockton	
Employment	Senior Information Scientist, NCCMH
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Dr Clare Taylor	
Employment	Research Assistant, NCCMH
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Ms Katherine Leggett	
Employment	Project Manager, NCCMH
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Ms Sabrina Naqvi	
Employment	Project Manager, NCCMH
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Ms Lucy Burt	
Employment	Research Assistant, NCCMH
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None

APPENDIX 3: SPECIAL ADVISORS TO THE GUIDELINE DEVELOPMENT GROUP

None

APPENDIX 4: STAKEHOLDERS WHO RESPONDED TO EARLY REQUESTS FOR EVIDENCE

None

APPENDIX 5: STAKEHOLDERS AND EXPERTS WHO SUBMITTED COMMENTS IN RESPONSE TO THE CONSULTATION DRAFT OF THE GUIDELINE

Stakeholders

Experts

APPENDIX 6: RESEARCHERS CONTACTED TO REQUEST INFORMATION ABOUT UNPUBLISHED OR SOON-TO-BE PUBLISHED STUDIES

Chloe Allen
Michael Aman
Eugene Arnold
Prof. Laila AL-Ayadhi
Diane Chugani
Professor Elisabeth Dykens
Eli Lilly Holdings Limited (Chief Medical Officer)
Glen Elliott
Craig Erickson
Professor Daniel Glaze
Professor Robert Hendren
Dr. Bobbi Hopkins
Dr. Susan Hyman
Dr. Connie Kasari
Luc Lecavalier
Dr. Eric Lemonnier
Prof. Helen McConachie
Dr. Christopher McDougle
Rebecca McNally Keehn
Professor Gary Mesibov
National Institutes of Health information request
Dr. Sherie Novotny
Dr. Nalin Payakachat
Professor Deborah Pearson
Dr. David Posey
Dr. Jeanette Ramer
Dr. Jo-Ann Reitzel
Repligen Bioprocessing Corporation
Dr. Wendy Roberts
Dr. Daniel Rossignol
Professor Laura Schreibman
Gemma Spiers
Dr. Susan Swedo
Dr. Frank Symons
Dr. Robert Voigt
Dr. Ting Wang
Dr. Robert Weiner

Dr. Luci Wiggs
Dr. John Wray
Dr. Susan White
Dr. David Wilensky

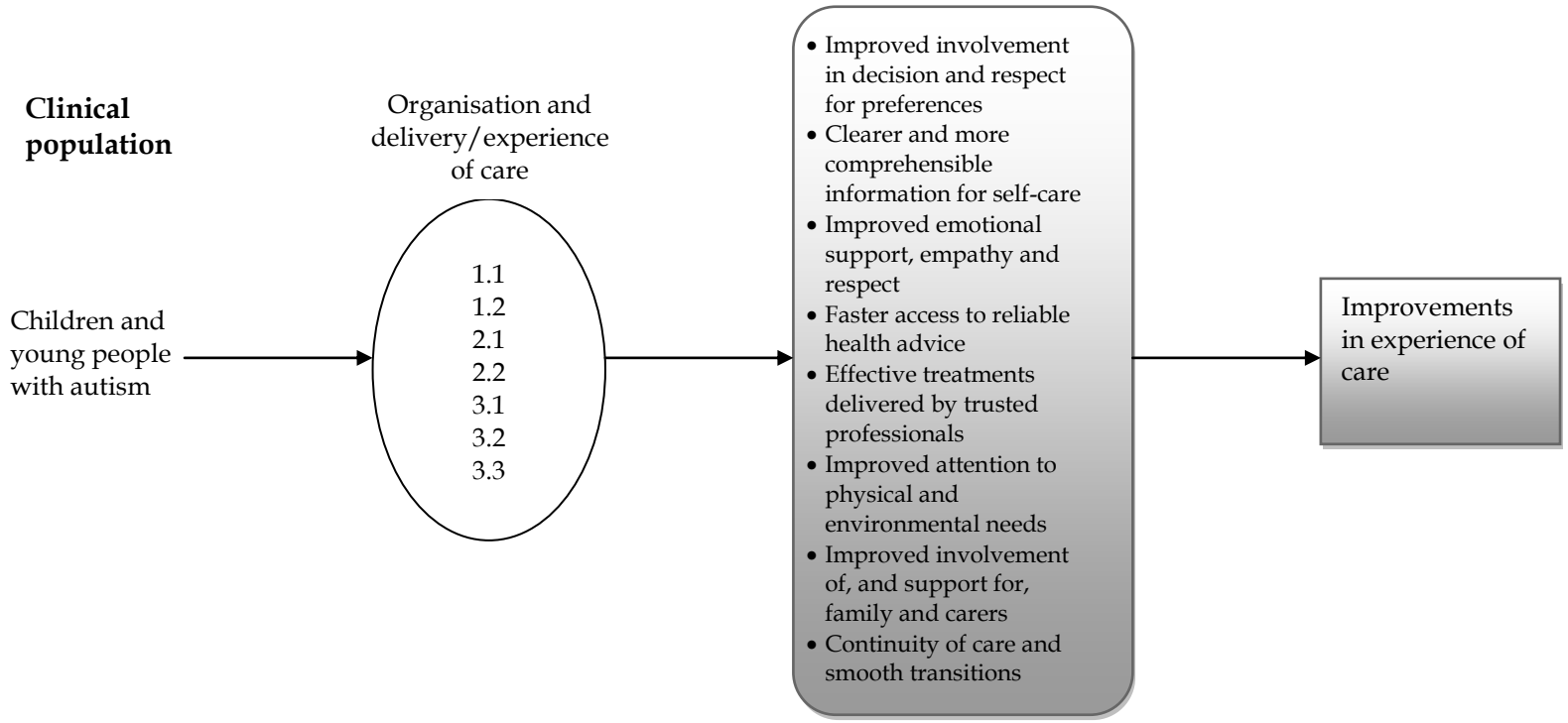
RESEARCHERS CONTACTED TO REQUEST FURTHER INFORMATION FROM PUBLISHED

Dr. James Adams (contacted three times regarding two studies)
Dr. Shahin Akhondzadeh (contacted twice regarding two studies)
Dr. Michael Aman (contacted three times regarding three studies)
Dr. Stephen Bent
Dr. Avril Brereton
Professor Agnes Chan
Dr. Michael Chez
Dr. Susan Coniglio
Dr. Geraldine Dawson (contacted twice regarding two studies)
Dr. Melissa DeRosier
Mila Amerine-Dickens
Dr. Dennis Dixon
Amy Drahota
Dr. Jennifer Dunn-Geier
Leonardo Fava
Dr. Tiffany Field (contacted twice regarding two studies)
Ellen Giarelli
Prof. Paul Gringas
Prof. Jonathan Green
Dr. Benjamin Handen
Dr. Jessica Hellings
Dr. Robert Hendren
Dr. Eric Hollander
Prof. Pat Howlin and Dr. Kate Gordon
Dr. Brooke Ingersoll
Dr. Betty Jarusiewicz
Dr. Connie Kasari
Dr. Janet Kern
Dr. Bryan King (contacted twice regarding two studies)
Dr. Rebecca Landa
Dr. Elizabeth Laugeson
Dr. Levy
Dr. Joan Luby

Dr. Sujeeva Munasinghe
Dr. Jeff Munson
Dr. Helmut Niederhofer
Dr. Iris Oosterling
Dr. Randall Owen
Dr. Gina Owens
Dr. Sally Ozonoff
Dr. Kingkaew Pajareya
Dr. Beth Pfeiffer
Dr. David Posey and Dr. Laudan Jahromi
Dr. Gary Remington
Dr. Anne Rickards
Dr. Wendy Roberts
Dr. Daniel Rossignol
Dr. Christian Ryan
Dr. Adrian Sandler
Dr. Sarah Shea
Prof. Louisa Silva
Dr. Miriam Silver
Dr. Pratibha Singhi
Dr. Kate Sofronoff (contacted twice regarding two studies)
Dr. James Tanaka and Dr. Robert Schultz
Dr. Christina Whalen
Dr. Paul Whiteley
Prof. Virginia Chun-Nei Wong (contacted twice regarding two studies)
Dr. Paul Yoder

APPENDIX 7: ANALYTIC FRAMEWORK AND REVIEW QUESTIONS

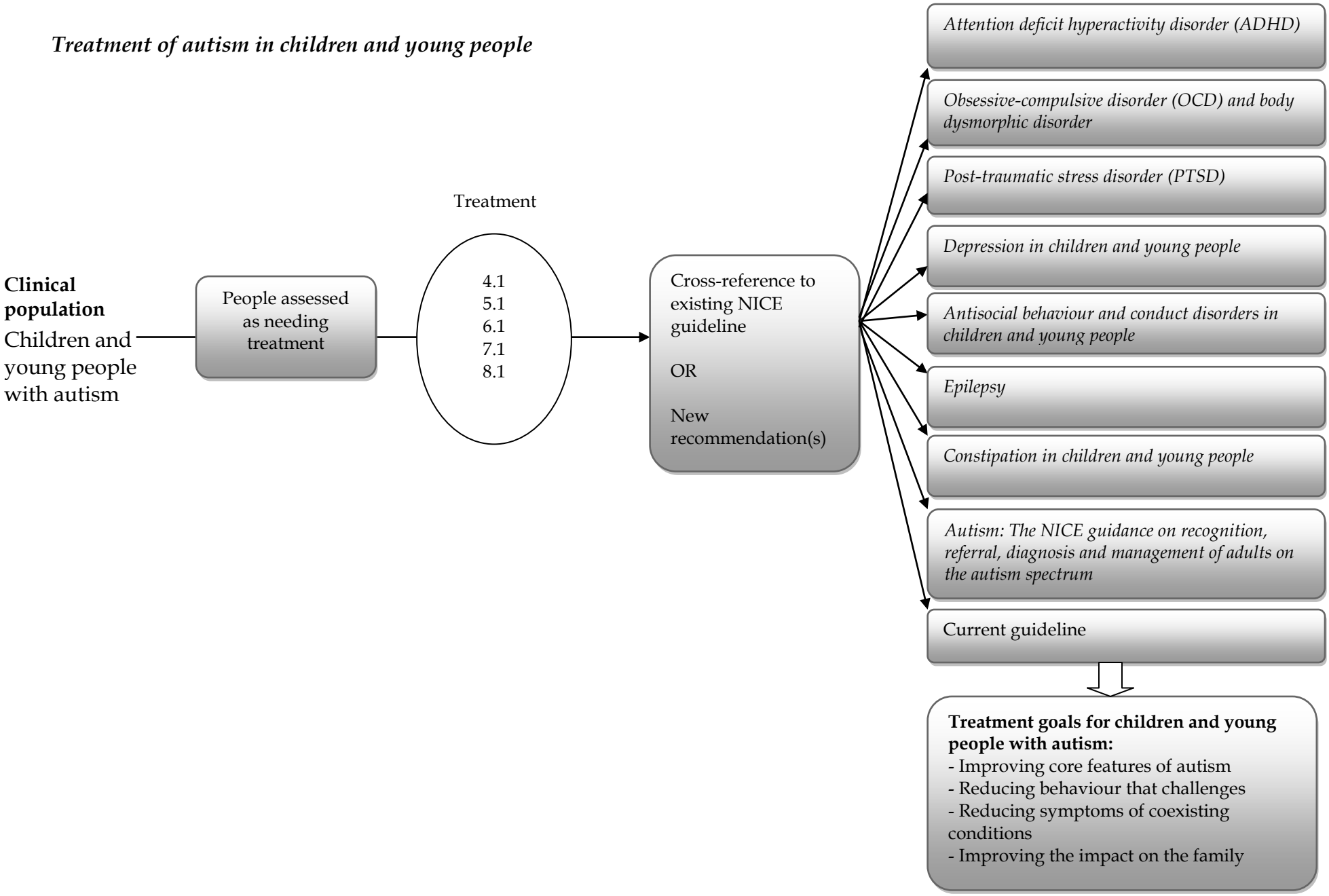
Care pathways/experience of care



Chapter 4: experience of care and the organisation and delivery of care

No.	Primary review questions
1.1	What services and treatments are effective in providing a positive experience of care for children and young people with autism and their families and carers?
1.2	What are the key problems associated with the experience of care for children and young people with autism and their families and carers?
1.3	For children and young people with autism, and their families and carers, what would help improve the experience of care?
2.1	What information and day-to-day support is effective in supporting children and young people with autism and their families and carers :- • in the post-diagnosis period (including genetic advice and advice about investigation for possible causes of autism including regression)? • when treatment and care is provided (including case coordination or case management)? • at intervention/management plan reviews? • during periods of crisis? • at key transitions (for example, school transitions and transition to adult services)?
2.2	What information and day-to-day support do children and young people with autism and their families and carers want:- • in the post-diagnosis period? • when treatment and care is provided? • at intervention/management plan reviews? • during periods of crisis? • at key transitions (for example, school transitions and transition to adult services)?
3.1	What are the essential elements that allow integration across services/agencies for the optimal organisation and delivery of care to children and young people with autism and their families and carers?
3.2	What are the essential elements that assist in the transition into adulthood services for young people with autism?
3.3	What are the effective ways of monitoring progress in children and young people with autism?
3.4	What alterations need to be made to routine and acute healthcare for children and young people with autism to ensure access for those with autism?

