National Institute for Health and Care Excellence

Draft for Consultation

Attention deficit hyperactivity disorder (update)

[A] Evidence reviews for risk factors for ADHD

NICE guideline CG72

Prognostic evidence review

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This evidence review was developed by the National Guideline Centre

Disclaimer

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

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ISBN:

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1 Risk factors for ADHD

1.1 Review question: Which groups of people are more likely than the general population to have ADHD or are more likely to have missed a diagnosis of ADHD?

1.2 Introduction

Although ADHD is a multifaceted condition that has different types of behavioural symptoms, the popular view of symptoms as mainly related to hyperactivity has led to under- diagnosis in certain populations. This chapter looks at the evidence for increased risk of ADHD in certain populations. Here risk refers to populations in which ADHD occurs at higher rates than in the general population, and where practitioners need to be alert to the diagnosis of ADHD.

There are two main reasons to raise awareness of ADHD in populations at high risk of ADHD. First, the overlap of symptoms with other neurodevelopmental and mental health problems can lead to diagnostic overshadowing and a failure to appropriately diagnosis and treat ADHD. Another problem is failure to identify and treat conditions co-existing with ADHD.

The findings on risk are therefore intended to identify the populations in which practitioners need to pay particular attention to the possibility of ADHD. Here screening for ADHD or how best to diagnose ADHD in the presence of co-existing conditions is not considered, the aim is to raise awareness among practitioners of the circumstances under which there is an increased risk of ADHD.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	Children, young people and adults

Prognostic variables under consideration	• Comorbidities/personal medical history
	  ○ Neurodevelopmental disorders
	  ○ Intellectual disability
	  ○ Autism spectrum disorder (ASD)
	  ○ Mental health disorders
	  ○ Preterm children
	• Social/environmental factors
	  ○ Looked after children
	  ○ Secure estate
	  ○ Children not in mainstream schooling
	  ○ Adults with unstable employment
	• Family history of ADHD
	• Female*

Confounding factors	No critical confounding factors were included in this review. The purpose was to identify those at higher risk of ADHD in the general, primary care population and not to prove causality or definitive association. The risk of bias and indirectness ratings have taken into account this impact and the implications discussed by the committee in forming recommendations.
Outcomes	• Diagnosis of ADHD by healthcare professional or trained lay interviewer

	• Missed diagnosis of ADHD *Only missed diagnosis outcome to be extracted for gender risk, as increased prevalence in boys/men compared to girls/women is an accepted aspect of ADHD epidemiology and not priority for this review.
Study design	• Studies including a general population and assessing prevalence • Studies assessing ADHD diagnosis rates in matched cohorts

1.4 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual.[186] Methods specific to this review question are described in the review protocol in appendix A.

Studies were pooled in this review as default given the lack of importance attached to confounders, however random effects meta-analysis was used to reflect the likely imprecision in effect sizes. Where studies were pooled and substantial heterogeneity was observed, studies were separated and downgraded for inconsistency.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy.

1.5 Clinical evidence

1.5.1 Included studies

Sixteen studies were included in the review;[13,18,44,51,61,65,81,84,139,155,172,189,225,229,261,286] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3). See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E, GRADE tables in appendix F and excluded studies list in appendix I.

Thirteen studies assessed ADHD diagnosis in childhood (aged 5 to 18) and four studies assessed ADHD diagnosis in adulthood (one study provided information on both children and young people 5 years and over and adults). No studies reported on missed ADHD diagnoses.

1.5.2 Excluded studies

See the excluded studies list in appendix I.

1.5.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Population	Prognostic variable(s)	Outcomes	Comments
Children and young people				
Anderson 1987[13]	General representative sample of children from Dunedin (New Zealand), n = 782 Age stratum – 5 to 18 (mean age interviewed 11)	Anxiety disorders CD/ODD	ADHD diagnosis Psychiatric interview (DISC-C (DSM-III))	Cross-sectional prevalence Univariable analysis

Study	Population	Prognostic variable(s)	Outcomes	Comments
Bora 2014[44]	Preterm group from regional hospital; control group selected from births occurring at same hospital and times as preterm group (New Zealand), n = 815 Age stratum – 5 to 18 (mean age interviewed 9)	Preterm children	ADHD diagnosis Psychiatric interview (DSM-IV)	Retrospective cohort study Univariable analysis
Burnett 2014[51]	Preterm group from state of Victoria; control group selected to match for mother's country of origin, health insurance and sex of the child (Australia), n = 560 Age stratum – 5 to 18 (mean age interviewed 18)	Preterm children	ADHD diagnosis Psychiatric interview (ChIPS (DSM-IV))	Retrospective cohort study Univariable analysis
Clark 1997[61]	Substance abuse group from adolescent substance abuse centre; control group recruited via advertisement and systematic community sampling (USA), n = 219 Age stratum – 5 to 18 (mean age interviewed 16)	Substance abuse	ADHD diagnosis Psychiatric interview (K-SADS (DSM-III-R))	Retrospective cohort study Univariable analysis
Costa 2015[65]	Epilepsy group consecutive patients treated in secondary care clinic; control group age, gender, SES matched - recruited from nearby primary school (Brazil), n = 73 Age stratum – 5 to 18 (mean age interviewed 11)	Epilepsy	ADHD diagnosis Psychiatric interview (DSM-IV)	Retrospective cohort study Univariable analysis
Elberling 2016[81]	Random sample of all children born around Copenhagen	ASD CD/ODD Mood disorders	ADHD diagnosis Trained lay interviewer	Cross-sectional prevalence

Study	Population	Prognostic variable(s)	Outcomes	Comments
	in the year 2000, sample enriched with 20% high risk group (Denmark), n = 1585 Age stratum – 5 to 18 (mean age interviewed 6)		(SDQ (ICD-10))	Univariable analysis
Emerson 2003[84]	Representative sample of children obtained from ONS (UK), n = 10438 Age stratum – 5 to 18 (interviewed between 5 and 15)	Intellectual disability	ADHD diagnosis Trained lay interviewer (DAWBA (ICD-10))	Cross-sectional prevalence Univariable analysis
Ford 2007[101]	Looked after group composed of random sample of all looked after children in UK, control group randomly sampled from child benefit register, n = 11691 Age stratum – 5 to 18 (interviewed when at least 11)	Looked after children	ADHD diagnosis Trained lay interviewer (DAWBA (ICD-10))	Retrospective cohort study Univariable analysis
Johnson 2010[139]	Preterm group composed of all surviving and consenting children born <26 weeks gestation in UK in 1995, control group from index classmates matched for sex, gender, age and ethnicity (UK), n = 321 Age stratum – 5 to 18 (mean age interviewed 11)	Preterm children	ADHD diagnosis Trained lay interviewer (DAWBA (ICD-10))	Retrospective cohort study Univariable analysis
Kurlan 2002[155]	General representative sample of children aged 9 to 17 (USA), n = 1596 Age stratum – 5 to 18 (interviewed between 9 and 17)	Tic disorders	ADHD diagnosis Psychiatric interview (DISC (DSM-IV))	Cross-sectional prevalence Univariable analysis
Neece 2011[189]	Samples drawn from Collaborative Family Study in California,	Intellectual disability	ADHD diagnosis	Retrospective cohort study

Study	Population	Prognostic variable(s)	Outcomes	Comments
	recruited both those with developmental delays and typical development; ID was defined by IQ <70 (USA), n = 228 Age stratum – 5 to 18 (mean age interviewed 8)		Psychiatric interview (DISC)	Univariable analysis
Roberts 2007[225]	Sample of households in Houston, oversampling for ethnic minorities (USA), n = 4175 Age stratum – 5 to 18 (interviewed between 11 and 17)	Substance abuse	ADHD diagnosis Trained lay interviewer (DISC-IV (DSM-IV))	Cross-sectional prevalence Univariable analysis
Romano 2005[229]	Random subsample of children from Quebec whose mothers had completed questionnaires in 1987 (Canada), n = 1201 Age stratum – 5 to 18 (mean age interviewed 15)	Mood disorders Anxiety disorders CD/ODD	ADHD diagnosis Trained lay interviewer (DISC-2.25 (DSM-IV))	Cross-sectional prevalence Univariable analysis
Adults				
Arias 2008[18]	Substance abuse group from larger genetic study and separately recruited control group (USA), n = 2466 Age stratum – over 18 (mean age interviewed 39)	Substance abuse	ADHD diagnosis Interview (SSADDA (DSM-IV))	Retrospective cohort study Univariable analysis
Marwaha 2015[172]	General representative sample of adults from English postcode file, stratified by region and socioeconomic characteristics (UK), n = 7403 Age stratum – over 18 (interviewed over age of 16)	Psychotic disorders	ADHD diagnosis Trained lay interviewer (ASRS (DSM-IV))	Cross-sectional prevalence Univariable analysis

Study	Population	Prognostic variable(s)	Outcomes	Comments
Stewart 2006[261]	FMH group recruited from Children and Adults with ADD association, clinic referrals, internet advertisements; control participants selected using random dialling procedure, matched on age, gender and area of residence (USA), n = 473 Age stratum – over 18 (mean age at interview approximately 30)	FMH of ADHD	ADHD diagnosis Trained lay interviewer (DSM-IV)	Retrospective cohort study Univariable analysis
Wozniak 1995[286]	Both groups recruited from pre-existing family genetic study (no other information provided) (USA), n = 523 Age stratum – provided information on both adults and children	FMH of ADHD	ADHD diagnosis Trained lay interviewer (DSM-III-R)	Retrospective cohort study Univariable analysis

1 See appendix D for full evidence tables.

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1.5.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: ADHD diagnosed at age 5 to 18

Risk factors	No of Participants (studies)	Quality of the evidence (GRADE)	Relative effect (95% CI)
Anxiety disorders	1877 (2 studies)	MODERATE[1] due to risk of bias	RR 3.59 (2.28 to 5.65)
ODD/CD	3502 (3 studies)	MODERATE[1] due to risk of bias	RR 6.96 (4.79 to 10.13)
Preterm birth	897 (3 studies)	MODERATE[2] due to indirectness	RR 2.35 (1.63 to 3.39)
Substance abuse (Clark 1997)	219 (1 study)	VERY LOW[1,2,3,4] due to risk of bias, inconsistency, indirectness, imprecision	RR 4.91 (2.01 to 11.99)
Substance abuse (Roberts 2007)	4175 (1 study)	VERY LOW[1,2,3,4] due to risk of bias, inconsistency, indirectness, imprecision	OR 1.60 (0.60 to 4.27)
Epilepsy	73 (1 study)	LOW[1,4] due to risk of bias, imprecision	RR 6.17 (0.78 to 48.71)
ASD	1585 (1 study)	MODERATE[1] due to risk of bias	RR 39.97 (17.85 to 89.53)
Mood disorders (Elberling 2016)	1585 (1 study)	VERY LOW[1,3,4] due to risk of bias, inconsistency, imprecision	RR 12.25 (4.67 to 32.13)
Mood disorders (Romano 2005)	1131 (1 study)	VERY LOW[1,3,4] due to risk of bias, inconsistency, imprecision	RR 1.56 (0.63 to 3.86)
Intellectual disability	10666 (2 studies)	LOW[1,3] due to risk of bias, inconsistency	RR 6.2 (2.39 to 16.12)
Tic disorder	1596	MODERATE[1]	RR 1.97

Risk factors	No of Participants (studies)	Quality of the evidence (GRADE)	Relative effect (95% CI)
	(1 study)	due to risk of bias	(1.65 to 2.35)
FMH of ADHD	153 (1 study)	VERY LOW[4,5] due to risk of bias, imprecision	RR 2.25 (0.88 to 5.79)
Looked after children	11691 (1 study)	HIGH	RR 7.76 (6.02 to 10.01)

1 Downgraded once as majority of evidence at high risk of bias (see evidence tables for more information)
2 Downgraded once due to indirectness of population (see evidence tables for more information)
3 Downgraded due to inconsistency as I squared ~ 75% when pooled with study of same risk factor
4 Downgraded due to imprecision as confidence intervals crossed the line of no effect
5 Downgraded twice as majority of evidence at very high risk of bias (see evidence tables)

Table 4: Clinical evidence summary: ADHD diagnosed at age >18

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Substance abuse	2466 (1 study)	LOW[1] due to risk of bias	RR 6.14 (2.7 to 13.95)
Psychotic disorders	7325 (1 study)	MODERATE[2] due to risk of bias	RR 22.51 (8.43 to 60.14)
FMH of ADHD	843 (2 studies)	LOW[1] due to risk of bias	RR 2.33 (1.23 to 4.4)

1 Downgraded twice as majority of evidence at very high risk of bias (see evidence tables)
2 Downgraded once as majority of evidence at high risk of bias (see evidence tables)

See appendix F for full GRADE tables.

1.6 Economic evidence

1.6.1 Included studies

No relevant health economic studies were identified.

1.6.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix G.

1.7 Resource impact

We do not expect recommendations resulting from this review area to have a significant impact on resources.

1.8 Evidence statements

1.8.1 Clinical evidence statements

ADHD diagnosed at age 5 to 18, there was an increased risk of ADHD diagnosis in children and young people with:

- Anxiety disorders, two studies of 1877 people (Moderate quality)
- ODD/CD, three studies of 3502 (Moderate quality)
- Prematurity, three studies of 897 people (Moderate quality)
- Substance abuse disorders, two studies of 4394 people (Very low quality)
- Epilepsy, one study of 73 people(Low quality)
- ASD, one study of 1585 people (Moderate quality)
- Mood disorders, two studies of 2716 people (Very low quality)
- Intellectual disability, two studies of 10666 people (Low quality)
- Tic disorder, one study of 1596 people (Moderate quality)
- Family history of ADHD, one study of 153 people (Very low quality)
- Looked after status, one study of 11691 people (High quality)

ADHD diagnosed at age >18, there was an increased risk of ADHD diagnosis in adults with:

- Substance abuse, one study of 2466 people, (Low quality)
- Psychotic disorders, one study of 7325 people, (Moderate quality)
- Family history of ADHD, two studies of 843 people (Low quality)

1.8.2 Health economic evidence statements

- No relevant economic evaluations were identified.

1.9 Recommendations

A1. Be aware that people in the following groups may have increased prevalence of ADHD compared with the general population:

- people born preterm (see NICE's guideline on developmental follow-up of children and young people born preterm)
- looked-after children and young people
- children and young people with oppositional defiant disorder or conduct disorder
- children and young people with mood disorders (for example, anxiety, and depression)
- people with a close family member diagnosed with ADHD
- people with epilepsy
- people with neurodevelopmental disorders [for example, autism spectrum disorder, tic disorders, learning disability (intellectual disability) and specific learning difficulties

- adults with a mental health condition (for example, psychosis)
- people with a history of substance misuse
- people within the secure estate
- people with acquired brain injury.

A2. Be aware that ADHD is thought to be under-recognised in girls and women and that they are:

- less likely to be referred for assessment for ADHD
- more likely to have undiagnosed ADHD
- more likely to receive an incorrect diagnosis of another mental health or neurodevelopmental condition.

1.10 Rationale and impact

1.10.1 Why the committee made the recommendations

Evidence showed that the prevalence of ADHD is higher in some groups than in the general population. The committee agreed that a recommendation was needed to raise awareness of these groups among non-specialists to help them avoid missing a diagnosis of ADHD. Although no evidence was identified for a higher prevalence in people within the secure estate and people with acquired brain injury, the committee agreed that in their experience these groups often receive a late diagnosis of ADHD or a misdiagnosis. No evidence was found on the increased risk of missing a diagnosis of ADHD in girls. But the committee discussed the different symptoms often found in this group, and agreed to make a recommendation to raise awareness.

1.10.2 Why we need recommendations on this topic

Although there is an established pathway for the identification and diagnosis of ADHD, there is still concern amongst ADHD specialists that diagnoses are missed in some groups where there is evidence that ADHD rates are higher than the general population. In the Committee's opinion, diagnostic overshadowing is common. Recommendations to raise awareness are needed to help non ADHD specialists to identify people in whom a diagnosis of ADHD is likely, but perhaps where ADHD symptoms are more difficult to recognise or to distinguish from another co–existing condition. Girls are more likely to present with symptoms other than hyperactivity.

This missed opportunity to recognise ADHD results in some people and their families having delayed access to effective treatment and support for their ADHD symptoms and some people may never get access to ADHD treatment. Not recognising ADHD symptoms risks more negative attributions of behaviour for the individual. Appropriate treatment for ADHD symptoms has benefits in both the short and long term in reducing the impairment that ADHD symptoms can have in all areas of people's lives.

1.10.3 Impact of the recommendations on practice

The recommendations are to raise awareness among non-specialists of a possible diagnosis of ADHD in groups of people that they are already seeing. The recommendations may increase the rates of diagnosis and referral for ADHD, but these should be accurate and therefore appropriate diagnoses and management..

1.11 The committee's discussion of the evidence

1.11.1 Interpreting the evidence

1.11.1.1 The outcomes that matter most

The committee considered increased prevalence rates of ADHD and increased rates of missed diagnoses to be critical outcomes in identifying at risk groups. Identifying groups that have higher rates of ADHD than the general population should raise awareness about people who are likely more likely to have ADHD. Identifying groups with high rates of missed diagnosis will raise awareness about people who are less likely to receive a diagnosis of ADHD, regardless of prevalence. No evidence was identified for the outcome of missed diagnoses.

1.11.1.2 The quality of the evidence

The evidence ranged from moderate to very low quality. The included evidence did not adjust for any confounding factors. This was a deliberate feature of the analysis in the guideline as the aim of the review was not to show causality but to identify risk factors that, in the population seen in primary care, may act as a marker to suggest a higher likelihood of ADHD.

The committee noted that the limitation of this strategy meant that little could be drawn from the magnitudes of association and no statements about causality could be made based on the evidence..

The committee agreed that the quality of the evidence was sufficient to make new recommendations to highlight particular groups that may merit increased attention from healthcare professionals to the possibility of exploring an ADHD diagnosis.

1.11.1.3 Benefits and harms

The committee noted that the benefits of identifying groups that are at higher risk of ADHD or having a missed diagnosis of ADHD than the general population would include reducing missed diagnoses and diagnostic overshadowing. This would result in people being offered and receiving treatment appropriate for their ADHD symptoms, reducing impairment and improving their quality of life.

A potential harm of identifying these groups, raising awareness and increasing diagnosis rates is an increase in rates of false diagnoses and some people receiving treatment that is not appropriate.

The committee considered that the benefits outweighed the harms. From the committee's experience, it is clear quite rapidly if medication for ADHD is effective and so if a false diagnosis had occurred this would be quickly identified and ineffective treatment stopped. The risks of treatment in the short term are relatively low compared to the benefits of more people receiving a correct diagnosis and treatment.

1.11.2 Cost effectiveness and resource use

No economic evidence was identified for this question.

The recommendations in relation to this question are intended to raise awareness about particular populations that may be underdiagnosed or misdiagnosed.

The committee noted that these recommendations have little in the way of costs or harms as they do not recommend a specific intervention and are intended to remind healthcare

professionals to be vigilant for the possibility of ADHD or a missed diagnosis of ADHD. There may be an impact from these recommendations if better identification leads on to a diagnosis of ADHD and then there is a potential resource use associated with specialist diagnoses and treatments for ADHD being initiated. Identifying misdiagnosis has the potential to be cost neutral, if the treatments that are stopped and the appropriate ones initiated have similar costs and resource use.

1.11.3 Other factors the committee took into account

The committee noted that girls and women are less likely to present with hyperactivity symptoms and as a consequence are less likely to be identified and referred for assessment than boys. They therefore made a separate recommendation to be aware of this based on their experience.