Treatment of autism in children and young people



Chapters 5-9: Core autism features, behaviour that challenges, common coexisting conditions, impact on the family and adverse events

No.	Primary review question
4.1	For children and young people with autism, what are the benefits of psychosocial, pharmacological or biomedical interventions for the core features of autism (overall autistic behaviours, impaired reciprocal social communication and interaction, and restricted interests and rigid and repetitive behaviours)* when compared with alternative management strategies? * Sub-group analyses will examine and compare treatment effects on core autism features when the interventions are specifically aimed at these features (direct outcomes) and when the primary target of the intervention was another outcome but effects on core autism features are examined (indirect outcomes)
5.1	For children and young people with autism, what are the benefits of psychosocial, pharmacological or biomedical interventions for anticipating, preventing or managing behaviour that challenges or poses a risk*, when compared with alternative management strategies? * Sub-group analyses will examine and compare treatment effects on behaviour that challenges when the interventions are specifically aimed at these behaviours (direct outcomes) and when the primary target of the intervention was another outcome but effects on behaviour that challenges are examined (indirect outcomes)
6.1	For children and young people with autism, what are the benefits of psychosocial, pharmacological or biomedical interventions for coexisting problems or disorders (including adaptive behaviour, speech and language problems, IQ and academic skills, sensory sensitivities, motor skills, common coexisting mental health problems and common functional problems)* when compared with alternative management strategies? * Sub-group analyses will examine and compare treatment effects on coexisting problems or disorders when the interventions are specifically aimed at these features (direct outcomes) and when the primary target of the intervention was another outcome but effects on coexisting problems or disorders are examined (indirect outcomes)
7.1	For children and young people with autism, what are the benefits of psychosocial, pharmacological or biomedical interventions for improving the impact on the family* when compared with alternative management strategies? * Sub-group analyses will examine and compare treatment effects on the impact for the family when the interventions are specifically aimed at improving the impact on the family (direct outcomes) and when the primary target of the intervention was another outcome but effects on the family are examined (indirect outcomes)
8.1	• For children and young people with autism, what are the potential harms associated with psychosocial, pharmacological or biomedical interventions?

APPENDIX 8: REVIEW PROTOCOLS

Experience of Care and the organisation and delivery of care

Topic	Description
Review question(s)	1.1 What services and treatments are effective in providing a positive experience of care for children and young people with autism and their families and carers? 1.2 What are the key problems associated with the experience of care for children and young people with autism and their families and carers? 1.3 For children and young people with autism, and their families and carers, what would help improve the experience of care? 2.1 What information and day-to-day support is effective in supporting children and young people with autism and their families and carers :- • in the post-diagnosis period (including genetic advice and advice about investigation for possible causes of autism including regression)? • when treatment and care is provided (including case coordination or case management)? • at intervention/management plan reviews? • during periods of crisis? • at key transitions (for example, school transitions and transition to adult services)? 2.2 What information and day-to-day support do children and young people with autism and their families and carers want:- • in the post-diagnosis period? • when treatment and care is provided? • at intervention/management plan reviews? • during periods of crisis? • at key transitions (for example, school transitions and transition to adult services)? 3.1 What are the essential elements that allow integration across services/agencies for the optimal organisation and delivery of care to children and young people with autism and their families and carers? 3.2 What are the essential elements that assist in the transition into adulthood services for young people with autism? 3.3 What are the effective ways of monitoring progress in children and young people with autism? 3.4 What alterations need to be made to routine and acute healthcare for children and young people with autism to ensure access for those with autism?
Sub-question(s)	For children and young people with autism, and their families and carers, is the experience of care and the organisation and delivery of care different for:- • looked after children?

	• immigrant groups? • children with regression in skills?
Chapter	Experience of Care and Organisation and Delivery of Care
Sub-section	
Topic Group	
Sub-section lead	
Objectives	To evaluate the experience of care, and the organisation and delivery of care for children and young people with autism and their families and carers.
Criteria for considering studies for the review	
• Population	Children and young people (from birth until their 19th birthday) with autism, (across the full range of intellectual ability) and their families and carers. If some, but not all, of a study's participants are eligible for our review, we will ask the study authors for disaggregated data. If we are unable to obtain the appropriate disaggregated data, then we will include a study if the majority (at least 51%) of its participants are eligible for our review. If we are unable to determine the exact percent of a study's participants who are eligible, then we will include the study if its participants are eligible on average (for example, the mean participant age is less than 19 years). Adults giving retrospective reports will also be included but results will be analysed separately. Consideration will be given to the particular management and support needs of: • looked after children • immigrant groups • children with regression in skills Excluded groups include: • adults (19 years and older).
• Intervention	The review will include: experience of care received by service users and carers; experience of access to care; experience of and/or views on care planning, delivery and/or management; service user experience reported indirectly (e.g. where service user has been facilitated/supported to provide feedback), however, this will be highlighted in analysis/reporting; experience of health, housing, education & social care services; experiences of living with autism where there are explicit implications for management, planning and/or delivery of care; experience of post-diagnosis information and support; and qualitative reports of perceived intervention effectiveness where a qualitative approach is the most appropriate methodology. This review will exclude: experiences of autism or of diagnosis with no explicit implications for management, planning and/or delivery of care; case studies; autobiographical accounts; and qualitative measures of perceived intervention effectiveness where a quantitative approach would have been more appropriate
• Comparator	Not applicable
• Critical outcomes	Service user and carer experience – emerging themes.

• Time points	Not applicable
• Study design	Systematic reviews of qualitative studies, primary qualitative studies, surveys and websites (such as healthtalkonline) Non-English language papers will be excluded, as will books, dissertation abstracts, trade magazines, policy and guidance, and non-empirical research.
• Include unpublished data?	Yes but only where: • the evidence was accompanied by a report containing sufficient detail to properly assess the quality of the data • the evidence was submitted with the understanding that data from the study and a summary of the study's characteristics will be published in the full guideline. Therefore, the GDG should not accept evidence submitted as commercial in confidence. However, the GDG should recognise that unpublished evidence submitted by investigators, might later be retracted by those investigators if the inclusion of such data would jeopardise publication of their research.
• Restriction by date?	Date of publication post-1992
• Minimum sample size	Not applicable
• Study setting	• Setting is in a country operating a developed service infrastructure. • Primary, secondary and tertiary health and social care. This guideline will also be relevant to other health and social care settings (including forensic services and youth justice settings) although they are not explicitly covered. • The guideline will also address interventions relevant to early years services and educational settings.
Search strategy	**Databases searched:** General medical databases: Embase, Medline, PreMedline, PsycINFO Topic specific databases: Australian Education Index (AEI), Applied Social Sciences Index and Abstracts (ASSIA), British Education Index (BEI), Cumulative Index to Nursing and Allied Health (CINAHL), Education Resources in Curriculum (ERIC), International Bibliography of the Social Sciences (IBSS), Sociological Abstracts, Social Service Abstracts (SSA), Social Science Citation Index (SSCI) Grey literature databases: Health Management Information Consortium (HMIC), PsycBOOKS, PsycEXTRA, Social Policy and Practice **Years searched:** 1995 to January 2013
Study design filter used	Qualitative systematic review, primary qualitative study, survey
Amendments to filter/ search strategy	None
Searching other resources	Hand-reference searching and citation searches of included studies, hand-searching of Research Autism and ISRCTN and ClinicalTrials.gov websites. Validation evidence will also be obtained from an expert advisory group of service users.
The review strategy	The review strategy will be a thematic analysis of primary qualitative studies, the

	results of which will be validated through the expert advisory group of service users

Interventions aimed at the core features of autism

Topic	Description
Review question(s)	4.1 For children and young people with autism, what are the benefits of psychosocial, pharmacological or biomedical interventions for the core features of autism (overall autistic behaviours, impaired reciprocal social communication and interaction, and restricted interests and rigid and repetitive behaviours)* when compared with alternative management strategies? • * Sub-group analyses will examine and compare treatment effects on core autism features when the interventions are specifically aimed at these features (direct outcomes) and when the primary target of the intervention was another outcome but effects on core autism features are examined (indirect outcomes)
Sub-question(s)	4.1.1 For children and young people with autism, and their families and carers, is the engagement with or effectiveness of interventions aimed at the core features of autism different for:- • looked after children? • immigrant groups? • children with regression in skills? 4.1.2 For children and young people with autism is the effectiveness of interventions aimed at the core features of autism moderated by:- • the nature and severity of the condition? • the presence of coexisting conditions (including, mental and behaviour, neurodevelopmental, medical or genetic, and functional, problems and disorders)? • age? • gender? • the presence of sensory differences? • IQ? • language level? • family/carer contextual factors (for example, socioeconomic status, parental education, parental mental health, sibling with special education needs)? 4.1.3 For children and young people with autism is the effectiveness of interventions aimed at the core features of autism mediated by:- • the intensity of the intervention? • the duration of the intervention? • the length of follow-up? • programme components?
Chapter	Interventions Aimed at the Core Features of Autism
Sub-section	
Topic Group	
Sub-section lead	

Objectives	To evaluate the clinical and cost effectiveness of interventions aimed at the core features of autism for children and young people with autism.
Criteria for considering studies for the review	
• Population	Children and young people (from birth until their 19th birthday) with autism, (across the full range of intellectual ability) and their families and carers. If some, but not all, of a study's participants are eligible for our review, we will ask the study authors for disaggregated data. If we are unable to obtain the appropriate disaggregated data, then we will include a study if the majority (at least 51%) of its participants are eligible for our review. If we are unable to determine the exact percent of a study's participants who are eligible, then we will include the study if its participants are eligible on average (for example, the mean participant age is less than 19 years). Consideration will be given to the particular management and support needs of: • looked after children • immigrant groups • children with regression in skills Excluded groups include: • adults (19 years and older).
• Intervention	Psychosocial, biomedical or pharmacological interventions which are aimed at improving the core features of autism as a direct or indirect outcome
• Comparator	No treatment or treatment-as-usual (includes placebo and waitlist control up until receiving intervention), other active interventions
• Critical outcomes	• **Overall autistic behaviours** (as measured by total scores on autistic behavior checklists or scales, including the Childhood Autism Rating Scale [CARS]) • **Impaired reciprocal social communication and interaction** (as measured by: diagnostic scales including the Autism Diagnostic Observation Schedule [ADOS/ADOS-G] Communication and Social Interaction domains; social skills scales including the Social Skills Rating Scale [SSRS]; joint attention and engagement as measured by behavioural observations) • **Restricted interests and rigid and repetitive behaviours** (as measured by: diagnostic scales including the Autism Diagnostic Observation Schedule [ADOS/ADOS-G] Repetitive Behavior domain; repetitive behavior scales; compulsions as measured by the Children's Yale Brown Obsessive Compulsive Scale [CYBOCS])
• Time points	Some studies may measure outcomes at multiple time points. We will run the following analyses: • Post-intervention (end of treatment) • Longest follow-up
• Study design	• RCTs • Systematic reviews Non-English language papers will be excluded, as will books, dissertation abstracts, trade magazines, policy and guidance, and non-empirical research.
• Include	Yes but only where:

unpublished data?	• the evidence was accompanied by a trial report containing sufficient detail to properly assess the quality of the data • the evidence was submitted with the understanding that data from the study and a summary of the study's characteristics will be published in the full guideline. Therefore, the GDG should not accept evidence submitted as commercial in confidence. However, the GDG should recognise that unpublished evidence submitted by investigators, might later be retracted by those investigators if the inclusion of such data would jeopardise publication of their research.
• Restriction by date?	No limit
• Minimum sample size	• N ≥ 10 per arm (ITT) Exclude studies with > 50% attrition from either arm of trial (unless adequate statistical methodology has been applied to account for missing data).
• Study setting	• Primary, secondary and tertiary health and social care. This guideline will also be relevant to other health and social care settings (including forensic services and youth justice settings) although they are not explicitly covered. • The guideline will also address interventions relevant to early years services and educational settings.
Search strategy	**Databases searched:** General medical databases: Embase, Medline, PreMedline, PsycINFO Topic specific databases: Australian Education Index (AEI), Applied Social Sciences Index and Abstracts (ASSIA), British Education Index (BEI), Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), Cumulative Index to Nursing and Allied Health (CINAHL), Database of Abstracts of Reviews of Effects (DARE), Education Resources in Curriculum (ERIC), Health Technology Assessment Database (HTA), International Bibliography of the Social Sciences (IBSS), Sociological Abstracts, Social Service Abstracts (SSA), Social Science Citation Index (SSCI) **Years searched:** Systematic review/grey literature: 1995 to January 2013 RCT: database inception to January 2013
Study design filter used	Quantitative systematic review, RCT
Amendments to filter/ search strategy	None
Searching other resources	Hand-reference searching and citation searches of included studies, hand-searching of Research Autism and ISRCTN and ClinicalTrials.gov websites
The review strategy	• The initial aim is to conduct a meta-analysis evaluating the clinical effectiveness of the interventions. However, in the absence of adequate data, the literature will be presented via a narrative synthesis of the available evidence. Consider subgroup meta-analyses that takes into account the effectiveness of interventions as moderated by:- • the nature and severity of the condition? • the presence of coexisting conditions (including, mental and behaviour,

	neurodevelopmental, medical or genetic, and functional, problems and disorders)? • age? • gender? • the presence of sensory differences? • IQ? • language level? • family/carer contextual factors (for example, socioeconomic status, parental education, parental mental health, sibling with special education needs)?

Interventions aimed at reducing behaviour that challenges

Topic	Description
Review question(s)	5.1 For children and young people with autism, what are the benefits of psychosocial, pharmacological or biomedical interventions for anticipating, preventing or managing behaviour that challenges or poses a risk*, when compared with alternative management strategies? • * Sub-group analyses will examine and compare treatment effects on behaviour that challenges when the interventions are specifically aimed at these behaviours (direct outcomes) and when the primary target of the intervention was another outcome but effects on behaviour that challenges are examined (indirect outcomes)
Sub-question(s)	5.1.1 For children and young people with autism, and their families and carers, is the engagement with or effectiveness of interventions aimed at reducing behaviour that challenges or poses a risk different for:- • looked after children? • immigrant groups? • children with regression in skills? 5.1.2 For children and young people with autism is the effectiveness of interventions aimed at reducing behaviour that challenges or poses a risk moderated by:- • the nature and severity of the condition? • the presence of coexisting conditions (including, mental and behaviour, neurodevelopmental, medical or genetic, and functional, problems and disorders)? • age? • gender? • the presence of sensory differences? • IQ? • language level? • family/carer contextual factors (for example, socioeconomic status, parental education, parental mental health, sibling with special education needs)? 5.1.3 For children and young people with autism is the effectiveness of interventions aimed at reducing behaviour that challenges or poses a risk

	mediated by:- • the intensity of the intervention? • the duration of the intervention? • the length of follow-up? • programme components?
Chapter	Interventions Aimed at Behaviour the Challenges
Sub-section	
Topic Group	
Sub-section lead	
Objectives	To evaluate the clinical and cost effectiveness of interventions aimed at reducing behaviour that challenges or poses a risk for children and young people with autism.
Criteria for considering studies for the review	
• Population	Children and young people (from birth until their 19th birthday) with autism, (across the full range of intellectual ability) and their families and carers. If some, but not all, of a study's participants are eligible for our review, we will ask the study authors for disaggregated data. If we are unable to obtain the appropriate disaggregated data, then we will include a study if the majority (at least 51%) of its participants are eligible for our review. If we are unable to determine the exact percent of a study's participants who are eligible, then we will include the study if its participants are eligible on average (for example, the mean participant age is less than 19 years). Consideration will be given to the particular management and support needs of: • looked after children • immigrant groups • children with regression in skills Excluded groups include: • adults (19 years and older).
• Intervention	Psychosocial, biomedical or pharmacological interventions which are aimed at reducing behaviour that challenges or poses a risk as a direct or indirect outcome
• Comparator	No treatment or treatment-as-usual (includes placebo and waitlist control up until receiving intervention), other active interventions
• Critical outcomes	• **Challenging behavior** (as measured by behavior checklists including the Aberrant Behavior Checklist [ABC]) • **Positive treatment response** (dichotomous measure of positive treatment response where adaptive or challenging behavior was the direct outcome) • **Global state-challenging behaviour** (as measured by the Clinical Global Impressions Scale [CGI] where challenging behavior was the direct outcome)
• Time points	Some studies may measure outcomes at multiple time points. We will run the following analyses: • Post-intervention (end of treatment) • Longest follow-up
• Study design	• RCTs • Systematic reviews Non-English language papers will be excluded, as will books, dissertation

	abstracts, trade magazines, policy and guidance, and non-empirical research.
• Include unpublished data?	Yes but only where: • the evidence was accompanied by a trial report containing sufficient detail to properly assess the quality of the data • the evidence was submitted with the understanding that data from the study and a summary of the study's characteristics will be published in the full guideline. Therefore, the GDG should not accept evidence submitted as commercial in confidence. However, the GDG should recognise that unpublished evidence submitted by investigators, might later be retracted by those investigators if the inclusion of such data would jeopardise publication of their research.
• Restriction by date?	No limit
• Minimum sample size	• N ≥ 10 per arm (ITT) Exclude studies with > 50% attrition from either arm of trial (unless adequate statistical methodology has been applied to account for missing data).
• Study setting	• Primary, secondary and tertiary health and social care. This guideline will also be relevant to other health and social care settings (including forensic services and youth justice settings) although they are not explicitly covered. • The guideline will also address interventions relevant to early years services and educational settings.
Search strategy	**Databases searched:** General medical databases: Embase, Medline, PreMedline, PsycINFO Topic specific databases: Australian Education Index (AEI), Applied Social Sciences Index and Abstracts (ASSIA), British Education Index (BEI), Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), Cumulative Index to Nursing and Allied Health (CINAHL), Database of Abstracts of Reviews of Effects (DARE), Education Resources in Curriculum (ERIC), Health Technology Assessment Database (HTA), International Bibliography of the Social Sciences (IBSS), Sociological Abstracts, Social Service Abstracts (SSA), Social Science Citation Index (SSCI) **Years searched:** Systematic review/grey literature: 1995 to January 2013 RCT: database inception to January 2013
Study design filter used	Quantitative systematic review, RCT
Amendments to filter/ search strategy	None
Searching other resources	Hand-reference searching and citation searches of included studies, hand-searching of Research Autism and ISRCTN and ClinicalTrials.gov websites
The review strategy	• The initial aim is to conduct a meta-analysis evaluating the clinical effectiveness of the interventions. However, in the absence of adequate data, the literature will be presented via a narrative synthesis of the available evidence. Consider subgroup meta-analyses that takes into account the effectiveness of interventions as moderated by:- • the nature and severity of the condition?

	• the presence of coexisting conditions (including, mental and behaviour, neurodevelopmental, medical or genetic, and functional, problems and disorders)? • age? • gender? • the presence of sensory differences? • IQ? • language level? • family/carer contextual factors (for example, socioeconomic status, parental education, parental mental health, sibling with special education needs)?

Interventions aimed at coexisting problems or disorders

Topic	Description
Review question(s)	6.1 For children and young people with autism, what are the benefits of psychosocial, pharmacological or biomedical interventions for coexisting problems or disorders (including adaptive behaviour, speech and language problems, IQ and academic skills, sensory sensitivities, motor skills, common coexisting mental health problems and common functional problems)* when compared with alternative management strategies? • * Sub-group analyses will examine and compare treatment effects on coexisting problems or disorders when the interventions are specifically aimed at these features (direct outcomes) and when the primary target of the intervention was another outcome but effects on coexisting problems or disorders are examined (indirect outcomes)
Sub-question(s)	6.1.1 For children and young people with autism, and their families and carers, is the engagement with or effectiveness of interventions aimed at coexisting problems or disorders different for:- • looked after children? • immigrant groups? • children with regression in skills? 6.1.2 For children and young people with autism is the effectiveness of interventions aimed at coexisting problems or disorders moderated by:- • the nature and severity of the condition? • the presence of coexisting conditions (including, mental and behaviour, neurodevelopmental, medical or genetic, and functional, problems and disorders)? • age? • gender? • the presence of sensory differences? • IQ? • language level? • family/carer contextual factors (for example, socioeconomic status, parental education, parental mental health, sibling with special education needs)?

	6.1.3 For children and young people with autism is the effectiveness of interventions aimed at coexisting problems or disorders mediated by:- • the intensity of the intervention? • the duration of the intervention? • the length of follow-up? • programme components?
Chapter	Interventions Aimed at Associated Features of Autism and Coexisting Conditions
Sub-section	
Topic Group	
Sub-section lead	
Objectives	To evaluate the clinical and cost effectiveness of interventions aimed at coexisting problems or disorders for children and young people with autism.
Criteria for considering studies for the review	
• Population	Children and young people (from birth until their 19th birthday) with autism, (across the full range of intellectual ability) and their families and carers. If some, but not all, of a study's participants are eligible for our review, we will ask the study authors for disaggregated data. If we are unable to obtain the appropriate disaggregated data, then we will include a study if the majority (at least 51%) of its participants are eligible for our review. If we are unable to determine the exact percent of a study's participants who are eligible, then we will include the study if its participants are eligible on average (for example, the mean participant age is less than 19 years). Consideration will be given to the particular management and support needs of: • looked after children • immigrant groups • children with regression in skills Excluded groups include: • adults (19 years and older).
• Intervention	Psychosocial, biomedical or pharmacological interventions which are aimed at coexisting problems or disorders as a direct or indirect outcome
• Comparator	No treatment or treatment-as-usual (includes placebo and waitlist control up until receiving intervention), other active interventions
• Critical outcomes	• **Adaptive behavior** (as measured by behavior checklists including the Vineland Adaptive Behavior Scales [VABS]) • **Speech and language** (receptive and expressive language as measured by rating scales including the Reynell Developmental Language Scales, the Preschool Language Scales-3 [PLS-3], the Mullen Scales of Early Learning [MSEL]; the MacArthur Communication Developmental Inventories [CDI]) • **IQ** (as measured by the MSEL early learning composite score) • **Academic skills** • **Sensory sensitivities** • **Fine and gross motor skills** (as measured by motor subscales of the Vineland Adaptive Behavior Scales [VABS] and theMSEL) • **Anxiety**

	• **Hyperactivity/ADHD symptoms** • **Sleep problems** • **Gastrointestinal or eating problems**
• Time points	Some studies may measure outcomes at multiple time points. We will run the following analyses: • Post-intervention (end of treatment) • Longest follow-up
• Study design	• RCTs • Systematic reviews Non-English language papers will be excluded, as will books, dissertation abstracts, trade magazines, policy and guidance, and non-empirical research.
• Include unpublished data?	Yes but only where: • the evidence was accompanied by a trial report containing sufficient detail to properly assess the quality of the data • the evidence was submitted with the understanding that data from the study and a summary of the study's characteristics will be published in the full guideline. Therefore, the GDG should not accept evidence submitted as commercial in confidence. However, the GDG should recognise that unpublished evidence submitted by investigators, might later be retracted by those investigators if the inclusion of such data would jeopardise publication of their research.
• Restriction by date?	No limit
• Minimum sample size	• N ≥ 10 per arm (ITT) Exclude studies with > 50% attrition from either arm of trial (unless adequate statistical methodology has been applied to account for missing data).
• Study setting	• Primary, secondary and tertiary health and social care. This guideline will also be relevant to other health and social care settings (including forensic services and youth justice settings) although they are not explicitly covered. • The guideline will also address interventions relevant to early years services and educational settings.
Search strategy	**Databases searched:** General medical databases: Embase, Medline, PreMedline, PsycINFO Topic specific databases: Australian Education Index (AEI), Applied Social Sciences Index and Abstracts (ASSIA), British Education Index (BEI), Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), Cumulative Index to Nursing and Allied Health (CINAHL), Database of Abstracts of Reviews of Effects (DARE), Education Resources in Curriculum (ERIC), Health Technology Assessment Database (HTA), International Bibliography of the Social Sciences (IBSS), Sociological Abstracts, Social Service Abstracts (SSA), Social Science Citation Index (SSCI) **Years searched:** Systematic review/grey literature: 1995 to January 2013 RCT: database inception to January 2013
Study design filter used	Quantitative systematic review, RCT

Amendments to filter/ search strategy	None
Searching other resources	Hand-reference searching and citation searches of included studies, hand-searching of Research Autism and ISRCTN and ClinicalTrials.gov websites
The review strategy	• The initial aim is to conduct a meta-analysis evaluating the clinical effectiveness of the interventions. However, in the absence of adequate data, the literature will be presented via a narrative synthesis of the available evidence. Consider subgroup meta-analyses that takes into account the effectiveness of interventions as moderated by:- • the nature and severity of the condition? • the presence of coexisting conditions (including, mental and behaviour, neurodevelopmental, medical or genetic, and functional, problems and disorders)? • age? • gender? • the presence of sensory differences? • IQ? • language level? • family/carer contextual factors (for example, socioeconomic status, parental education, parental mental health, sibling with special education needs)?

Interventions aimed at improving the impact on the family

Topic	Description
Review question(s)	7.1 For children and young people with autism, what are the benefits of psychosocial, pharmacological or biomedical interventions for improving the impact on the family* when compared with alternative management strategies? • * Sub-group analyses will examine and compare treatment effects on the impact for the family when the interventions are specifically aimed at improving the impact on the family (direct outcomes) and when the primary target of the intervention was another outcome but effects on the family are examined (indirect outcomes)
Sub-question(s)	7.1.1 For children and young people with autism, and their families and carers, is the engagement with or effectiveness of interventions aimed at improving the impact on the family different for:- • looked after children? • immigrant groups? • children with regression in skills? 7.1.2 For children and young people with autism is the effectiveness of interventions aimed at improving the impact on the family moderated by:- • the nature and severity of the condition? • the presence of coexisting conditions (including, mental and behaviour,

	neurodevelopmental, medical or genetic, and functional, problems and disorders)? • age? • gender? • the presence of sensory differences? • IQ? • language level? • family/carer contextual factors (for example, socioeconomic status, parental education, parental mental health, sibling with special education needs)? 7.1.3 For children and young people with autism is the effectiveness of interventions aimed at improving the impact on the family mediated by:- • the intensity of the intervention? • the duration of the intervention? • the length of follow-up? • programme components?
Chapter	Interventions Aimed at Improving the Impact on the Family
Sub-section	
Topic Group	
Sub-section lead	
Objectives	To evaluate the clinical and cost effectiveness of interventions aimed at improving the impact on the family for children and young people with autism.
Criteria for considering studies for the review	
• Population	Children and young people (from birth until their 19th birthday) with autism, (across the full range of intellectual ability) and their families and carers. If some, but not all, of a study's participants are eligible for our review, we will ask the study authors for disaggregated data. If we are unable to obtain the appropriate disaggregated data, then we will include a study if the majority (at least 51%) of its participants are eligible for our review. If we are unable to determine the exact percent of a study's participants who are eligible, then we will include the study if its participants are eligible on average (for example, the mean participant age is less than 19 years). Consideration will be given to the particular management and support needs of: • looked after children • immigrant groups • children with regression in skills Excluded groups include: • adults (19 years and older).
• Intervention	Psychosocial, biomedical or pharmacological interventions which are aimed at improving the impact of autism on the family as a direct or indirect outcome
• Comparator	No treatment or treatment-as-usual (includes placebo and waitlist control up until receiving intervention), other active interventions
• Critical outcomes	• **Parental mental health** • **Parental stress**

• Time points	Some studies may measure outcomes at multiple time points. We will run the following analyses: • Post-intervention (end of treatment) • Longest follow-up
• Study design	• RCTs • Systematic reviews Non-English language papers will be excluded, as will books, dissertation abstracts, trade magazines, policy and guidance, and non-empirical research.
• Include unpublished data?	Yes but only where: • the evidence was accompanied by a trial report containing sufficient detail to properly assess the quality of the data • the evidence was submitted with the understanding that data from the study and a summary of the study's characteristics will be published in the full guideline. Therefore, the GDG should not accept evidence submitted as commercial in confidence. However, the GDG should recognise that unpublished evidence submitted by investigators, might later be retracted by those investigators if the inclusion of such data would jeopardise publication of their research.
• Restriction by date?	No limit
• Minimum sample size	• N ≥ 10 per arm (ITT) Exclude studies with > 50% attrition from either arm of trial (unless adequate statistical methodology has been applied to account for missing data).
• Study setting	• Primary, secondary and tertiary health and social care. This guideline will also be relevant to other health and social care settings (including forensic services and youth justice settings) although they are not explicitly covered. • The guideline will also address interventions relevant to early years services and educational settings.
Search strategy	**Databases searched:** General medical databases: Embase, Medline, PreMedline, PsycINFO Topic specific databases: Australian Education Index (AEI), Applied Social Sciences Index and Abstracts (ASSIA), British Education Index (BEI), Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), Cumulative Index to Nursing and Allied Health (CINAHL), Database of Abstracts of Reviews of Effects (DARE), Education Resources in Curriculum (ERIC), Health Technology Assessment Database (HTA), International Bibliography of the Social Sciences (IBSS), Sociological Abstracts, Social Service Abstracts (SSA), Social Science Citation Index (SSCI) **Years searched:** Systematic review/grey literature: 1995 to January 2013 RCT: database inception to January 2013
Study design filter used	Quantitative systematic review, RCT
Amendments to filter/ search strategy	None
Searching other resources	Hand-reference searching and citation searches of included studies, hand-searching of Research Autism and ISRCTN and ClinicalTrials.gov websites

The review strategy	• The initial aim is to conduct a meta-analysis evaluating the clinical effectiveness of the interventions. However, in the absence of adequate data, the literature will be presented via a narrative synthesis of the available evidence. Consider subgroup meta-analyses that takes into account the effectiveness of interventions as moderated by:- • the nature and severity of the condition? • the presence of coexisting conditions (including, mental and behaviour, neurodevelopmental, medical or genetic, and functional, problems and disorders)? • age? • gender? • the presence of sensory differences? • IQ? • language level? • family/carer contextual factors (for example, socioeconomic status, parental education, parental mental health, sibling with special education needs)?