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Appendices

Appendix A: Review protocols

Table 5: Review protocol: Risk factors for ADHD

Field	Content
Review question	Which groups of people are more likely than the general population to have ADHD or are more likely to have missed a diagnosis of ADHD?
Type of review question	Prognostic
Objective of the review	To identify groups of people in whom ADHD is more prevalent than the general population, to encourage clinicians to actively consider whether people in their care may have ADHD
Eligibility criteria – population / disease / condition / issue / domain	Children, young people and adults with ADHD
Eligibility criteria – prognostic factor(s)	• Comorbidities/personal medical history ○ Neurodevelopmental disorders ○ Intellectual disability ○ ASD ○ Mental health disorders ○ Preterm children • Social/environmental factors ○ Looked after children ○ Secure estate ○ Children not in mainstream schooling ○ Adults with unstable employment • Family history of ADHD • Female (only missed diagnoses outcomes) Key confounders: Raw effect sizes only – no confounders to be adjusted. Team and GC to pay particular attention to broader demographics and setting of participants
Outcomes and prioritisation	Formal research diagnoses of ADHD (i.e. diagnoses done as per validated diagnostic criteria on the basis of universally screening the population in question as opposed to incidental diagnoses from health care contacts) Missed diagnoses of ADHD (no diagnosis prior to assessment and new diagnosis after assessment)
Eligibility criteria – study design	Studies in which participants are divided into two groups by the presence/absence of a specified risk factor from the list specified by the GC and all participants are formally assessed for a research diagnosis of ADHD, including both cohort and cross-sectional prevalence studies.
Other inclusion exclusion criteria	Exclusions: Studies in which ADHD diagnosis is based purely on self-report/questionnaire (minimum lay interviewer diagnosis) or ADHD diagnosis is based on previously noted diagnoses and whole population is not formally assessed Cross-sectional prevalence studies including a population that is selected so as not to be generally representative of the primary care population

Proposed sensitivity / subgroup analysis, or meta-regression	All meta-analyses to use random effects on the basis of likely presence of confounders No subgroup analysis was done
Selection process – duplicate screening / selection / analysis	A sample of at least 10% of the abstract lists were double-sifted by a senior research fellow and discrepancies rectified, with committee input where consensus could not be reached, for more information please see the separate Methods report for this guideline.
Data management (software)	• Pairwise meta-analyses were performed using Cochrane Review Manager (RevMan5). • GRADEpro was used to assess the quality of evidence for each outcome. • Endnote for bibliography, citations, sifting and reference management
Information sources – databases and dates	Clinical search databases to be used: Medline, Embase, Cochrane Library,PsycINFO Date: From 1978 Health economics search databases to be used: Medline, Embase, NHSEED, HTA Date: Medline, Embase from 2014 NHSEED, HTA – from 2008 Language: Restrict to English only Supplementary search techniques: backward citation searching Key papers: Not known
Identify if an update	Not an update
Author contacts	https://www.nice.org.uk/guidance/cg72
Highlight if amendment to previous protocol	Not an amendment to previous protocol
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see the separate Methods report for this guideline. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report for this guideline.
Meta-bias assessment – publication bias, selective	For details please see section 6.2 of Developing NICE guidelines: the manual.

reporting bias	
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Gillian Baird in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

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2 **Table 6: Health economic review protocol**

Review question	**All questions – health economic evidence**
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	Populations, interventions and comparators must be as specified in the clinical review protocols in appendix A above. Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) Unpublished reports will not be considered unless submitted as part of a call for evidence. Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B. For questions being updated, the search will be run from December 2007, which was the cut-off date for the searches conducted for NICE guideline CG72
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2001, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published after 2001 that were included in the previous guideline will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[186] Inclusion and exclusion criteria

Review question	All questions – health economic evidence
	If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. Where there is discretion The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation as excluded health economic studies in appendix I. The health economist will be guided by the following hierarchies. Setting: UK NHS (most applicable). OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). OECD countries with predominantly private health insurance systems (for example, Switzerland). Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. Health economic study type: Cost–utility analysis (most applicable). Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). Comparative cost analysis. Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. Year of analysis: The more recent the study, the more applicable it will be. Studies published in 2001 or later (including any such studies included in the previous guideline) but that depend on unit costs and resource data entirely or predominantly from before 2001 will be rated as 'Not applicable'. Studies published before 2001 (including any such studies included in the previous guideline) will be excluded before being assessed for applicability and methodological limitations. Quality and relevance of effectiveness data used in the health economic analysis: The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline. Economic evaluations that are based on studies excluded from the clinical review will be excluded.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual, Oct 2014, updated 2017 https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches for this review were run in Medline (OVID), Embase (OVID), the Cochrane Library (Wiley). and PsycINFO (ProQuest]. Filters were applied where appropriate.

Table 7: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1978 – 28 April 2017	Exclusions
Embase (OVID)	1978 – 28 April 2017	Exclusions
The Cochrane Library (Wiley)	Cochrane Reviews 1978 to 2017 Issue 4 of 12 CENTRAL 1978 to 2017 Issue 3 of 12 DARE and NHSEED 1978 to 2015 Issue 1 of 4 HTA 1978 to 2017 Issue 1 of 4	None
PsycINFO (ProQuest)	1978 – 28 April 2017	Exclusions

Medline (Ovid) search terms

1.	"attention deficit and disruptive behavior disorders"/ or attention deficit disorder with hyperactivity/
2.	((attenti* or disrupt*) adj3 (adolescent* or adult* or behav* or child* or class or classes or classroom* or condition* or difficult* or disorder* or learn* or people or person* or poor or problem* or process* or youngster*)).ti.
3.	((attenti* or disrupt*) adj3 disorder*).ab.
4.	(adhd or addh or ad hd or ad??hd).ti,ab.
5.	(attenti* adj3 deficit*).ti,ab.
6.	(((hyperkin* or hyper kin*) adj1 (syndrome* or disorder*)) or hkd).ti,ab.
7.	(minimal brain adj2 (dysfunct* or disorder*)).ti,ab.
8.	or/1-7
9.	limit 8 to English language
10.	letter/
11.	editorial/
12.	news/
13.	exp historical article/
14.	Anecdotes as Topic/
15.	comment/
16.	case report/

17.	(letter or comment*).ti.
18.	or/10-17
19.	randomized controlled trial/ or random*.ti,ab.
20.	18 not 19
21.	animals/ not humans/
22.	Animals, Laboratory/
23.	exp animal experiment/
24.	exp animal model/
25.	exp Rodentia/
26.	(rat or rats or mouse or mice).ti.
27.	or/20-26
28.	9 not 27
29.	incidence/ or prevalence/
30.	Epidemiology/
31.	(prevalen* or incidence* or epidemiolog*).ti,ab.
32.	or/29-31
33.	28 and 32

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2 **Embase (Ovid) search terms**

1.	*attention deficit disorder/
2.	((attenti* or disrupt*) adj3 (adolescent* or adult* or behav* or child* or class or classes or classroom* or condition* or difficult* or disorder* or learn* or people or person* or poor or problem* or process* or youngster*)).ti.
3.	((attenti* or disrupt*) adj3 disorder*).ab.
4.	(adhd or addh or ad hd or ad??hd).ti,ab.
5.	(attenti* adj3 deficit*).ti,ab.
6.	(((hyperkin* or hyper kin*) adj1 (syndrome* or disorder*)) or hkd).ti,ab.
7.	(minimal brain adj2 (dysfunct* or disorder*)).ti,ab.
8.	or/1-7
9.	limit 8 to English language
10.	letter.pt. or letter/
11.	note.pt.
12.	editorial.pt.
13.	case report/ or case study/
14.	(letter or comment*).ti.
15.	or/10-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animal/ not human/
19.	nonhuman/
20.	exp Animal Experiment/
21.	exp Experimental Animal/
22.	animal model/
23.	exp Rodent/
24.	(rat or rats or mouse or mice).ti.

25.	or/17-24
26.	9 not 25
27.	epidemiology/ or incidence/ or prevalence/
28.	(prevalen* or incidence* or epidemiolog*).ti,ab.
29.	27 or 28
30.	26 and 29

Cochrane Library (Wiley) search terms

#1.	[mh ^"attention deficit and disruptive behavior disorders"]
#2.	[mh ^"attention deficit disorder with hyperactivity"]
#3.	((attenti* or disrupt*) near/3 (adolescent* or adult* or behav* or child* or class or classes or classroom* or condition* or difficult* or disorder* or learn* or people or person* or poor or problem* or process* or youngster*)):ti
#4.	((attenti* or disrupt*) near/3 disorder*):ab
#5.	(adhd or addh or ad next hd or ad-hd):ti,ab
#6.	(attenti* near/3 deficit*):ti,ab
#7.	(((hyperkin* or (hyper next kin*)) near/1 (syndrome* or disorder*)) or hkd):ti,ab
#8.	(minimal next brain near/2 (dysfunct* or disorder*)):ti,ab
#9.	(or #1-#8)
#10.	[mh ^incidence]
#11.	[mh ^prevalence]
#12.	[mh ^Epidemiology]
#13.	(prevalen* or incidence* or epidemiolog*):ti,ab
#14.	(or #10-#13)
#15.	#9 and #14

PsycINFO (ProQuest) search terms

1.	SU.EXACT.EXPLODE("Attention Deficit Disorder") OR TI((attenti* OR disrupt*) NEAR/3 (adolescent* OR adult* OR behav* OR child* OR class OR classes OR classroom* OR condition* OR difficult* OR disorder* OR learn* OR people OR person* OR poor OR problem* OR process* OR youngster*)) OR AB((attenti* OR disrupt*) NEAR/3 disorder*) OR TI,AB(adhd OR addh OR ad-hd OR ad??hd) OR TI,AB(attenti* NEAR/3 deficit*) OR TI,AB(((hyperkin* OR (hyper-kin*)) NEAR/1 (syndrome* OR disorder*)) OR hkd) OR TI,AB(minimal NEAR/1 brain NEAR/2 (dysfunct* OR disorder*))
2.	SU.EXACT("Epidemiology") or TI,AB(prevalen* or incidence* or epidemiolog*)
3.	1 AND 2
4.	NOT (Dissertations & Theses AND Books)
5.	English (limit)

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to ADHD population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase.