Adverse events associated with interventions

Topic	**Description**
Review question(s)	9.1 For children and young people with autism, what are the potential harms associated with psychosocial, pharmacological or biomedical interventions?
Sub-question(s)	
Chapter	Adverse Events Associated with Interventions
Sub-section	
Topic Group	
Sub-section lead	
Objectives	To evaluate the potential harms associated with psychosocial, pharmacological and biomedical interventions for children and young people with autism.
Criteria for considering studies for the review	
• Population	Children and young people (from birth until their 19th birthday) with autism, (across the full range of intellectual ability) and their families and carers. If some, but not all, of a study's participants are eligible for our review, we will ask the study authors for disaggregated data. If we are unable to obtain the appropriate disaggregated data, then we will include a study if the majority (at least 51%) of its participants are eligible for our review. If we are unable to determine the exact percent of a study's participants who are eligible, then we will include the study if its participants are eligible on average (for example, the mean participant age is less than 19 years). Consideration will be given to the particular management and support needs of: • looked after children • immigrant groups

	• children with regression in skills Excluded groups include: • adults (19 years and older).
• Intervention	Any psychosocial, pharmacological or biomedical intervention for children and young people with autism
• Comparator	No treatment or treatment-as-usual (includes placebo and waitlist control up until receiving intervention), other active interventions
• Critical outcomes	• **Any adverse event** (dichotomous measure of number of participants expericing any adverse event during the treatment period) • **Discontinuation due to adverse events** • **Weight gain** • **Prolactin concentration** • **Extrapyramidal symptoms** • **Metabolic measures** • **Blood pressure**
• Time points	Some studies may measure outcomes at multiple time points. We will run the following analyses: • Post-intervention (end of treatment) • Longest follow-up
• Study design	• RCTs • Systematic reviews Non-English language papers will be excluded, as will books, dissertation abstracts, trade magazines, policy and guidance, and non-empirical research.
• Include unpublished data?	Yes but only where: • the evidence was accompanied by a trial report containing sufficient detail to properly assess the quality of the data • the evidence was submitted with the understanding that data from the study and a summary of the study's characteristics will be published in the full guideline. Therefore, the GDG should not accept evidence submitted as commercial in confidence. However, the GDG should recognise that unpublished evidence submitted by investigators, might later be retracted by those investigators if the inclusion of such data would jeopardise publication of their research.
• Restriction by date?	No limit
• Minimum sample size	• N ≥ 10 per arm (ITT) Exclude studies with > 50% attrition from either arm of trial (unless adequate statistical methodology has been applied to account for missing data).
• Study setting	• Primary, secondary and tertiary health and social care. This guideline will also be relevant to other health and social care settings (including forensic services and youth justice settings) although they are not explicitly covered. • The guideline will also address interventions relevant to early years services and educational settings.
Search strategy	**Databases searched:** General medical databases: Embase, Medline, PreMedline, PsycINFO Topic specific databases: Australian Education Index (AEI), Applied Social Sciences Index and Abstracts (ASSIA), British Education Index (BEI), Cochrane

	Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), Cumulative Index to Nursing and Allied Health (CINAHL), Database of Abstracts of Reviews of Effects (DARE), Education Resources in Curriculum (ERIC), Health Technology Assessment Database (HTA), International Bibliography of the Social Sciences (IBSS), Sociological Abstracts, Social Service Abstracts (SSA), Social Science Citation Index (SSCI) **Years searched:** Systematic review/grey literature: 1995 to January 2013 RCT: database inception to January 2013
Study design filter used	Quantitative systematic review, RCT
Amendments to filter/ search strategy	None
Searching other resources	Hand-reference searching and citation searches of included studies, hand-searching of Research Autism and ISRCTN and ClinicalTrials.gov websites
The review strategy	• The initial aim is to conduct a meta-analysis evaluating the clinical effectiveness of the interventions. However, in the absence of adequate data, the literature will be presented via a narrative synthesis of the available evidence. Consider subgroup meta-analyses that takes into account the effectiveness of interventions as moderated by:- • the nature and severity of the condition? • the presence of coexisting conditions (including, mental and behaviour, neurodevelopmental, medical or genetic, and functional, problems and disorders)? • age? • gender? • the presence of sensory differences? • IQ? • language level? • family/carer contextual factors (for example, socioeconomic status, parental education, parental mental health, sibling with special education needs)?

APPENDIX 9: SEARCH STRATEGIES FOR THE IDENTIFICATION OF CLINICAL STUDIES

Each search was constructed using the groups of terms set out in Text Box 1. The full set of search terms is documented in sections 1 to 3.24. The selection of search terms was kept broad to maximise retrieval of evidence in a wide range of areas of interest to the GDG.

Text Box 1: Summary of systematic search strategies: Search strategy construction

Summary of systematic search strategies for clinical evidence					
Section 1					
Review area/s	**Search type**	**Search construction**	**Study design searched**	**Databases searched**	**Date range searched**
Review questions: 4.1,5.1,6.1,7.1, 9.1 (also includes sub questions)	Generic, evidence mapped to all review areas	General medical /topic specific databases – generic search: [(population terms) AND (systematic review/RCT study design filter)] Grey literature databases – generic search: (population search terms only)	Quantitative systematic review, RCT	General medical databases: Embase, Medline, PreMedline, PsycINFO Topic specific databases: AEI*, ASSIA*, BEI*, CDSR*, CENTRAL*, CINAHL*, DARE*, ERIC*, HTA*, IBSS*, Sociological Abstracts, SSA*, SSCI* Grey literature databases: HMIC*, PsycEXTRA, Social Policy and Practice	SR: 1995 to January 2013 RCT: database inception to January 2013
Notes: ***Evidence resulting from generic searches mapped to all review areas***					

Section 2					
Review area/s	**Search type**	**Search construction**	**Study design searched**	**Databases searched**	**Date range searched**
Experience of care and the organisation and delivery of care, RQ 1.1-1.3,2.1-2.2,3.1-3.4 (also includes sub questions)	Focused search, supplements evidence retrieved from evidence retrieved from searches detailed in Section 1	General medical databases: [(population terms) AND (qualitative systematic review terms OR qualitative study terms OR ((service user experience, sensitive terms) AND survey terms) OR service user experience, specific terms)] Topic specific databases: [(population terms) and (qualitative systematic review filter)]	General medical databases: qualitative systematic reviews, qualitative primary studies, surveys Topic specific databases: qualitative systematic reviews	General medical databases: Embase, Medline, PreMedline, PsycINFO Topic specific databases: AEI*, ASSIA*, BEI*, CINAHL, ERIC*, IBSS*, Sociological Abstracts, SSA*, SSCI*	1995 to January 2013
Notes: Supplements evidence captured by searches set out in Section 1					
* AEI (Australian Education Index), ASSIA (Applied Social Services Index and Abstracts), BEI (British Education Index), CDSR (Cochrane Database of Systematic Reviews), CENTRAL [COCHRANE database of RCTs and other controlled trials), CINAHL, (Cumulative Index to Nursing and Allied Health Literature), DARE (Database of Abstracts of Reviews and Effectiveness), ERIC (Education Resources in Curriculum), HMIC (Health Management Information Consortium), HTA (Health Technology Assessment database), IBSS (International Bibliography of Social Science), SSA (Social Services Abstracts), SSCI (Social Sciencies Citation Index – Web of Science)					

1 Population search terms – all databases

1.1 STEM – General medical databases
Embase, Medline, PreMEDLINE, PsycINFO – OVID SP

1	autism/ or asperger syndrome/ or childhood disintegrative disorder/ or "pervasive developmental disorder not otherwise specified"/
2	1 use emez
3	child development disorders, pervasive/ or asperger syndrome/ or autistic disorder/
4	3 use mesz, prem
5	aspergers syndrome/ or autism/ or autistic thinking/ or pervasive developmental disorders/
6	5 use psyh
7	asperger$.ti,ab.
8	autis$.ti,ab.
9	childhood schizophrenia.ti,ab.
10	((communicat$ or speech) adj3 disorder$).ti,ab.
11	(heller$ or (disintegrative adj2 (disorder$ or psychos$))).ti,ab.
12	kanner$.ti,ab.
13	(language adj3 delay$).ti,ab.
14	(((left or right) adj2 hemispher$ adj3 (damag$ or deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$)) or hemisphere functioning).ti,ab.
15	(neurodiverse$ or neurodiversit$).ti,ab.
16	((nonverbal or non verbal) adj2 learning adj2 (deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$)).ti,ab.
17	pathological demand avoidance.ti,ab.
18	((pervasive$ adj2 (development$ or neurodevelopment$)) or pdd nos or pddnos).ti,ab.
19	((pragmatic language or semantic pragmatic) adj3 (deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$)).ti,ab.
20	or/2,4,6-19

1.2 STEM - topic specific databases
HTA, CDSR, DARE, CENTRAL – Wiley

id	search
#1	mesh descriptor **child development disorders, pervasive** explode all trees
#2	(asperger*):ti or (asperger*):ab
#3	(autis*):ti or (autis*):ab
#4	"childhood schizophrenia":ti or "childhood schizophrenia":ab
#5	((communicat* or speech) near/3 disorder*):ti or ((communicat* or speech) near/3 disorder*):ab
#6	(heller* or (disintegrative near/2 (disorder* or psychos*))):ti or (heller* or (disintegrative near/2 (disorder* or psychos*))):ab
#7	(kanner*):ti or (kanner*):ab
#8	(language near/3 delay*):ti or (language near/3 delay*):ab
#9	((left or right) near/2 hemispher* near/3 (damag* or deficit* or disabilit* or disorder* or impair* or dysfunction*)) or "hemisphere functioning":ti or ((left or right) near/2 hemispher* near/3 (damag* or deficit* or disabilit* or disorder* or impair* or dysfunction*)) or "hemisphere functioning":ab
#10	(neurodiverse* or neurodiversit*):ti or (neurodiverse* or neurodiversit*):ab
#11	((nonverbal or non verbal) near/2 learning near/2 (deficit* or disabilit* or disorder* or impair* or dysfunction*)):ti or ((nonverbal or non verbal) near/2 learning near/2 (deficit* or disabilit* or disorder* or impair* or dysfunction*)):ab
#12	"pathological demand avoidance":ti or "pathological demand avoidance":ab
#13	((pervasive* near/2 (development* or neurodevelopment*)) or "pdd nos" or pddnos):ti or ((pervasive* near/2 (development* or neurodevelopment*)) or "pdd nos" or pddnos):ab
#14	(("pragmatic language" or "semantic pragmatic") near/3 (deficit* or disabilit* or disorder* or impair* or dysfunction*)):ti or (("pragmatic language" or "semantic pragmatic") near/3 (deficit* or disabilit* or disorder* or impair* or dysfunction*)):ab
#15	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or

#14)

1.3 STEM - topic specific databases
Applied Social Sciences Index and Abstracts (ASSIA), Australian Education Index (AEI), British Education Index (BEI), Education Resources in Curriculum (ERIC), Social Services Abstracts (SSA), Sociological Abstracts, Applied Social Sciences Index and Abstracts (ASSIA), International Bibliography of Social Sciences (IBSS) - ProQUEST

s1	all(asperger* or autis* or "childhood schizophrenia" or ((communicat* or speech) near/3 disorder*) or heller* or (disintegrative near/2 (disorder* or psychos*)) or kanner* or (language near/3 delay*) or ((left or right) near/2 hemispher* near/3 (damag* or deficit* or disabilit* or disorder* or impair* or dysfunction*)) or "hemisphere functioning" or neurodiverse* or neurodiversit* or ((nonverbal or non verbal) and learning and (deficit* or disabilit* or disorder* or impair* or dysfunction*)) or "pathological demand avoidance" or (pervasive* near/2 (development* or neurodevelopment*)) or "pdd nos" or pddnos or (("pragmatic language" or "semantic pragmatic") near/3 (deficit* or disabilit* or disorder* or impair* or dysfunction*)))

1.4 STEM- topic specific databases
CINAHL – Ebsco

s15	s1 or s2 or s3 or s4 or s5 or s6 or s7 or s8 or s9 or s10 or s11 or s12 or s13 or s14
s14	ti ((("pragmatic language" or "semantic pragmatic") n3 (deficit* or disabilit* or disorder* or impair* or dysfunction*))) or ab ((("pragmatic language" or "semantic pragmatic") n3 (deficit* or disabilit* or disorder* or impair* or dysfunction*)))
s13	ti (((pervasive* n2 (development* or neurodevelopment*)) or "pdd nos" or pddnos)) or ab (((pervasive* n2 (development* or neurodevelopment*)) or "pdd nos" or pddnos))
s12	ti "pathological demand avoidance" or ab "pathological demand avoidance"
s11	ti (((nonverbal or "non verbal") n2 learning n2 (deficit* or disabilit* or disorder* or impair* or dysfunction*))) or ab (((nonverbal or "non verbal") n2 learning n2 (deficit* or disabilit* or disorder* or impair* or dysfunction*)))
s10	ti ((neurodiverse* or neurodiversit*)) or ab ((neurodiverse* or neurodiversit*))
s9	ti ((((left or right) n2 hemispher* n3 (damag* or deficit* or disabilit* or disorder* or impair* or dysfunction*)) or "hemisphere functioning")) or ab ((((left or right) n2 hemispher* n3 (damag* or deficit* or disabilit* or disorder* or impair* or

	dysfunction*)) or “hemisphere functioning”))
s8	ti (language n3 delay*) or ab (language n3 delay*)
s7	ti kanner* or ab kanner*
s6	ti ((heller* or (disintegrative n2 (disorder* or psychos*)))) or ab ((heller* or (disintegrative n2 (disorder* or psychos*))))
s5	ti (((communicat* or speech) n3 disorder*)) or ab (((communicat* or speech) n3 disorder*))
s4	ti “childhood schizophrenia” or ab “childhood schizophrenia”
s3	ti autis* or ab autis*
s2	ti asperger* or ab asperger*
s1	(mh "child development disorders, pervasive" explode all trees)