Table 8: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 28 April 2017	Exclusions Health economics
Embase	2014 – 28 April 2017	Exclusions Health economics
Centre for Research and Dissemination (CRD)	HTA - 2008 – 28 April 2017 NHSEED - 2008 to March 2015	None

Medline (Ovid) search terms

1.	"attention deficit and disruptive behavior disorders"/ or attention deficit disorder with hyperactivity/
2.	((attenti* or disrupt*) adj3 (adolescent* or adult* or behav* or child* or class or classes or classroom* or condition* or difficult* or disorder* or learn* or people or person* or poor or problem* or process* or youngster*)).ti.
3.	((attenti* or disrupt*) adj3 disorder*).ab.
4.	(adhd or addh or ad hd or ad??hd).ti,ab.
5.	(attenti* adj3 deficit*).ti,ab.
6.	(((hyperkin* or hyper kin*) adj1 (syndrome* or disorder*)) or hkd).ti,ab.
7.	(minimal brain adj2 (dysfunct* or disorder*)).ti,ab.
8.	or/1-7
9.	limit 8 to English language
10.	letter/
11.	editorial/
12.	news/
13.	exp historical article/
14.	Anecdotes as Topic/
15.	comment/
16.	case report/
17.	(letter or comment*).ti.
18.	or/10-17
19.	randomized controlled trial/ or random*.ti,ab.
20.	18 not 19
21.	animals/ not humans/
22.	Animals, Laboratory/
23.	exp animal experiment/
24.	exp animal model/
25.	exp Rodentia/
26.	(rat or rats or mouse or mice).ti.
27.	or/20-26
28.	9 not 27
29.	Economics/
30.	Value of life/
31.	exp "Costs and Cost Analysis"/
32.	exp Economics, Hospital/

33.	exp Economics, Medical/
34.	Economics, Nursing/
35.	Economics, Pharmaceutical/
36.	exp "Fees and Charges"/
37.	exp Budgets/
38.	budget*.ti,ab.
39.	cost*.ti.
40.	(economic* or pharmaco?economic*).ti.
41.	(price* or pricing*).ti,ab.
42.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
43.	(financ* or fee or fees).ti,ab.
44.	(value adj2 (money or monetary)).ti,ab.
45.	or/29-44
46.	exp models, economic/
47.	*Models, Theoretical/
48.	*Models, Organizational/
49.	markov chains/
50.	monte carlo method/
51.	exp Decision Theory/
52.	(markov* or monte carlo).ti,ab.
53.	econom* model*.ti,ab.
54.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
55.	or/46-54
56.	28 and (45 or 55)

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2 **Embase (Ovid) search terms**

1.	attention deficit disorder/
2.	((attenti* or disrupt*) adj3 (adolescent* or adult* or behav* or child* or class or classes or classroom* or condition* or difficult* or disorder* or learn* or people or person* or poor or problem* or process* or youngster*)).ti.
3.	((attenti* or disrupt*) adj3 disorder*).ab.
4.	(adhd or addh or ad hd or ad??hd).ti,ab.
5.	(attenti* adj3 deficit*).ti,ab.
6.	(((hyperkin* or hyper kin*) adj1 (syndrome* or disorder*)) or hkd).ti,ab.
7.	(minimal brain adj2 (dysfunct* or disorder*)).ti,ab.
8.	or/1-7
9.	limit 8 to English language
10.	letter.pt. or letter/
11.	note.pt.
12.	editorial.pt.
13.	case report/ or case study/
14.	(letter or comment*).ti.
15.	or/10-14

16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animal/ not human/
19.	nonhuman/
20.	exp Animal Experiment/
21.	exp Experimental Animal/
22.	animal model/
23.	exp Rodent/
24.	(rat or rats or mouse or mice).ti.
25.	or/17-24
26.	9 not 25
27.	statistical model/
28.	exp economic aspect/
29.	27 and 28
30.	*theoretical model/
31.	*nonbiological model/
32.	stochastic model/
33.	decision theory/
34.	decision tree/
35.	monte carlo method/
36.	(markov* or monte carlo).ti,ab.
37.	econom* model*.ti,ab.
38.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
39.	or/29-38
40.	*health economics/
41.	exp *economic evaluation/
42.	exp *health care cost/
43.	exp *fee/
44.	budget/
45.	funding/
46.	budget*.ti,ab.
47.	cost*.ti.
48.	(economic* or pharmaco?economic*).ti.
49.	(price* or pricing*).ti,ab.
50.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
51.	(financ* or fee or fees).ti,ab.
52.	(value adj2 (money or monetary)).ti,ab.
53.	or/40-52
54.	26 and (39 or 53)

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2 **NHS EED and HTA (CRD) search terms**

#1.	MeSH DESCRIPTOR Attention Deficit and Disruptive Behavior Disorders
#2.	MeSH DESCRIPTOR Attention Deficit Disorder with Hyperactivity
#3.	(((attenti* or disrupt*) adj3 (adolescent* or adult* or behav* or child* or class or classes or classroom* or condition* or difficult* or disorder* or learn* or people or person* or

	poor or problem* or process* or youngster*))):TI
#4.	(((attenti* or disrupt*) adj3 disorder*))
#5.	((adhd or addh or ad hd or ad??hd))
#6.	((attenti* adj3 deficit*))
#7.	((((hyperkin* or hyper kin*) adj1 (syndrome* or disorder*)) or hkd))
#8.	((minimal brain adj2 (dysfunct* or disorder*)))
#9.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
#10.	(#9) IN NHSEED, HTA

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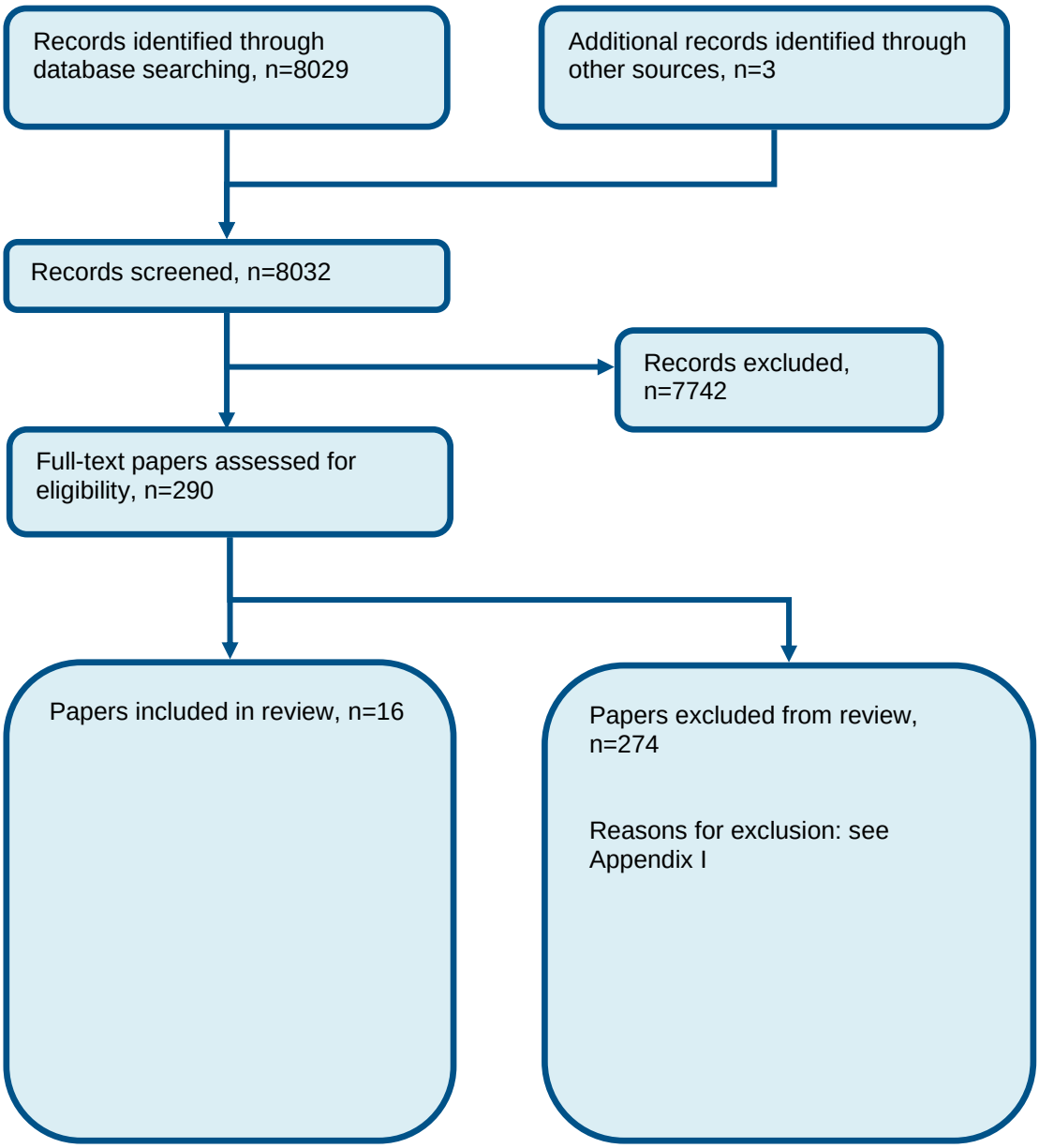
Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of ADHD risk factors



Appendix D: Clinical evidence tables

Reference	Anderson 1987[13,174]
Study type and analysis	Prevalence study using structured psychiatric interview with DISC-C (DSM-III), unadjusted data
Number of participants and characteristics	Total n = 782, representative sample of general population from New Zealand, 925 in original sample, 782 with interview data Children were 11 years old at interview New Zealand
Prognostic variable(s)	Anxiety disorders Oppositional defiant disorder/conduct disorder
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Anxiety disorders RR 4.40 (2.54 to 7.62) ODD/CD RR 6.69 (3.94 to 11.37)
Comments	Risk of bias low for anxiety disorders, ODD/CD

Reference	Arias 2008[18]
Study type and analysis	Cross-sectional cohort study using structured psychiatric interview with SSADDA (DSM-IV), unadjusted data
Number of participants and characteristics	Substance abuse group n = 1761, controls n = 705 Substance abuse group identified from larger genetic study, controls identified from group specifically chosen to provide controls for genetic study Mean age of participants was 39 at interview USA
Prognostic variable(s)	Substance abuse (opioid or cocaine abuse)
Confounders	No confounders adjusted for

strategy	
Outcomes and effect sizes	Substance abuse RR 6.14 (2.70 to 13.95)
Comments	Risk of bias very high for substance abuse due to selection and detection bias

Reference	**Bora 2014[44]**
Study type and analysis	Cross-sectional cohort study using structured psychiatric interview with DSM-IV, unadjusted data
Number of participants and characteristics	Preterm group n = 110, controls n = 705 Preterm group were consecutive preterm births at regional hospital, controls selected from same hospital as infant born second previously or after each index preterm birth Children were interviewed at 9 years old New Zealand
Prognostic variable(s)	Preterm birth (less than or equal to 32 weeks gestation)
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Preterm birth RR 2.16 (1.34 to 3.49)
Comments	Risk of bias low