1.5 STEM - topic specific databases
Social Sciences Citation Index - WoK

title=(asperger* or autis* or “childhood schizophrenia” or “communicat* disorder*”
1 or “speech disorder*” or heller* or (disintegrative near (disorder* or psychos*)) or kanner* or “language delay*” or ((left or right) near hemispher* near (damag* or deficit* or disabilit* or disorder* or impair* or dysfunction*)) or “hemisphere functioning” or neurodiverse* or neurodiversit* or ((nonverbal or “non verbal”) near learning near (deficit* or disabilit* or disorder* or impair* or dysfunction*)) or “pathological demand avoidance” or (pervasive* near (development* or neurodevelopment*)) or “pdd nos” or pddnos or ((“pragmatic language” or “semantic pragmatic”) near (deficit* or disabilit* or disorder* or impair* or dysfunction*))) or topic=(asperger* or autis* or “childhood schizophrenia” or “communicat* disorder*” or “speech disorder*” or heller* or (disintegrative near (disorder* or psychos*)) or kanner* or “language delay*” or ((left or right) near hemispher* near (damag* or deficit* or disabilit* or disorder* or impair* or dysfunction*)) or “hemisphere functioning” or neurodiverse* or neurodiversit* or ((nonverbal or “non verbal”) near learning near (deficit* or disabilit* or disorder* or impair* or dysfunction*)) or “pathological demand avoidance” or (pervasive* near (development* or neurodevelopment*)) or “pdd nos” or pddnos or ((“pragmatic language” or “semantic pragmatic”) near (deficit* or disabilit* or disorder* or impair* or dysfunction*)))

1.6 STEM – grey literature databases
Social Policy and Practice – OVID SP

1. (autism$ or autistic$ or asperger$ or pervasive developmental disorder$).de.
2. asperger$.ti,ab.
3. autis$.ti,ab.
4. childhood schizophrenia.ti,ab.
5. ((communicat$ or speech) adj3 disorder$).ti,ab.
6. (heller$ or (disintegrative adj2 (disorder$ or psychos$))).ti,ab.
7. kanner$.ti,ab.
8. (language adj3 delay$).ti,ab.
9. (((left or right) adj2 hemispher$ adj3 (damag$ or deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$)) or hemisphere functioning).ti,ab.
10. (neurodiverse$ or neurodiversit$).ti,ab.
11. ((nonverbal or non verbal) adj2 learning adj2 (deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$)).ti,ab.
12. pathological demand avoidance.ti,ab.
13. ((pervasive$ adj2 (development$ or neurodevelopment$)) or pdd nos or pddnos).ti,ab.
14. ((pragmatic language or semantic pragmatic) adj3 (deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$)).ti,ab.
15. or/1-14

1.7 STEM - grey literature databases
Health Management Information Consortium (HMIC), PsycEXTRA – OVID SP

(asperger$ or autis$ or childhood schizophrenia or ((communicat$ or speech) adj3 disorder$) or heller$ or (disintegrative adj2 (disorder$ or psychos$)) or kanner$ or (language adj3 delay$) or ((left or right) adj2 hemispher$ adj3 (damag$ or deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$)) or hemisphere functioning or
1 neurodiverse$ or neurodiversit$ or ((nonverbal or non verbal) adj2 learning adj2 (deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$)) or pathological demand avoidance or (pervasive$ adj2 (development$ or neurodevelopment$)) or pdd nos or pddnos or ((pragmatic language or semantic pragmatic) adj3 (deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$))).ti,ab.

2. Question specific search strategies - all databases

2.1 Experience of care and the organisation and delivery of care

Review questions:

1.1 What services and treatments are effective in providing a positive experience of care for children and young people with autism and their families and carers?

1.2 What are the key problems associated with the experience of care for children and young people with autism and their families and carers?

1.3 For children and young people with autism, and their families and carers, what would help improve the experience of care?

2.1 What information and day-to-day support is effective in supporting children and young people with autism and their families and carers :-

- in the post-diagnosis period (including genetic advice and advice about investigation for possible causes of autism including regression)?
- when treatment and care is provided (including case coordination or case management)?
- at intervention/management plan reviews?
- during periods of crisis?
- at key transitions (for example, school transitions and transition to adult services)?

2.2 What information and day-to-day support do children and young people with autism and their families and carers want:-

- in the post-diagnosis period?
- when treatment and care is provided?
- at intervention/management plan reviews?
- during periods of crisis?
- at key transitions (for example, school transitions and transition to adult services)?

3.1 What are the essential elements that allow integration across services/agencies for the optimal organisation and delivery of care to children and young people with autism and their families and carers?

3.2 What are the essential elements that assist in the transition into adulthood services for young people with autism?

3.3 What are the effective ways of monitoring progress in children and young people with autism?

3.4 What alterations need to be made to routine and acute healthcare for children and young people with autism to ensure access for those with autism?

2.11 Service user experience, general medical databases
Embase, Medline, PreMedline, PsycINFO – OVID SP

1	cluster analysis/ or constant comparative method/ or content analysis/ or cultural anthropology/ or discourse analysis/ or ethnographic research/ or ethnography/ or ethnology/ or ethnonursing research/ or field study/ or grounded theory/ or information processing/ or nursing methodology research/ or personal experience/ or phenomenology/ or purposive sample/ or qualitative research/ or exp recording/ or semi structured interview/ or storytelling/ or structured interview/ or thematic analysis/ or theoretical sample/
2	1 use emez
3	anthropology, cultural/ or focus groups/ or exp tape recording/ or interview/ or personal narratives/ or exp interviews as topic/ or narration/ or nursing methodology research/ or observation/ or qualitative research/ or sampling studies/ or cluster analysis/ or videodisc recording/
4	3 use mesz, prem
5	"culture (anthropological)"/ or cluster analysis/ or content analysis/ or discourse analysis/ or ethnography/ or "experiences (events)"/ or grounded theory/ or interviews/ or life experiences/ or narratives/ or observation methods/ or phenomenology/ or qualitative research/ or structured clinical interview/ or exp tape recorders/ or storytelling/ or (field study or interview or focus group or qualitative study).md.
6	5 use psyh
7	(action research or audiorecord$ or ((audio or tape or video$) adj5 record$) or colaizzi$ or (constant adj (comparative or comparison)) or content analy$ or critical social$ or (data adj1 saturat$) or discourse analys?s or emic or ethical enquiry or ethno$ or etic or fieldnote$ or (field adj (note$ or record$ or stud$ or research)) or (focus adj4 (group$ or sampl$)) or ((focus$ or structured) adj2 interview$) or giorgi$ or glaser or (grounded adj (theor$ or study or studies or research)) or heidegger$ or hermeneutic$ or heuristic or human science or husserl$ or ((life or lived) adj experience$) or maximum variation or merleau or narrat$ or ((participant$ or nonparticipant$) adj3 observ$) or ((philosophical or social) adj research$) or (pilot testing and survey) or purpos$ sampl$ or qualitative$ or ricoeur or semiotics or shadowing or snowball or spiegelberg$ or stories or story or storytell$ or strauss or structured categor$ or tape record$ or taperecord$ or testimon$ or (thematic$ adj3

analys$) or Themes or theoretical sampl$ or unstructured categor$ or van kaam$ or van manen or videorecord$ or video record$ or videotap$ or video tap$).ti,ab.

8 or/2,4,6-7

9 health care survey/ or health survey/

10 9 use emez

11 health care surveys/ or exp health surveys/

12 11 use mesz, prem

13 exp surveys/

14 13 use psyh

15 (survey$ or question$).ti,ab.

16 caregiver/ or consumer attitude/ or attitude/ or family assessment/ or exp child parent relation/ or exp family attitude/ or family coping/ or family functioning/ or family health/ or family interaction/ or exp family life/ or family nursing/ or exp family relation/ or family therapy/ or family/ or friend/ or *home care/ or exp nuclear family/ or exp patient acceptance of health care/ or exp patient attitude/ or patient education/or patient satisfaction/ or patient-centered care/ or stepfamily/

17 16 use emez

18 attitude/ or exp attitude to health/ or caregivers/ or community networks/ or consumer satisfaction/ or exp family characteristics/ or family health/ or family nursing/ or family relations/ or family therapy/ or family/ or home nursing/ or intergenerational relations/ or exp parents/ or exp *parent-child relations/ or exp patient acceptance of health care/ or patient education handout/ or patient education/ or patient-centered care/ or exp patient satisfaction/ or sibling relations/ or siblings/ or spouses/ or visitors to patients/

19 18 use mesz, prem

20 adult attitudes/ or attitude change/ or attitude formation/ or attitudes/ or caregiver burden/ or caregivers/ or child attitudes/ or exp client attitudes/ or client education/ or client education/ or exp consumer attitudes/ or exp consumer surveys/ or family/ or exp family conflict/ or exp family members/ or exp family relations/ or exp family therapy/ or female attitudes/ or friendship/ or health attitudes/ or exp health attitudes/ or exp marital relations/ or home care/ or intergenerational relations/ or marriage attitudes/ or nuclear family/ or exp parent child relations/ or exp parental attitudes/ or exp patient attitude/ or parental role/ or patient education/ or patient satisfaction/ or patient-centered care/ or sibling relations/ or significant others/ or spouses/ or stepfamily/

21 20 use psyh

22 (account$ or anxieties or attitude$ or barriers or belief$ or buyin or buy in$1 or cooperat$ or co operat$ or expectation$ or experienc$ or feedback or involv$ or

opinion$ or participat$ or perceived need$ or (perception$ not speech perception) or perspective$ or preferen$ or satisf$ or view$ or voices or worry).ti,ab.

23 (or/10,12,14-15) and (or/17,19,21-22)

24 ((information adj (need$ or requirement$ or support$)) or patient information).ti,ab.

25 (service$ adj2 (acceptab$ or unacceptab$)).ti,ab.

26 or/24-25

27 ((adult$ or attender$ or carer$ or caregiver$ or care giver$ or client$ or consumer$ or couples or customer$ or daughter$ or famil$ or father$ or friend$ or husband$ or individual$ or marital$ or mentor$ or mother$ or multifamil$ or niece or nephew$ or parent$ or partner$ or patient$ or people$ or person$ or relative$ or sibling$ or spouse$ or step relationship$ or teacher$ or wife or wives or women or user$ or adolescen$ or boy$1 or child$ or girl$1 or graders or infant$ or junior$1 or juvenile$ or kindergarten or minors or p?ediatric$ or postpubert$ or postpubescen$ or preadolescen$ or prepubert$ or prepubescen$ or preschool$ or preteen$ or pubert$ or pubescen$ or school$ or teen$ or (young$ adj (people or person$ or patient$ or population$)) or youngster$ or youth$1) adj3 (account$ or anxieties or attitude$ or barriers or belief$ or buyin or buy in$1 or cooperat$ or co operat$ or expectation$ or experienc$ or feedback or involv$ or opinion$ or participat$ or perceived need$ or (perception$ not speech perception) or perspective$ or preferen$ or satisf$ or view$ or voices or worry)).ti,ab.

28 or/8,23,26-27

2.12 Service user experience, topic specific databases

CINAHL – Wiley

s39	s21 or s35 or s36 or s37 or s38
s38	ti (((adult* or attender* or carer* or caregiver* or care giver* or client* or consumer* or couples or customer* or daughter* or famil* or famil* or father* or friend* or husband* or individual* or marital or mentor* or mother* or multifam* or parent* or partner* or patient* or people* or person* or relative* or sibling* or spouse* or step relationship* or son or sons or teacher* or wife or wives or women or user* or adolescen* or boy* or child* or girl* or graders or infant* or junior* or juvenile* or kindergarten or minors or neice or nephew* or p?ediatric* or postpubert* or postpubescen* or preadolescen* or prepubert* or prepubescen* or preschool* or preteen* or pubert* or pubescen* or school* or teen* or (young* n1 (people or person* or patient* or population*)) or youngster* or youth*) n3 (account* or anxieties or attitude* or barriers or belief* or buyin or "buy in*" or cooperat* or co

	operat* or expectation* or experienc* or feedback or involv* or opinion* or participat* or perceived need* or (perception* not speech perception) or perspective* or preferen* or satisf* or view* or voices or worry))) or ab (((adult* or attender* or carer* or caregiver* or care giver* or client* or consumer* or couples or customer* or daughter* or famil* or famil* or father* or friend* or husband* or individual* or marital or mentor* or mother* or multifam* or parent* or partner* or patient* or people* or person* or relative* or sibling* or spouse* or step relationship* or son or sons or teacher* or wife or wives or women or user* or adolescen* or boy* or child* or girl* or graders or infant* or junior* or juvenile* or kindergarten or minors or niece or nephew* or p?ediatric* or postpubert* or postpubescen* or preadolescen* or prepubert* or prepubescen* or preschool* or preteen* or pubert* or pubescen* or school* or teen* or (young* n1 (people or person* or patient* or population*)) or youngster* or youth*) n3 (account* or anxieties or attitude* or barriers or belief* or buyin or "buy in*" or cooperat* or co operat* or expectation* or experienc* or feedback or involv* or opinion* or participat* or perceived need* or (perception* not speech perception) or perspective* or preferen* or satisf* or view* or voices or worry)))
s37	ti ((service* n2 (acceptab* or unacceptab*))) or ab ((service* n2 (acceptab* or unacceptab*)))
s36	ti ((information n1 (need* or requirement* or support*)) or ((carer* or care giv* or caregiv* or famil*) n2 information")) or ab ((information n1 (need* or requirement* or support*)) or ((carer* or care giv* or caregiv* or famil*) n2 information"))
s35	s33 and s34
s34	s25 or s26 or s27 or s28 or s29 or s30 or s31 or s32
s33	s22 or s23 or s24
s32	ti ((account* or anxieties or attitude* or barriers or belief* or buyin or "buy in*" or cooperat* or co operat* or expectation* or experienc* or feedback or involv* or opinion* or participat* or "perceived need*" or (perception* not speech perception) or perspective* or preferen* or satisf* or view* or voices or worry)) or ab ((account* or anxieties or attitude* or barriers or belief* or buyin or "buy in*" or cooperat* or co operat* or expectation* or experienc* or feedback or involv* or opinion* or participat* or "perceived need*" or (perception* not speech perception) or perspective* or preferen* or satisf* or view* or voices or worry))
s31	(mh "adult-child relations")