Reference	**Burnett 2014[51]**
Study type and analysis	Cross-sectional cohort study using structured psychiatric interview with ChIPS (DSM-IV), unadjusted data
Number of participants and characteristics	Preterm group n = 298, controls n = 262 Preterm group were consecutive extremely premature/extremely low birth weight infants at from Victoria (Australia), controls were normal birthweight and selected from same region and matched for maternal ethnicity, sex of child and health insurance status Participants mean age at interview was 18 Australia

Prognostic variable(s)	Preterm birth (<28 weeks gestation or <1000g)
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Preterm birth RR 2.05 (1.06 to 3.96)
Comments	Risk of bias low Indirectness due to extremely preterm cut-off

Reference	**Clark 1997[61]**
Study type and analysis	Cross-sectional cohort study using structured psychiatric interview with K-SADS (DSM-III-R), unadjusted data
Number of participants and characteristics	Substance abuse group n = 133, controls n = 86 Substance abuse group from adolescent substance abuse centre, control group recruited through advertisements and systematic community sampling Participants mean age at interview was 16 USA
Prognostic variable(s)	Substance abuse (alcohol dependence)
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Substance abuse RR 2.05 (1.06 to 3.96)
Comments	Risk of bias high due to selection bias

Reference	**Costa 2014[65]**
Study type and analysis	Cross-sectional cohort study using structured psychiatric interview DSM-IV, unadjusted data
Number of participants	Epilepsy group n = 36, controls n = 37 Epilepsy group from consecutive attendances at outpatient clinic, control group age, gender, SES matched - recruited from nearby

and characteristics	primary school Participants mean age at interview was 11 Brazil
Prognostic variable(s)	Epilepsy
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Substance abuse RR 6.17 (0.78 to 48.71)
Comments	Risk of bias high due to selection bias

Reference	**Elberling 2016[81]**
Study type and analysis	Prevalence study using trained lay person interview with SDQ (ICD-10), unadjusted data
Number of participants and characteristics	Total n = 1585 Random sample of all children born in area around Copenhagen in 2000, 20% of sample selected to enrich group based on positive screening scores Interviews conducted at ages 5 to 7 Brazil
Prognostic variable(s)	ASD (pervasive developmental disorders) Mood disorders (emotional disorders) ODD/CD (behavioural disorders)
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	ASD RR 39.97 (17.85 to 89.53) Mood disorders RR 12.25 (4.67 to 32.13) ODD/CD RR 10.18 (3.17 to 32.71)
Comments	Risk of bias high due to selection bias, detection bias

Reference	Emerson 2003[84]
Study type and analysis	Prevalence study using trained lay person interview with DAWBA (ICD-10), unadjusted data , study split into population with and without intellectual disability and risk of being diagnosed with ADHD compared between groups.
Number of participants and characteristics	Total n = 10438 Stratified sample (ONSSSD) of all children aged 5 to 15 in the UK, 83% of target sample interviewed UK
Prognostic variable(s)	Intellectual disability
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	ID RR 9.63 (6.20 to 14.96)
Comments	Risk of bias low

Reference	Ford 2007[101]
Study type and analysis	Cross-sectional cohort study using structured psychiatric interview with DAWBA (ICD 10), unadjusted data
Number of participants and characteristics	Total n = 11691, looked after group (n = 1253) composed of random sample of all looked after children in UK, control group (n = 10438) randomly sampled from child benefit register Children were at least 11 years old at interview United Kingdom
Prognostic variable(s)	Looked after children
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Looked after children RR 7.76 (6.02 to 10.01)
Comments	Risk of bias low

Reference	Johnson 2010[139]

Study type and analysis	Cross-sectional cohort study using structured psychiatric interview with DAWBA (DSM-IV), unadjusted data
Number of participants and characteristics	Total n = 321 Premature birth group representing all surviving babies born at <26 weeks gestation in UK in 1995 with parental consent to participate in interview at age 11 (n = 183), control group selected at random from 3 term classmates closest in age and of the same sex and ethnicity (n = 138) not including for those children not in mainstream education UK
Prognostic variable(s)	Preterm birth (<26 weeks gestation)
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Pre term birth RR 9.63 (6.20 to 14.96)
Comments	Risk of bias high due to selection bias and detection bias Indirectness due to extremely preterm cut-off

Reference	**Kurlan 2002[155]**
Study type and analysis	Prevalence study using structured psychiatric interview with DISC (DSM-IV), unadjusted data
Number of participants and characteristics	Total n = 1596 1596 children aged 9 to 17 in 10 school districts in New York State, little additional information provided on selection of participants. Technician performed psychiatric interviewing for diagnosis of both tic disorders (n = 339) and ADHD. USA
Prognostic variable(s)	Tic disorders
Confounders strategy	No confounders adjusted for
Outcomes and	Tic disorders RR 1.97 (1.65 to 2.35)

effect sizes	
Comments	Risk of bias high due to selection bias and detection bias

Reference	**Marwaha 2015[172]**
Study type and analysis	Prevalence study using face to face interview with ASRS (DSM-IV), unadjusted data
Number of participants and characteristics	Total n = 7403 7403 adults aged over 16 identified from UK postcode file and stratified by socioeconomic data and ethnicity to provide representative sample, ADHD n = 39, psychosis n = 37 UK
Prognostic variable(s)	Psychotic disorders
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Psychotic disorders RR 22.51 (8.43 to 60.14)
Comments	Risk of bias high due to selection bias and detection bias

Reference	**Neece 2011[189]**
Study type and analysis	Cross-sectional cohort study using structured psychiatric interview with DISC, unadjusted data
Number of participants and characteristics	Total n = 228 Samples drawn from Collaborative Family Study in California, recruited both those with developmental delays and typical development; ID was defined by IQ <70 (n = 63) USA
Prognostic variable(s)	Intellectual disability

Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Intellectual disability RR 22.51 (8.43 to 60.14)
Comments	Risk of bias very high due to selection bias and detection bias

Reference	**Roberts 2007[225]**
Study type and analysis	Prevalence study using face to face interview with DISC-IV (DSM-IV), unadjusted data
Number of participants and characteristics	Total n = 4175 Samples drawn from Houston metropolitan area, children aged 11-17 with oversampling for ethnic minorities. Assessed ORs for substance abuse predicting psychiatric disorder in the previous year. USA
Prognostic variable(s)	Substance abuse (any substance abuse)
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Substance abuse OR 1.6 (0.6 to 4.6)
Comments	Risk of bias very high due to selection bias and detection bias

Reference	**Romano 2005[229]**
Study type and analysis	Prevalence study using face to face interview with DISC-2.25 (DSM-IV), unadjusted data
Number of participants and characteristics	Total n = 1201 Samples drawn from group of children in Canada whose mothers had completed questionnaire whilst they were in kindergarten in 1987, children were interviewed once between the ages of 14 to 17 (mean 15).

	USA
Prognostic variable(s)	Anxiety disorder (any) Mood disorder (depression) ODD/CD
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	Anxiety disorder RR 2.78 (1.48 to 5.23) Mood disorder RR 1.56 (0.63 to 3.86) ODD/CD RR 7.89 (4.39 to 14.15)
Comments	Risk of bias high due to detection bias and attrition bias

Reference	**Stewart 2006[261]**
Study type and analysis	Cross-sectional cohort study using structured psychiatric interview with DSM-IV criteria, unadjusted data
Number of participants and characteristics	Total n = 473 FMH group recruited from Children and Adults with ADD association (n = 319), clinic referrals, internet advertisements; control participants (n = 154) selected using random dialling procedure, matched on age, gender and area of residence. USA
Prognostic variable(s)	FMH of ADHD (FMH of ADHD +/- Tourette's disorder)
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	FMH of ADHD RR 1.74 (0.89 to 3.41)
Comments	Risk of bias high due to selection and detection bias

Reference	**Wozniak 1995[286]**
Study type and analysis	Cross-sectional cohort study using structured psychiatric interview with DSM-IV criteria, unadjusted data

Number of participants and characteristics	Total n = 523 FMH group (n = 211 (adults) and 92 (children and adolescents)) and control group (n = 159 (adults) and 61 (children)) recruited from pre-existing genetic study, no other information provided USA
Prognostic variable(s)	FMH of ADHD
Confounders strategy	No confounders adjusted for
Outcomes and effect sizes	FMH of ADHD (>18) RR 3.34 (1.51 to 7.38) FMH of ADHD (5 to 18) RR 2.25 (0.88 to 5.79)
Comments	Risk of bias very high due to selection and detection bias

Appendix E: Forest plots

E.1 ADHD diagnosis in childhood (aged 5 to 18)

Figure 2: Anxiety disorders

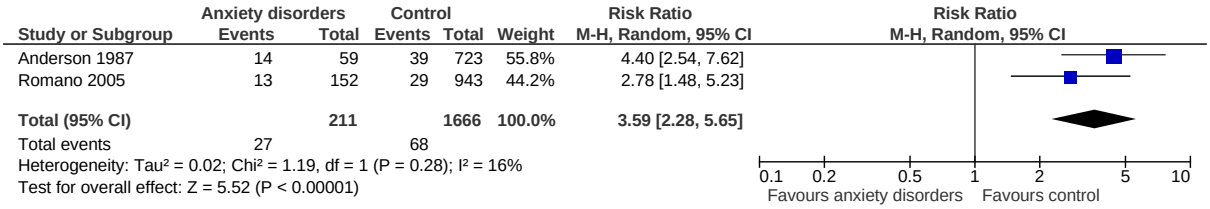


Figure 3: ODD/CD

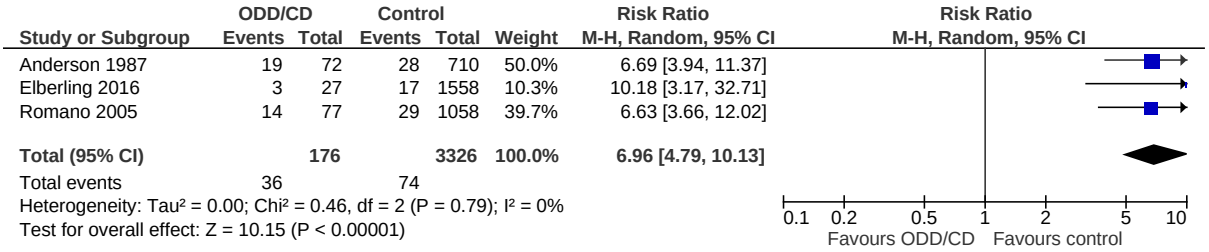


Figure 4: Premature birth

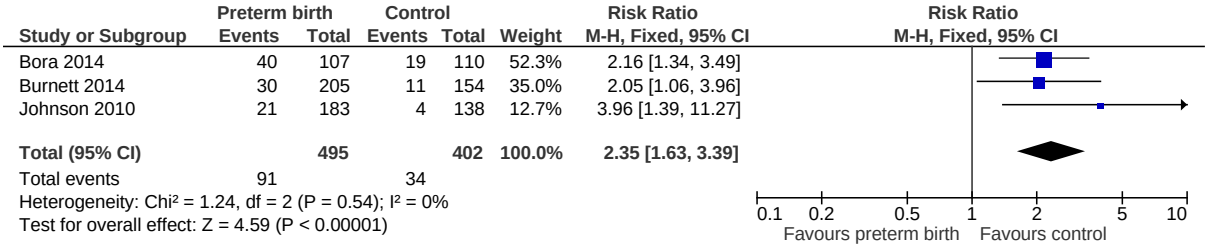


Figure 5: Substance abuse

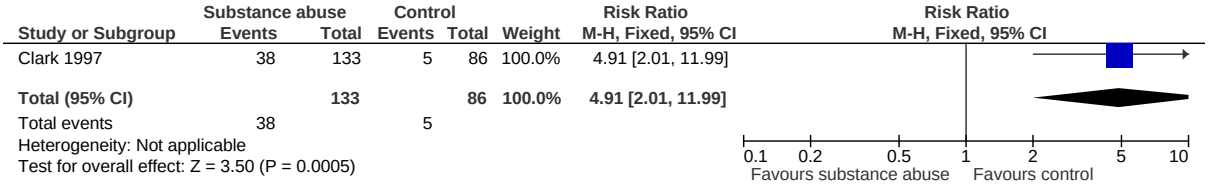
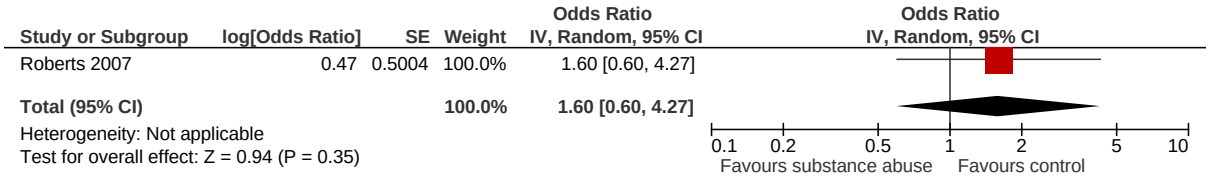
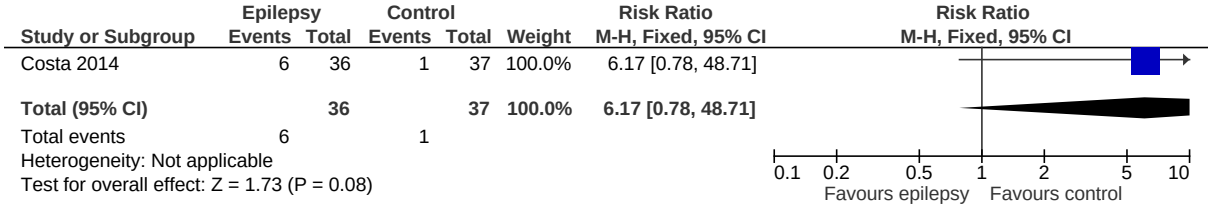


Figure 6: Substance abuse (Roberts 2007)



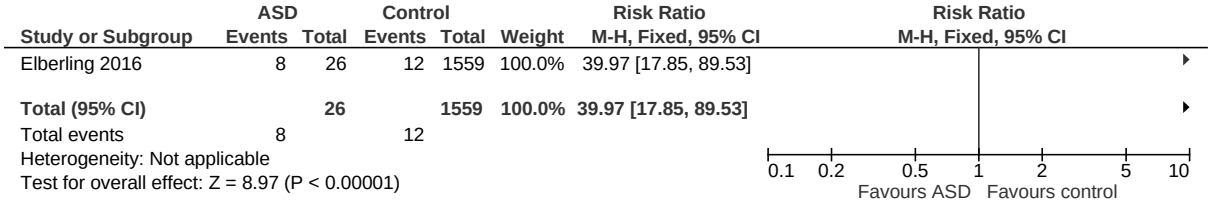
1

Figure 7: Epilepsy



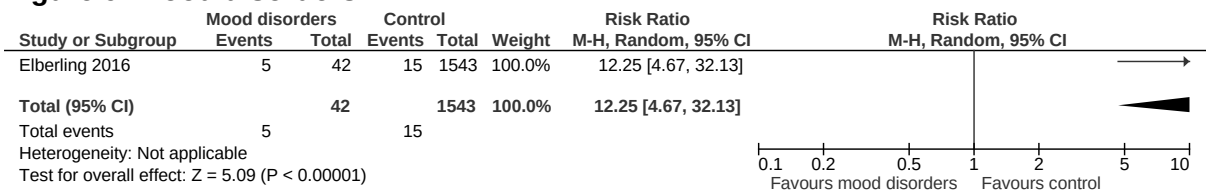
2

Figure 8: ASD



3

Figure 9: Mood disorders



4

Figure 10: Mood disorders

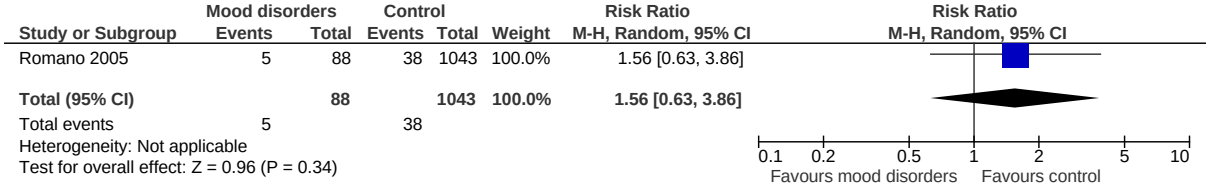
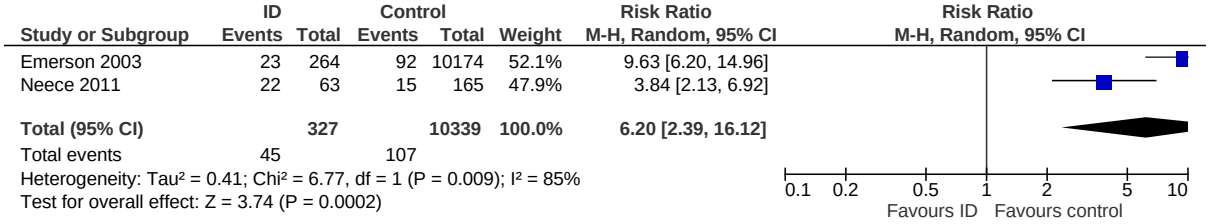
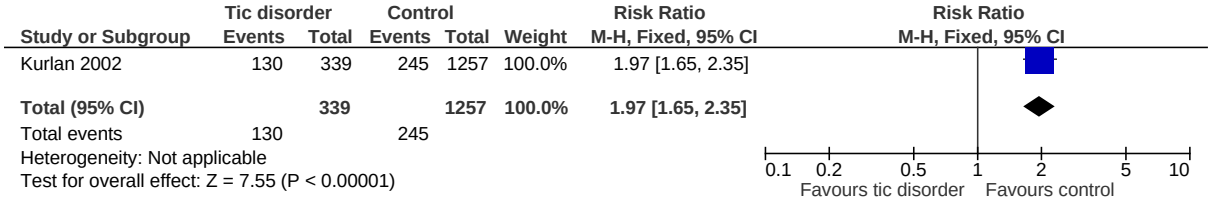


Figure 11: Intellectual disability



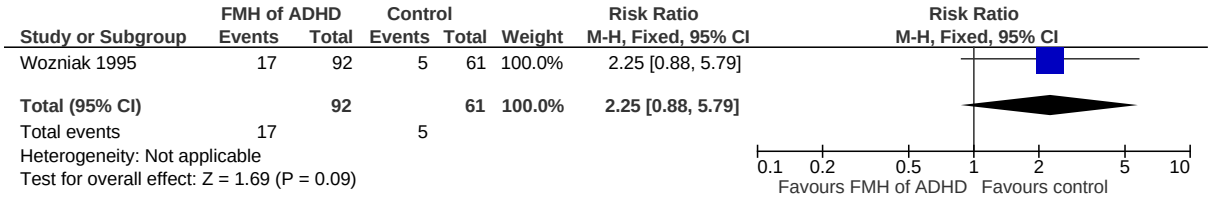
1

Figure 12: Tic disorder



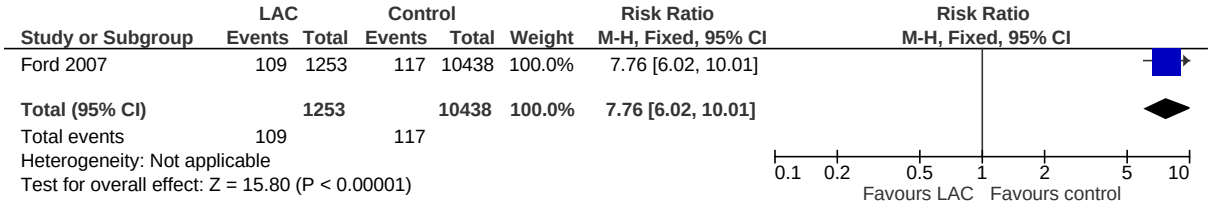
2

Figure 13: FMH of ADHD



3

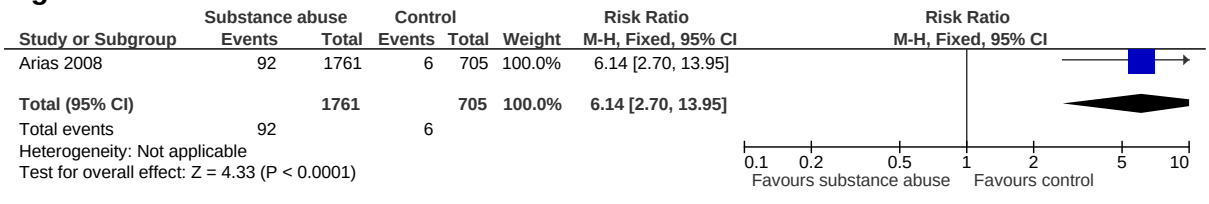
Figure 14: Looked after children



4

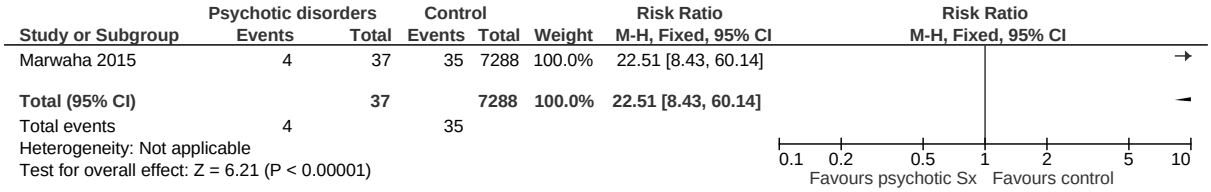
5 E.2 ADHD diagnosis in adulthood (aged >18)