s30	(mh "caregiver adaptation to patient institutionalization (iowa noc)") or (mh "caregiver burden") or (mh "caregiver emotional health (iowa noc)") or (mh "caregiver home care readiness (iowa noc)") or (mh "caregiver lifestyle disruption (iowa noc)") or (mh "caregiver performance: direct care (iowa noc)") or (mh "caregiver performance: indirect care (iowa noc)") or (mh "caregiver physical health (iowa noc)") or (mh "caregiver role strain (nanda)") or (mh "caregiver role strain (saba ccc)") or (mh "caregiver strain index") or (mh "caregiver stressors (iowa noc)") or (mh "caregiver support") or (mh "caregivers")
s29	(mh "children of impaired parents+") or (mh "community networks") or (mh "family health (iowa noc) (non-cinahl)") or (mh "family health") or (mh "family member health status (iowa noc) (non-cinahl)") or (mh "family nursing") or (mh "family services") or (mh "family+") or (mh "home health aides") or (mh "home health care") or (mh "home nursing") or (mh "intergenerational relations") or (mh "parents+") or (mh "risk for caregiver role strain (nanda)") or (mh "siblings") or (mh "significant other") or (mh "spouses") or (mh "visitors to patients")
s28	(mh "attitude") or (mh "consumer attitudes") or (mh "attitude to health+") or (mh "attitude to illness+") or (mh "family attitudes+")
s27	(mh "patient education") or (mh "patient education (iowa nic) (non-cinahl)") or (mh "patient satisfaction")
s26	(mh "patient centered care")
s25	(mh "patient compliance+")
s24	ti (question* or survey*) or ab (question* or survey*)
s23	(mh "surveys")
s22	(mh "questionnaires+")
s21	s1 or s2 or s3 or s4 or s5 or s6 or s7 or s8 or s9 or s10 or s11 or s12 or s13 or s14 or s15 or s16 or s17 or s18 or s19 or s20
s20	tx ((qualitative* and (metaanal* or meta anal* or synthes* or systematic review*))) or pt ((qualitative* and (metaanal* or meta anal* or synthes* or systematic review*))) or mw ((qualitative* and (metaanal* or meta anal* or synthes* or systematic review*)))
s19	ti ((“action research” or audiorecord* or ((audio or tape or video*) n5 record*) or colaizzi* or (constant n1 (comparative or comparison)) or “content analy*” or

	"critical social*" or (data n1 saturat*) or "discourse analys?s" or emic or "ethical enquiry" or ethno* or etic or fieldnote* or (field n1 (note* or record* or stud* or research)) or (focus n4 (group* or sampl*)) or ((focus* or structured) n2 interview*) or giorgi* or glaser or (grounded n1 (theor* or study or studies or research)) or heidegger* or hermeneutic* or heuristic or "human science" or husserl* or ((life or lived) n1 experience*) or "maximum variation" or merleau or narrat* or ((participant* or nonparticipant*) n3 observ*) or ((philosophical or social) n1 research*) or (pilot testing and survey) or "purpos* sampl*" or qualitative* or ricoeur or semiotics or shadowing or snowball or spiegelberg* or stories or story or storytell* or strauss or "structured categor*" or "tape record*" or taperecord* or testimon* or (thematic* n3 analys*) or themes or "theoretical sampl*" or "unstructured categor*" or "van kaam*" or "van manen" or videorecord* or "video record*" or videotap* or "video tap*")) or ab (("action research" or audiorecord* or ((audio or tape or video*) n5 record*) or colaizzi* or (constant n1 (comparative or comparison)) or "content analy*" or "critical social*" or (data n1 saturat*) or "discourse analys?s" or emic or "ethical enquiry" or ethno* or etic or fieldnote* or (field n1 (note* or record* or stud* or research)) or (focus n4 (group* or sampl*)) or ((focus* or structured) n2 interview*) or giorgi* or glaser or (grounded n1 (theor* or study or studies or research)) or heidegger* or hermeneutic* or heuristic or "human science" or husserl* or ((life or lived) n1 experience*) or "maximum variation" or merleau or narrat* or ((participant* or nonparticipant*) n3 observ*) or ((philosophical or social) n1 research*) or (pilot testing and survey) or "purpos* sampl*" or qualitative* or ricoeur or semiotics or shadowing or snowball or spiegelberg* or stories or story or storytell* or strauss or "structured categor*" or "tape record*" or taperecord* or testimon* or (thematic* n3 analys*) or themes or "theoretical sampl*" or "unstructured categor*" or "van kaam*" or "van manen" or videorecord* or "video record*" or videotap* or "video tap*"))
s18	(mh "videorecording")
s17	(mh "theoretical sample")
s16	(mh "thematic analysis")
s15	(mh "qualitative validity")
s14	(mh "qualitative studies+")
s13	(mh "purposive sample")
s12	(mh "phenomenology")

s11	(mh "observational methods+")
s10	(mh "narratives")
s9	(mh "interviews+")
s8	(mh "information processing (iowa noc)")
s7	(mh "focus groups")
s6	(mh "field studies")
s5	(mh "discourse analysis")
s4	(mh "content analysis")
s3	(mh "constant comparative method")
s2	(mh "cluster analysis")
s1	(mh "audiorecording")

3 Study design filters – all databases

3.1 Quantitative and qualitative systematic review study design filters

3.11 Quantitative systematic review study design filter, general medical databases Embase, Medline, PreMEDLINE, PsycINFO – OVID SP

1 meta analysis/ or systematic review/

2 1 use emez

3 meta analysis.sh,pt. or "meta-analysis as topic"/ or "review literature as topic"/

4 3 use mesz, prem

5 (literature review or meta analysis).sh,id,md. or systematic review.id,md.

6 5 use psyh

7 (exp bibliographic database/ or (((electronic or computer$ or online) adj database$) or bids or cochrane or embase or index medicus or isi citation or medline or psyclit or psychlit or scisearch or science citation or (web adj2 science)).ti,ab.) and (review$.ti,ab,sh,pt. or systematic$.ti,ab.)

8 7 use emez

9 (exp databases, bibliographic/ or (((electronic or computer$ or online) adj database$)

or bids or cochrane or embase or index medicus or isi citation or medline or psyclit or psychlit or scisearch or science citation or (web adj2 science)).ti,ab.) and (review$.ti,ab,sh,pt. or systematic$.ti,ab.)

10 9 use mesz, prem

11 (computer searching.sh,id. or (((electronic or computer$ or online) adj database$) or bids or cochrane or embase or index medicus or isi citation or medline or psyclit or psychlit or scisearch or science citation or (web adj2 science)).ti,ab.) and (review$.ti,ab,pt. or systematic$.ti,ab.)

12 11 use psyh

13 ((analy$ or assessment$ or evidence$ or methodol$ or quantitativ$ or systematic$) adj2 (overview$ or review$)).tw. or ((analy$ or assessment$ or evidence$ or methodol$ or quantitativ$ or systematic$).ti. and review$.ti,pt.) or (systematic$ adj2 search$).ti,ab.

14 (metaanal$ or meta anal$).ti,ab.

15 (research adj (review$ or integration)).ti,ab.

16 reference list$.ab.

17 bibliograph$.ab.

18 published studies.ab.

19 relevant journals.ab.

20 selection criteria.ab.

21 (data adj (extraction or synthesis)).ab.

22 (handsearch$ or ((hand or manual) adj search$)).ti,ab.

23 (mantel haenszel or peto or dersimonian or der simonian).ti,ab.

24 (fixed effect$ or random effect$).ti,ab.

25 ((pool$ or combined or combining) adj2 (data or trials or studies or results)).ti,ab.

26 or/2,4,6,8,10,12-25

3.12 Qualitative systematic review study design filter, general medical databases

Embase, Medline, PreMEDLINE, PsycINFO – OVID SP

1	(cross case analys$ or eppi approach or metaethno$ or meta ethno$ or metanarrative$ or meta narrative$ or meta overview or metaoverview or metastud$ or meta stud$ or metasummar$ or meta summar$ or qualitative

	overview$).ti,ab.
2	(((critical interpretative or evidence or meta or mixed methods or multilevel or multi level or narrative or parallel or realist) adj synthes$) or metasynthes$).ti,ab.
3	(qualitative$ and (metaanal$ or meta anal$ or synthes$ or systematic review$)).ti,ab,hw,pt.
4	or/1-3

3.13 Quantitative systematic review study design filter, topic specific databases

Applied Social Sciences Index and Abstracts (ASSIA), Australian Education Index (AEI), British Education Index (BEI), Education Resources in Curriculum (ERIC), Social Services Abstracts (SSA), Sociological Abstracts, Applied Social Sciences Index and Abstracts (ASSIA), International Bibliography of Social Sciences (IBSS) – ProQUEST [high specificity]

S1	all (("meta anal*" or "systematic overview" or "systematic review" or "systematic search"))

3.14 Qualitative systematic review study design filter, topic specific databases

Applied Social Sciences Index and Abstracts (ASSIA), Australian Education Index (AEI), British Education Index (BEI), Education Resources in Curriculum (ERIC), International Bibliography of Social Sciences (IBSS), National Criminal Justice Reference Service (NCJRS), Social Services Abstracts (SSA), Sociological Abstracts – ProQUEST

s1	all(("cross case analys*" or "eppi approach" or metaethno* or "meta ethno*" or metanarrative* or "meta narrative*" or "meta overview" or metaoverview or metastud* or "meta stud*" or metasummar* or "meta summar*" or "qualitative overview*"))
s2	all((((("critical interpretative" or evidence or meta or "mixed methods" or multilevel or "multi level" or narrative or parallel or realist) near/1 synthes*) or metasynthes*))
s3	all((qualitative* and (metaanal* or "meta anal*" or synthes* or "systematic review*")))
s4	s1 or s2 or s3

3.15 Quantitative systematic review study design filter, topic specific databases CINAHL – EBSCO HOST

s33	s1 or s2 or s3 or s4 or s5 or s6 or s7 or s8 or s9 or s10 or s11 or s12 or s13 or s14 or s15 or s16 or s22 or s23 or s26 or s27 or s28 or s29 or s30 or s31 or s32
s32	ti (analy* n5 review* or assessment* n5 review* or evidence* n5 review* or methodol* n5 review* or quantativ* n5 review* or systematic* n5 review*) or ab (analy* n5 review* or assessment* n5 review* or evidence* n5 review* or methodol* n5 review* or quantativ* n5 review* or systematic* n5 review*)
s31	ti (analy* n5 overview* or assessment* n5 overview* or evidence* n5 overview* or methodol* n5 overview* or quantativ* n5 overview* or systematic* n5 overview*) or ab (analy* n5 overview* or assessment* n5 overview* or evidence* n5 overview* or methodol* n5 overview* or quantativ* n5 overview* or systematic* n5 overview*)
s30	ti (pool* n2 results or combined n2 results or combining n2 results) or ab (pool* n2 results or combined n2 results or combining n2 results)
s29	ti (pool* n2 studies or combined n2 studies or combining n2 studies) or ab (pool* n2 studies or combined n2 studies or combining n2 studies)
s28	ti (pool* n2 trials or combined n2 trials or combining n2 trials) or ab (pool* n2 trials or combined n2 trials or combining n2 trials)
s27	ti (pool* n2 data or combined n2 data or combining n2 data) or ab (pool* n2 data or combined n2 data or combining n2 data)
s26	s24 and s25
s25	ti review* or pt review*
s24	ti analy* or assessment* or evidence* or methodol* or quantativ* or systematic*
s23	ti “systematic* n5 search*” or ab “systematic* n5 search*”
s22	(s17 or s18 or s19) and (s20 or s21)
s21	ti systematic* or ab systematic*
s20	tx review* or mw review* or pt review*
s19	(mh "cochrane library")
s18	ti (bids or cochrane or index medicus or “isi citation” or psyclit or psychlit or scisearch or “science citation” or web n2 science) or ab (bids or cochrane or index medicus or “isi citation” or psyclit or psychlit or scisearch or “science citation” or

	web n2 science)
s17	ti (“electronic database*” or “bibliographic database*” or “computeri?ed database*” or “online database*”) or ab (“electronic database*” or “bibliographic database*” or “computeri?ed database*” or “online database*”)
s16	(mh "literature review")
s15	pt systematic* or pt meta*
s14	ti (“fixed effect*” or “random effect*”) or ab (“fixed effect*” or “random effect*”)
s13	ti (“mantel haenszel” or peto or dersimonian or “der simonian”) or ab (“mantel haenszel” or peto or dersimonian or “der simonian”)
s12	ti (handsearch* or "hand search*" or "manual search*") or ab (handsearch* or "hand search*" or "manual search*")
s11	ab "data extraction" or "data synthesis"
s10	ab "selection criteria"
s9	ab "relevant journals"
s8	ab "published studies"
s7	ab bibliograph*
s6	ab "reference list*"
s5	ti (“research review*” or “research integration”) or ab (“research review*” or “research integration”)
s4	ti (metaanal* or “meta anal*”) or ab (metaanal* or “meta anal*”)
s3	(mh "meta analysis")
s2	(mh "systematic review")
s1	(mh "literature searching+")

3.16 Qualitative systematic review study design filter, topic specific databases

CINAHL – EBSCO HOST

s1	ti (“cross case analys*” or “eppi approach” or metaethno* or “meta ethno*” or metanarrative* or “meta narrative*” or “meta overview” or metaoverview or metastud* or “meta stud*” or metasummar* or “meta summar*” or “qualitative

	overview*") or ab ("cross case analys*" or "eppi approach" or metaethno* or "meta ethno*" or metanarrative* or "meta narrative*" or "meta overview" or metaoverview or metastud* or "meta stud*" or metasummar* or "meta summar*" or "qualitative overview*")
s2	ti ((("critical interpretative" or evidence or meta or "mixed methods" or multilevel or "multi level" or narrative or parallel or realist) near synthes*) or metasynthes*) or ab ((("critical interpretative" or evidence or meta or "mixed methods" or multilevel or "multi level" or narrative or parallel or realist) near synthes*) or metasynthes*)
s3	ti qualitative* or ab qualitative* or mw qualitative* or pt qualitative*
s4	ti (metaanal* or "meta anal*" or synthes* or "systematic review*") or ab (metaanal* or "meta anal*" or synthes* or "systematic review*") or mw (metaanal* or "meta anal*" or synthes* or "systematic review*") or pt (metaanal* or "meta anal*" or synthes* or "systematic review*")
s5	s3 and s4
s6	s1 or s2 or s5

3.17 Quantitative systematic review study design filter, topic specific databases
SSCI – Web of Knowledge

#1	title=("electronic database*" or "computer* database*" or "online database*" or bids or cochrane or embase or "index medicus" or "isi citation" or medline or psyclit or psychlit or scisearch or "science citation" or "web of science")
#2	title=(review* or systematic*) or topic=(review* or systematic*)
#3	#1 and #2
#4	topic=((systematic* near search* or metaanal* or "meta anal*" or "research review*" or "research integration" or "reference list*" or bibliograph* or "published studies" or "relevant journals" or "selection criteria" or "data extraction" or "data synthesis" or handsearch* or "hand search*" or "manual search*" or "mantel haenszel" or peto or dersimonian or "der simonian" or "fixed effect*" or "random effect*" or ((pool* or combined or combining) near (data or trials or studies or results)))) or title=((systematic* near search* or metaanal* or "meta anal*" or "research review*" or "research integration" or "reference list*" or bibliograph* or "published studies" or "relevant journals" or "selection criteria" or "data extraction" or "data synthesis" or handsearch* or "hand search*" or "manual search*" or "mantel haenszel" or peto or dersimonian or "der simonian" or "fixed effect*" or "random effect*") or ((pool* or combined or

	combining) near (data or trials or studies or results))))
#5	topic=(((analy* or assessment* or evidence* or methodol* or quantitativ* or systematic*) near (overview* or review*))) or title=(((analy* or assessment* or evidence* or methodol* or qualitativ* or quantitativ* or systematic*) near (overview* or review*)))
#6	#3 or #4 or #5

3.18 Qualitative systematic review study design filter, topic specific databases

SSCI – Web of Knowledge

#1	topic=((“cross case analys*” or “eppi approach” or metaethno* or “meta ethno*” or metanarrative* or “meta narrative*” or “meta overview” or metaoverview or metastud* or “meta stud*” or metasummar* or “meta summar*” or “qualitative overview*”)) or title=((“cross case analys*” or “eppi approach” or metaethno* or “meta ethno*” or metanarrative* or “meta narrative*” or “meta overview” or metaoverview or metastud* or “meta stud*” or metasummar* or “meta summar*” or “qualitative overview*”))
#2	topic=((((“critical interpretative” or evidence or meta or “mixed methods” or multilevel or “multi level” or narrative or parallel or realist) near synthes*) or metasynthes*)) or title=((((“critical interpretative” or evidence or meta or “mixed methods” or multilevel or “multi level” or narrative or parallel or realist) near synthes*) or metasynthes*))
#3	topic=((qualitative* and (metaanal* or “meta anal*” or synthes* or “systematic review*”))) or title=((qualitative* and (metaanal* or “meta anal*” or synthes* or “systematic review*”)))
#4	#1 or #2 or #3

3.2 Randomised controlled trial filters

3.21 Randomized controlled trial study design filter, general medical databases
Embase, Medline, PreMEDLINE, PsycINFO – OVID SP

1	exp "clinical trial (topic)"/ or exp clinical trial/ or crossover procedure/ or double blind procedure/ or placebo/ or randomization/ or random sample/ or single blind procedure/
2	1 use emez
3	exp clinical trial/ or cross-over studies/ or double-blind method/ or placebos/ or

random allocation/ or "randomized controlled trials as topic"/ or single-blind method/

4 3 use mesz, prem

5 (clinical trials or placebo or random sampling).sh,id.

6 5 use psyh

7 (clinical adj2 trial$).ti,ab.

8 (crossover or cross over).ti,ab.

9 (((single$ or doubl$ or trebl$ or tripl$) adj2 blind$) or mask$ or dummy or doubleblind$ or singleblind$ or trebleblind$ or tripleblind$).ti,ab.

10 (placebo$ or random$).ti,ab.

11 treatment outcome$.md. use psyh

12 animals/ not human$.mp. use emez

13 animal$/ not human$/ use mesz, prem

14 (animal not human).po. use psyh

15 (or/2,4,6-11) not (or/12-14)

3.22 Randomized controlled trial study design filter, topic specific databases Applied Social Sciences Index and Abstracts (ASSIA), Australian Education Index (AEI), British Education Index (BEI), Education Resources in Curriculum (ERIC), Social Services Abstracts (SSA), Sociological Abstracts, Applied Social Sciences Index and Abstracts (ASSIA), International Bibliography of Social Sciences (IBSS) – PRO QUEST

S1 all ((clinical near/1 trial* or crossover or “cross over”) or ((single* or doubl* or trebl* or tripl*) near/1 (blind* or mask* or dummy)) or (singleblind* or doubleblind* or trebleblind* or tripleblind* or placebo* or random*))

3.23 Randomized controlled trial study design filter, topic specific databases CINAHL– EBSCO Host

s10	s9 not s8
s9	s1 or s2 or s3 or s4 or s5 or s6 or s7
s8	(mh "animals") not (mh "human")

s7	(pt "clinical trial") or (pt "randomized controlled trial")
s6	ti (placebo* or random*) or ab (placebo* or random*)
s5	ti (single blind* or double blind* or treble blind* or mask* or dummy* or singleblind* or doubleblind* or trebleblind*) or ab (single blind* or double blind* or treble blind* or mask* or dummy* or singleblind* or doubleblind* or trebleblind*)
s4	ti (crossover or cross over) or ab (crossover or cross over)
s3	ti clinical n2 trial* or ab clinical n2 trial*
s2	(mh "crossover design") or (mh "placebos") or (mh "random assignment") or (mh "random sample")
s1	(mh "clinical trials+")

3.24 Randomized controlled trial study design filter, topic specific databases
SSCI – Web of Knowledge

#1	topic=(((clinical near trial* or crossover or "cross over") or ((single* or doubl* or trebl* or tripl*) near (blind* or mask* or dummy)) or (singleblind* or doubleblind* or trebleblind* or tripleblind* or placebo* or random*))) or title=(((clinical near trial* or crossover or "cross over") or ((single* or doubl* or trebl* or tripl*) near (blind* or mask* or dummy)) or (singleblind* or doubleblind* or trebleblind* or tripleblind* or placebo* or random*)))

APPENDIX 10: QUALITY CHECKLISTS FOR CLINICAL STUDIES AND REVIEWS

The methodological quality of each study was evaluated using NICE checklists (NICE, 2009). The checklists for systematic reviews and for RCTs are reproduced below (for other checklists and further information about how to complete each checklist, see *The Guidelines Manual* [NICE, 2009]). The completed checklists can be found in Appendix 16.

Methodology checklist: systematic reviews and meta-analyses

Study identification *Include author, title, reference, year of publication*	
Guideline topic:	Review question no:
Checklist completed by:	
SCREENING QUESTIONS	
In a well-conducted, relevant systematic review:	*Circle one option for each question*
The review addresses an appropriate and clearly focused question that is relevant to the guideline review question	Yes No Unclear
The review collects the type of studies you consider relevant to the guideline review question	Yes No Unclear
The literature search is sufficiently rigorous to identify all the relevant studies	Yes No Unclear
Study quality is assessed and reported	Yes No Unclear
An adequate description of the methodology used is included, and the methods used are appropriate to the question	Yes No Unclear

Methodology checklist: RCTs

Study identification Include author, title, reference, year of publication		
Guideline topic:		Review question no:
Checklist completed by:		
		Circle one option for each question
A. Selection bias (systematic differences between the comparison groups)		
A1	An appropriate method of randomisation was used to	Yes No Unclear N/A

	allocate participants to treatment groups (which would have balanced any confounding factors equally across groups)	
A2	There was adequate concealment of allocation (such that investigators, clinicians and participants cannot influence enrolment or treatment allocation)	Yes No Unclear N/A
A3	The groups were comparable at baseline, including all major confounding and prognostic factors	Yes No Unclear N/A
Based on your answers to the above, in your opinion was selection bias present? If so, what is the likely direction of its effect?		
Low risk of bias Unclear/unknown risk High risk of bias		
Likely direction of effect:		
B. Performance bias (systematic differences between groups in the care provided, apart from the intervention under investigation)		
B1	The comparison groups received the same care apart from the intervention(s) studied	Yes No Unclear N/A
B2	Participants receiving care were kept 'blind' to treatment allocation	Yes No Unclear N/A
B3	Individuals administering care were kept 'blind' to treatment allocation	Yes No Unclear N/A
Based on your answers to the above, in your opinion was performance bias present? If so, what is the likely direction of its effect?		
Low risk of bias Unclear/unknown risk High risk of bias		
Likely direction of effect:		
C. Attrition bias (systematic differences between the comparison groups with respect to loss of participants)		
C1	All groups were followed up for an equal length of time (or analysis was adjusted to allow for differences in length of follow-up)	Yes No Unclear N/A
C2	a. How many participants did not complete treatment in each group?	
	b. The groups were comparable for treatment completion (that is, there were no important or systematic differences between groups in terms of those who did not complete treatment)	Yes No Unclear N/A
C3	a. For how many participants in each group were no outcome data available?	
	b. The groups were comparable with respect to the availability of outcome data (that is, there were no important or systematic differences between groups in terms of those for whom outcome data were not available).	Yes No Unclear N/A
Based on your answers to the above, in your opinion was attrition bias present? If so, what is the likely direction of its effect?		
Low risk of bias Unclear/unknown risk High risk of bias		
Likely direction of effect:		

D. Detection bias (bias in how outcomes are ascertained, diagnosed or verified)		
D1	The study had an appropriate length of follow-up	Yes No Unclear N/A
D2	The study used a precise definition of outcome	Yes No Unclear N/A
D3	A valid and reliable method was used to determine the outcome	Yes No Unclear N/A
D4	Investigators were kept 'blind' to participants' exposure to the intervention	Yes No Unclear N/A
D5	Investigators were kept 'blind' to other important confounding and prognostic factors	Yes No Unclear N/A
Based on your answers to the above, in your opinion was detection bias present? If so, what is the likely direction of its effect?		
Low risk of bias Unclear/unknown risk High risk of bias		
Likely direction of effect:		

APPENDIX 11: SEARCH STRATEGIES FOR THE IDENTIFICATION OF HEALTH ECONOMICS EVIDENCE

Each search was constructed using the groups of terms set out in Text Box 1. The full set of search terms is documented in sections 1 to 2.1. The selection of search terms was kept broad to maximise retrieval of evidence in a wide range of areas of interest to the GDG.

Text Box 1: Summary of systematic search strategies: Search strategy construction

Summary of systematic search strategies for health economic evidence					
Section 1					
Review area/s	**Search type**	**Search construction**	**Study design searched**	**Databases searched**	**Date range searched**
All review areas/ questions	Generic, evidence mapped to all review areas	General mainstream databases – generic search: [(population terms) AND (health economic/quality of life filter)] Topic specific databases – generic search: [(population terms only)]	Economic evidence (including full and partial economic evaluations and health technology assessment reports)	General mainstream databases: Embase, Medline, PreMedline, PsycINFO Topic specific databases: HTA*, NHS EED*	1995 to January 2013
Notes: ***Evidence resulting from generic searches mapped to all review areas***					
**** HTA (Health Technology Assessment database), NHS EED (NHS Economic Evaluation Database)***					

1 Population search terms – all databases

1.1 STEM – general medical databases
Embase, Medline, PreMEDLINE, PsycINFO – OVID SP

1	autism/ or asperger syndrome/ or childhood disintegrative disorder/ or "pervasive developmental disorder not otherwise specified"/
2	1 use emez
3	child development disorders, pervasive/ or asperger syndrome/ or autistic disorder/
4	3 use mesz, prem
5	aspergers syndrome/ or autism/ or autistic thinking/ or pervasive developmental disorders/
6	5 use psyh
7	asperger$.ti,ab.
8	autis$.ti,ab.
9	childhood schizophrenia.ti,ab.
10	((communicat$ or speech) adj3 disorder$).ti,ab.
11	(heller$ or (disintegrative adj2 (disorder$ or psychos$))).ti,ab.
12	kanner$.ti,ab.
13	(language adj3 delay$).ti,ab.
14	(((left or right) adj2 hemispher$ adj3 (damag$ or deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$)) or hemisphere functioning).ti,ab.
15	(neurodiverse$ or neurodiversit$).ti,ab.
16	((nonverbal or non verbal) adj2 learning adj2 (deficit$ or disabilit$ or disorder$ or impair$ or dysfunction$)).ti,ab.
17	pathological demand avoidance.ti,ab.
18	((pervasive$ adj2 (development$ or neurodevelopment$)) or pdd nos or pddnos).ti,ab.
19	((pragmatic language or semantic pragmatic) adj3 (deficit$ or disability$ or disorder$ or impair$ or dysfunction$)).ti,ab.
20	or/2,4,6-19