Figure 15: Substance abuse



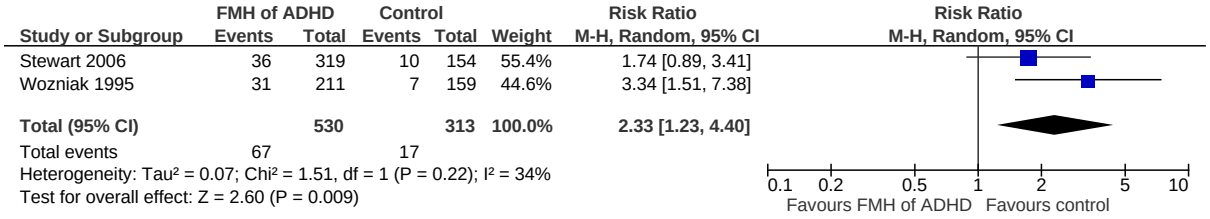
6

Figure 16: Psychotic disorders



1

Figure 17: FMH of ADHD



2

3

4

Appendix F:GRADE tables

Table 9: Clinical evidence profile: Children aged 5 to 18

Quality assessment							No of patients with ADHD		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risk factor	Control	Relative (95% CI)	Absolute		
Anxiety disorders												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	27/211 (12.8%)	68/1666 (4.1%)	RR 3.59 (2.28 to 5.65)	106 more per 1000 (from 52 more to 190 more)	⊕⊕⊕O MODERATE	CRITICAL
ODD/CD												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	36/176 (20.5%)	74/3326 (2.2%)	RR 6.96 (4.79 to 10.13)	133 more per 1000 (from 84 more to 203 more)	⊕⊕⊕O MODERATE	CRITICAL
Preterm birth												
3	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	91/495 (18.4%)	34/402 (8.5%)	RR 2.35 (1.63 to 3.39)	114 more per 1000 (from 53 more to 202 more)	⊕⊕⊕O MODERATE	CRITICAL
Substance abuse (Clark 1997)												
1	randomised trials	serious[1]	serious[3]	serious[2]	serious[4]	none	38/133 (28.6%)	5/86 (0.6%)	RR 4.91 (2.01 to 11.99)	227 more per 1000 (from 59 more to 639 more)	⊕OOO VERY LOW	CRITICAL
Substance abuse (Roberts 2007)												
1	randomised trials	serious[1]	serious[3]	serious[2]	serious[4]	none	-	-	OR 1.60 (0.60 to 4.27)	-	⊕OOO VERY LOW	CRITICAL

Epilepsy												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	6/36 (16.7%)	1/37 (2.7%)	RR 6.17 (0.78 to 48.71)	140 more per 1000 (from 6 fewer to 1000 more)	⊕⊕OO LOW	CRITICAL
ASD												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	8/26 (30.8%)	12/1559 (0.77%)	RR 39.97 (17.85 to 89.53)	300 more per 1000 (from 130 more to 681 more)	⊕⊕⊕O MODERATE	CRITICAL
Mood disorders (Elberling 2016)												
1	randomised trials	serious[1]	serious[3]	no serious indirectness	serious[4]	none	5/42 (11.9%)	15/1543 (0.97%)	RR 12.25 (4.67 to 32.13)	109 more per 1000 (from 36 more to 303 more)	⊕OOO VERY LOW	CRITICAL
Mood disorders (Romano 2005)												
1	randomised trials	serious[1]	serious[3]	no serious indirectness	serious[4]	none	5/88 (5.7%)	38/1043 (3.6%)	RR 1.56 (0.63 to 3.86)	20 more per 1000 (from 13 fewer to 104 more)	⊕OOO VERY LOW	CRITICAL
Intellectual disability												
2	randomised trials	serious[1]	serious[3]	no serious indirectness	no serious imprecision	none	45/327 (13.8%)	107/10339 (1%)	RR 6.2 (2.39 to 16.12)	54 more per 1000 (from 14 more to 156 more)	⊕⊕OO LOW	CRITICAL
Tic disorder												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	130/339 (38.3%)	245/1257 (19.5%)	RR 1.97 (1.65 to 2.35)	189 more per 1000 (from 127 more to 263 more)	⊕⊕⊕O MODERATE	CRITICAL
FMH of ADHD												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	17/92 (18.5%)	5/61 (8.2%)	RR 2.25 (0.88 to 5.79)	102 more per 1000 (from 10 fewer to 393 more)	⊕OOO VERY LOW	CRITICAL
Looked after children												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	109/1253 (8.7%)	117/10438 (1.1%)	RR 7.76 (6.02 to 10.01)	76 more per 1000 (from 56 more to 101 more)	⊕⊕⊕⊕ HIGH	CRITICAL

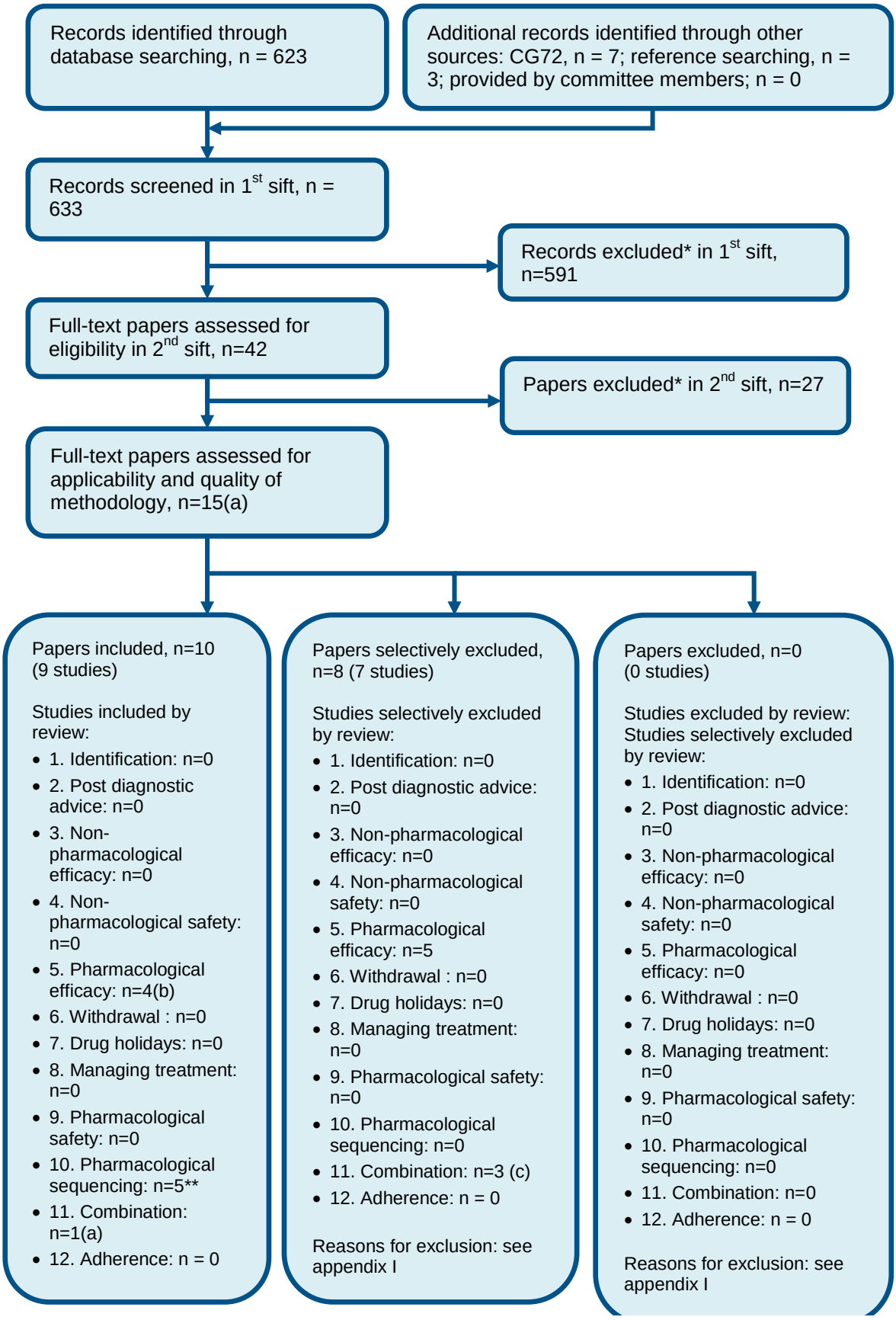
[1] Downgraded once as majority of evidence at high risk of bias or twice as majority of evidence at very high risk of bias (see evidence tables for more information)
[2] Downgraded once due to indirectness of population (see evidence tables for more information)
[3] Downgraded due to inconsistency as I squared ~ 75%
[4] Downgraded due to imprecision as confidence intervals crossed the line of no effect

Table 10: Clinical evidence profile: Adults over 18

Quality assessment							No of patients with ADHD		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Risk factor**	**Control**	**Relative (95% CI)**	**Absolute**		
Substance abuse												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	92/1761 (5.2%)	6/705 (0.85%)	RR 6.14 (2.7 to 13.95)	44 more per 1000 (from 14 more to 110 more)	⊕⊕OO LOW	
Psychotic disorders												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	4/37 (10.8%)	35/7288 (0.48%)	RR 22.51 (8.43 to 60.14)	103 more per 1000 (from 36 more to 284 more)	⊕⊕⊕O MODERATE	
FMH of ADHD												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67/530 (12.6%)	17/313 (5.4%)	RR 2.33 (1.23 to 4.4)	72 more per 1000 (from 12 more to 185 more)	⊕⊕OO LOW	

[1] Downgraded once as majority of evidence at high risk of bias or twice as majority of evidence at very high risk of bias (see evidence tables for more information)

Appendix G: Health economic evidence selection



* Non-relevant population, intervention, comparison, design or setting; non-English language

(a) note that there were 2 original models from the previous guideline (either included or excluded) which is why the numbers add to more than 15.