1.2 STEM - topic specific databases
HTA, NHS EED – Wiley

id	search
#1	mesh descriptor **child development disorders, pervasive** explode all trees
#2	(asperger*):ti or (asperger*):ab
#3	(autis*):ti or (autis*):ab
#4	"childhood schizophrenia":ti or "childhood schizophrenia":ab
#5	((communicat* or speech) near/3 disorder*):ti or ((communicat* or speech) near/3 disorder*):ab
#6	(heller* or (disintegrative near/2 (disorder* or psychos*))):ti or (heller* or (disintegrative near/2 (disorder* or psychos*))):ab
#7	(kanner*):ti or (kanner*):ab
#8	(language near/3 delay*):ti or (language near/3 delay*):ab
#9	((left or right) near/2 hemispher* near/3 (damag* or deficit* or disabilit* or disorder* or impair* or dysfunction*)) or "hemisphere functioning":ti or ((left or right) near/2 hemispher* near/3 (damag* or deficit* or disabilit* or disorder* or impair* or dysfunction*)) or "hemisphere functioning":ab
#10	(neurodiverse* or neurodiversit*):ti or (neurodiverse* or neurodiversit*):ab
#11	((nonverbal or non verbal) near/2 learning near/2 (deficit* or disabilit* or disorder* or impair* or dysfunction*)):ti or ((nonverbal or non verbal) near/2 learning near/2 (deficit* or disabilit* or disorder* or impair* or dysfunction*)):ab
#12	"pathological demand avoidance":ti or "pathological demand avoidance":ab
#13	((pervasive* near/2 (development* or neurodevelopment*)) or "pdd nos" or pddnos):ti or ((pervasive* near/2 (development* or neurodevelopment*)) or "pdd nos" or pddnos):ab
#14	(("pragmatic language" or "semantic pragmatic") near/3 (deficit* or disability* or disorder* or impair* or dysfunction*)):ti or (("pragmatic language" or "semantic pragmatic") near/3 (deficit* or disability* or disorder* or impair* or dysfunction*)):ab
#15	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14)

2 Study design filters – all databases

2.1 Health economic/quality of life filter
Embase, Medline, PreMEDLINE, PsycINFO – OVID SP

1	budget/ or exp economic evaluation/ or exp fee/ or funding/ or exp health care cost/ or health economics/ or exp pharmacoeconomics/ or resource allocation/
2	1 use emez
3	exp budgets/ or exp "costs and cost analysis"/ or economics/ or exp economics, hospital/ or exp economics, medical/ or economics, nursing/ or economics, pharmaceutical/ or exp "fees and charges"/ or exp resource allocation/ or value of life/
4	3 use mesz
5	exp "costs and cost analysis"/ or "cost containment"/ or economics/ or finance/ or funding/ or health care economics/ or pharmacoeconomics/ or exp professional fees/ or resource allocation/
6	5 use psyh
7	(cost$ or economic$ or pharmacoeconomic$ or pharmaco economic$).ti. or (cost$ adj2 (effective$ or utilit$ or benefit$ or minimi$)).ab. or economic model$.tw. or (budget$ or fee or fees or financ$ or price or prices or pricing or resource$ allocat$ or (value adj2 (monetary or money))).ti,ab.
8	decision theory/ or decision tree/ or monte carlo method/ or *nonbiological model/ or (statistical model/ and exp economic aspect/) or stochastic model/ or *theoretical model/
9	8 use emez
10	exp decision theory/ or markov chains/ or exp models, economic/ or *models, organizational/ or *models, theoretical/ or monte carlo method/
11	10 use mesz
12	exp decision theory/ or exp stochastic modeling/
13	12 use psyh
14	((decision adj (analy$ or model$ or tree$)) or economic model$ or markov or monte carlo).ti,ab.
15	quality adjusted life year/ or "quality of life index"/ or short form 12/ or short form 20/ or short form 36/ or short form 8/ or sickness impact profile/
16	15 use emez
17	quality-adjusted life years/ or sickness impact profile/
18	17 use mesz
19	"*quality of life"/
20	19 use psyh
21	(((disability or quality) adj adjusted) or (adjusted adj2 life)).ti,ab.
22	(disutili$ or (utilit$ adj1 (health or score$ or value$ or weigh$))).ti,ab.
23	(health year equivalent or hye or hyes).ti,ab.

24	(daly or qal or qald or qale or qaly or qtime$ or qwb$).ti,ab.
25	discrete choice.ti,ab.
26	(euroqol$ or euro qol$ or eq5d$ or eq 5d$).ti,ab.
27	(hui or hui1 or hui2 or hui3).ti,ab.
28	((quality adj2 (wellbeing or well being)) or quality adjusted life or qwb or (value adj2 (money or monetary))).ti,ab.
29	(qol or hql$ or hqol$or h qol$ or hrqol or hr qol or hr ql or hrql).ti,ab.
30	rosser.ti,ab.
31	sickness impact profile.ti,ab.
32	(standard gamble or time trade$ or tto or willingness to pay).ti,ab.
33	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab.
34	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab.
35	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab.
36	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab
37	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab.
38	or/ 2,4,6-7,9,11,13-14,16,18,20-37

APPENDIX 12: METHODOLOGY CHECKLIST FOR ECONOMIC STUDIES

This checklist is designed to determine whether an economic evaluation provides evidence that is useful to inform the decision-making of the GDG. It is not intended to judge the quality of the study per se or the quality of reporting. For further information about how to complete the checklist, see *The Guidelines Manual* [NICE, 2009].

Study identification *Including author, title, reference, year of publication*			
Guideline topic:			Question no:
Section 1: Applicability (relevance to specific guideline review question(s) and the NICE reference case). This checklist should be used first to filter out irrelevant studies.		Yes/ Partly/ No/Unclear /NA	Comments
1.1	Is the study population appropriate for the guideline?		
1.2	Are the interventions and services appropriate for the guideline?		
1.3	Is the healthcare system in which the study was conducted sufficiently similar to the current UK NHS context?		
1.4	Are costs measured from the NHS and personal social services (PSS) perspective?		
1.5	Are non-direct health effects on individuals excluded?		
1.6	Are both costs and health effects discounted at an annual rate of 3.5%?		
1.7	Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?		
1.8	Are changes in health-related quality of life (HRQoL) reported directly from patients and/or carers?		
1.9	Is the valuation of changes in HRQoL (utilities) obtained from a representative sample of the general public?		
1.10	Overall judgement: Directly applicable/Partially applicable/Not applicable There is no need to use section 2 of the checklist if the study is considered 'not applicable'.		
Other comments:			

Section 2: Study limitations (the level of methodological quality) This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline.		**Yes/ Partly /No/ Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the health condition under evaluation?		
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?		

2.3	Are all important and relevant health outcomes included?		
2.4	Are the estimates of baseline health outcomes from the best available source?		
2.5	Are the estimates of relative treatment effects from the best available source?		
2.6	Are all important and relevant costs included?		
2.7	Are the estimates of resource use from the best available source?		
2.8	Are the unit costs of resources from the best available source?		
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?		
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?		
2.11	Is there no potential conflict of interest?		
2.12	Overall assessment: Minor limitations/Potentially serious limitations/Very serious limitations		
Other comments:			

APPENDIX 13: RESEARCH RECOMMENDATIONS

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

1. ***Case management for children (aged 6-11 years) with autism***

What is the value of case management (defined by protocol and delivered in addition to usual care) for children (aged 6-11 years) with autism in terms of parental satisfaction, functioning and stress and child psychopathology?

Why is this important
Autism is well characterised as a chronic disorder with lifelong disability, yet the current health management structure is usually organised around single episodes of care. There is a significant body of international research into the management of chronic conditions such as diabetes and asthma, but nothing on autism. Key to commonly accepted strategies in chronic illness is the provision of case management. The theory and practice of management of chronic illness, as well as widely expressed service-user opinion, indicate that a chronic care model for the organisation of autism services could be appropriate and cost effective.

Case management for children with autism should be formally evaluated in a randomised controlled trial (RCT) reporting short- and medium-term outcomes (including cost-effectiveness) with a follow-up of at least 6 months and again at 12 months. The outcomes (parental satisfaction, functioning and stress and child psychopathology) should be assessed by structured clinical interviews, parent- and self-reports using validated questionnaires and objective measures of behaviour. The study needs to be large enough to determine the presence of clinically important effects, and mediators and moderators (in particular the child or young person's age) should be investigated.

2. ***Managing behaviour that challenges in children and young people with autism***

Is a group-based parent training intervention for parents or carers of children and young people with autism clinically and cost effective in reducing early and emerging behaviour that challenges in the short- and medium-term compared with treatment as usual?

Why this is important
Behaviour that challenges is a common and potentially very serious problem for children and young people with autism. It is not only an indicator of distress but often limits their participation in family life, education and community activities. Once behaviour that challenges has become established, it is unlikely to diminish

without intervention. Presently, many children and young people are referred only when the behaviour has become severely impairing to themselves and/or others, when they represent a threat to themselves and others or when there is a breakdown in everyday life (often leading to high levels of educational support including residential schooling, long-term hospital admissions and social service support). At this point, behavioural interventions may be difficult or impossible to initiate and antipsychotic medication is used. However, antipsychotic medication is undesirable as a first-line intervention because it is symptomatic in its benefits, has significant long-term adverse effects and behaviour problems typically recur when it is stopped.

This question would be answered using an RCT design reporting short- and medium-term outcomes The intervention should consider the main causes of behaviour that challenges that are likely to be amenable to a behavioural intervention, such as educating parents about simple functional behaviour analysis to identify triggers and examine patterns of reinforcement. The primary outcomes should be short- and medium-term reduction in behaviour that challenges; a priority will be to include or develop robust and ecologically valid blinded outcome measures. Secondary outcomes should include parental and sibling stress, quality of life and adaptive function of the child or young person. In addition, the use of medication in the medium term to manage behaviour that challenges should be assessed. Cost effectiveness should include use of a wide range of services, such as additional educational support and social services as well as the use of health services by other family members.

3. ***Managing sleep problems in children with autism***

Is a sleep hygiene intervention or melatonin a clinically and cost effective treatment of sleep onset, night waking and reduced total sleep in children (aged 4-10 years) with autism?

Why is this important?
Sleep problems are common in autism and have a significant negative impact on parental coping as well as on the child. There is some evidence that sleep hygiene techniques and use of melatonin are effective in autism. However existing studies of melatonin have used different groups and different preparations of melatonin precluding meta-analysis.

The intervention being assessed should be formally evaluated in an RCT in 3 stages: (1) recording sleep onset, night waking and total sleep time over 3 months using a diary completed by parents and actigraphy; (2) random allocation to sleep hygiene treatment by booklet or by professional contact for those with a sleep problem; (3) after 3 months random allocation to slow-release melatonin or placebo for those with persistent sleep problems; after a further 3 months, those on placebo would be offered the active preparation.

It should report primary and secondary outcomes with a follow-up at 12 months for all participants. Primary outcomes should include increased total sleep time and decreased night waking. Secondary outcomes should include improved sleep onset, a change in Aberrant Behaviour Checklist measures of behaviour that challenges, and improvement in parental stress index and satisfaction and the child's cognitive function.

4. ***Treating comorbid anxiety in children and young people with autism***

What is the comparative clinical and cost effectiveness of pharmacological and psychosocial interventions for anxiety disorders in children and young people with autism?

Why this is important
Anxiety disorders are common in children and young people, including in those with autism. Early trials of CBT for anxiety in children and young people with autism have shown promising results but individual studies have methodological shortcomings. Furthermore, the common pharmacological approaches have not been evaluated, despite their demonstrated efficacy in otherwise typically developing children and their suggested effects in adults with anxiety and autism. In some regions, selective serotonin reuptake inhibitors (SSRIs) are being prescribed for this indication despite the absence of an evidence base or a licence. Having evidence-based alternative interventions would provide greater choice for children and young people and their parents or carers, and the possibility of offering an alternative intervention if the first is unsuccessful.

This question should be answered using a parallel-arm RCT design comparing pharmacological and psychosocial interventions with placebo in children and young people with autism and an anxiety disorder (generalised anxiety disorder, separation anxiety disorder, social anxiety, panic disorder and agoraphobia). Pharmacological treatment should be with an SSRI and the dosing protocol should follow that used in research in typically developing children but should have the option of evaluating outcome at a lower dose than that usually expected to be effective (because of the suggestion that children and young people with autism may respond to lower doses). The SSRI should be blinded with an identical placebo and the use of an 'attention' or other psychosocial control group. The psychosocial intervention should be manualised and based on the cognitive behavioural approach used in children and young people with and without autism that has been shown to be effective in previous trials. The sample size should be powered to deliver precise effect size estimates for medication and CBT arms. If possible the full age and intellectual range of children and young people should be included and there should be demonstrable impairment secondary to the anxiety disorder.

Primary outcome measures should be reduction in anxiety symptoms. It is likely that parent-reported measures will be most pragmatic but self- and teacher-reported

measures should also be considered as secondary outcomes, as well as blinded measures such as heart rate, heart rate variability and skin conductance. Additional secondary outcome measures should include patient satisfaction, changes in adaptive function and quality of life and disruptive behaviour. Adverse effects should be evaluated. An economic evaluation should be included.

5. Sensory sensitivities in children with autism

Does sensory integration therapy reduce sensory sensitivities in children (aged 5-10 years) with autism across a range of contexts?

Why is this important?
First-hand accounts describe the considerable negative impact that sensory sensitivities can have on the daily lives of both affected individuals and their families or carers. A wide range of sensory-based interventions are used in the UK across health and education for people with autism. Currently sensory integration therapy is one of the most frequently requested interventions by parents of young children with autism and sensory processing difficulties. There is some limited evidence the sensory integration therapy can elicit improvements in sensory problems, however, the quality was low and there are no adequately powered RCTs or UK-funded research. Moreover the intervention itself is very labour intensive.

The intervention should be formally evaluated in an RCT. The intervention being assessed would be a manualised sensory integration treatment in children aged 5-10 years with a diagnosis of autism, who are in full-time education, and who have been identified, using a standardised measure, as having sensory sensitivities. It should be administered by an appropriately qualified professional (an occupational therapist) for a specified period of time using fidelity measures to ensure adherence to the programme. The intervention should be supported with a programme of activities in school to encourage generalisation of skills. It should be compared with a programme of school-based activities to meet the participants' sensory needs as identified using the standardised measure. This intervention should be of the same intensity and have the same number of sessions as the primary intervention.

There should be blinded assessment of the individuals' sensory sensitivity, pre- and post-intervention, using primary measures specified at the outset of the study and standardised assessment of parent-reported change in repetitive, stereotypical behaviours including motor mannerisms such as hand flapping or spinning. Secondary outcomes may include change in on-task behaviour as observed by a blinded assessor measuring amount of time taken on tasks in the classroom. The research will also need to include the systematic monitoring of any adverse effects during the course of the intervention and a health economic analysis. Investigators should also consider any ongoing support in order to maintain any observed gains after the initial treatment period.