(b) Two articles identified were applicable to Q5 and Q10, for the purposes of this diagram it has been included under Q5 only.

(c) One of these is a model from the previous guideline that was exclude. Two articles identified were applicable to both Q5 and Q11 and have only been included here under Q11. One paper here was selectively excluded in Q11 but included in Q5 and so is double counted in this flowchart.

1

Appendix H: Health economic evidence tables

None.

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 11: Studies excluded from the clinical review

Reference	Reason for exclusion
Aarons 2008[1]	No usable outcomes
Abiodun 2011[2]	No usable outcomes
Al Hamed 2008[4]	No usable outcomes
Alfonsson 2013[5]	No usable outcomes
Alizadeh 2015[6]	No usable outcomes
Al-Mamari 2015[3]	No usable outcomes
Almeida Montes 2007[7]	Inappropriate population
Almqvist 1999[8]	No usable outcomes
Alpaslan 2015[9]	No usable outcomes
Alyanak 2011[203]	Not in English
Ambuabunos 2011[10]	No usable outcomes
Amiri 2014[12]	No usable outcomes
Amiri 2010[11]	No usable outcomes
Andreassen 2016[14]	No usable outcomes
Andres 1999[15]	No usable outcomes
Antshel 2016[16]	No usable outcomes
Antshel 2008[17]	No usable outcomes
Arnold 2005[19]	Inappropriate population
Arruda 2015[20]	No usable outcomes
August 1992[21]	Inappropriate population
August 1996[22]	Inappropriate population
Ayoub 2009[71]	No usable outcomes
Baker 2010[23]	No usable outcomes
Ballon 2015[24]	Inappropriate population
Bansal 2011[25]	No usable outcomes
Barbaresi 2004[26]	No usable outcomes
Barbaresi 2002[27]	No usable outcomes
Bellelli 2015[28]	No usable outcomes
Bener 2014[29]	Inadequate ADHD diagnosis
Bertelsen 2016[30]	Unable to access
Bhatia 1991[31]	Inappropriate population
Biederman 2012[33]	No usable outcomes
Biederman 2013[32]	No usable outcomes
Bijlenga 2013[34]	No usable outcomes
Bird 1994[35]	Inappropriate population
Birmaher 2010[36]	No usable outcomes
Birmaher 2009[37]	No usable outcomes

Reference	Reason for exclusion
Bishry 2014[38]	No usable outcomes
Bitter 2010[39]	No usable outcomes
Bittner 2007[40]	Inappropriate population
Black 2013[41]	No usable outcomes
Bleck 2013[42]	No usable outcomes
Bleck 2015[43]	Inadequate ADHD diagnosis
Boulet 2011[45]	Inadequate ADHD diagnosis
Boyle 1991[46]	No usable outcomes
Breslau 2000[47]	No usable outcomes
Brewerton 2016[48]	Inappropriate population
Brogan 2014[49]	No usable outcomes
Brook 1998[50]	No usable outcomes
Byrd 2013[52]	No usable outcomes
Canals 2016[53]	Inappropriate population
Cantwell 1991[54]	Systematic review not matching PICO
Capusan 2016[55]	Inadequate ADHD diagnosis
Chen 2007[56]	Inadequate ADHD diagnosis
Chen 2015[58]	No usable outcomes
Chou 2013[59]	Inadequate ADHD diagnosis
Chudal 2015[60]	No usable outcomes
Copeland 2013[62]	No usable outcomes
Cortese 2016[64]	No usable outcomes
Cortese 2013[63]	No usable outcomes
Costello 2003[66]	Inappropriate population
Cuffe 2001[67]	Inappropriate population
Cuffe 2015[68]	No usable outcomes
De Alwis 2014[69]	No usable outcomes
de Zwaan 2012[70]	Inadequate ADHD diagnosis
Disney 1999[72]	Inappropriate population
Dopfner 2008[74]	No usable outcomes
Dougherty 2014[75]	No usable outcomes
Dowson 2008[76]	No usable outcomes
DuPaul 2014[77]	No usable outcomes
Egan 2000[78]	No usable outcomes
El Marroun 2012[79]	Inadequate ADHD diagnosis
Elberling 2010[80]	No usable outcomes
Elgen 2013[82]	No usable outcomes
Elumour 2014[83]	No usable outcomes
Ercan 2016[85]	No usable outcomes
Ersan 2004[86]	No usable outcomes
Esser 1990[87]	No usable outcomes
Estevez 2014[88]	No usable outcomes
Eyestone 1994[89]	No usable outcomes
Ezpeleta 2014[90]	Inappropriate population
Famularo 1992[91]	Inappropriate population

Reference	Reason for exclusion
Farahat 2014[92]	No usable outcomes
Faraone 2000[93]	Inappropriate population
Faravelli 2009[94]	No usable outcomes
Farbstein 2014[95]	No usable outcomes
Fayyad 2016[97]	No usable outcomes
Fayyad 2007[96]	Inadequate ADHD diagnosis
Fevang 2016[98]	Inadequate ADHD diagnosis
Field 2014[99]	No usable outcomes
Fombonne 1994[100]	No usable outcomes
Fornaro 2013[102]	No usable outcomes
Fortes 2016[103]	No usable outcomes
Frank-Briggs 2010[104]	No usable outcomes
Freeman 2016[105]	Inappropriate population
Fullana 2013[106]	No usable outcomes
Gada 1987[107]	No usable outcomes
Gadow 2002[108]	Inadequate ADHD diagnosis
Gadow 2001[109]	No usable outcomes
George 2006[110]	No usable outcomes
Ghanizadeh 2008[111]	No usable outcomes
Ghossoub 2017[112]	No usable outcomes
Giacobini 2014[113]	Inadequate ADHD diagnosis
Gomez 2016[114]	No usable outcomes
Gonzalez-Heydrich 2012[115]	No usable outcomes
Gordon 2005[116]	Inappropriate population
Gordon 2014[117]	Inappropriate population
Gorlin 2016[118]	No usable outcomes
Gross-Tsur 1991[119]	No usable outcomes
Gudjonsson 2014[120]	No usable outcomes
Gudmundsson 2013[121]	No usable outcomes
Hack 2009[122]	Inadequate ADHD diagnosis
Halldner 2014[123]	No usable outcomes
Halmoy 2012[124]	No usable outcomes
Hanc 2015[125]	No usable outcomes
Hanprathet 2015[126]	No usable outcomes
Harris 2013[127]	Inadequate ADHD diagnosis
Hastings 2005[128]	No usable outcomes
Hauck 2017[129]	Inadequate ADHD diagnosis
Heiervang 2007[130]	Inappropriate population
Heneghan 2013[131]	No usable outcomes
Hernandez Vega 2015[276]	Inappropriate population
Hirschtritt 2015[132]	Inappropriate population
Hirshfeld-Becker 2006[133]	No usable outcomes
Hong-Chen 2013[57]	Inadequate ADHD diagnosis
Huang 2016[134]	Inadequate ADHD diagnosis
Huss 2008[135]	No usable outcomes

Reference	Reason for exclusion
Hysing 2016[136]	No usable outcomes
Indredavik 2004[137]	Results reported elsewhere
Ivanov 2013[138]	No usable outcomes
Kashala 2005[140]	No usable outcomes
Katusic 2005[141]	Inadequate ADHD diagnosis
Kay 2016[142]	No usable outcomes
Kerekes 2015[143]	No usable outcomes
Keshavan 2008[144]	No usable outcomes
Keshavan 2003[145]	No usable outcomes
Kessler 2005[146]	Results reported elsewhere
Khalifa 2005[147]	No usable outcomes
Kim 2015[148]	No usable outcomes
Kim 2017[149]	No usable outcomes
Kirino 2015[150]	No usable outcomes
Kolla 2016[151]	No usable outcomes
Korczak 2014[152]	No usable outcomes
Korsgaard 2016[153]	Inappropriate population
Kovess 2015[154]	No usable outcomes
Kwak 2015[156]	No usable outcomes
Lakhan 2013[157]	No usable outcomes
Landgren 1996[158]	Inappropriate population
Lavigne 2009[159]	No usable outcomes
Lecendreux 2015[160]	No usable outcomes
Lecendreux 2011[161]	No usable outcomes
Lee 2008[73]	No usable outcomes
Lehti 2016[162]	Inadequate ADHD diagnosis
Lindblad 2011[163]	No usable outcomes
Linnet 2006[164]	Inadequate ADHD diagnosis
Liu 2014[165]	No usable outcomes
Love 1988[166]	No usable outcomes
Lumley 2002[167]	No usable outcomes
Lund 2011[168]	No usable outcomes
Lundstrom 2015[169]	No usable outcomes
Manor 2010[170]	No usable outcomes
Martin 2006[171]	Inappropriate population
McClellan 1990[173]	No usable outcomes
McGee 1990[174]	Outcomes reported elsewhere
McLeer 1994[175]	Inappropriate population
Meyer 1998[176]	No usable outcomes
Milin 1991[177]	Inappropriate population
Modestino 2013[178]	No usable outcomes
Molina 2002[179]	No usable outcomes
Morgan 2014[180]	Inadequate ADHD diagnosis
Musser 2014[181]	Inadequate ADHD diagnosis
Myers 1993[182]	Inappropriate population

Reference	Reason for exclusion
Nafi 2011[184]	No usable outcomes
Namdari 2012[185]	No usable outcomes
Nazar 2014[187]	No usable outcomes
Ndukuba 2014[188]	No usable outcomes
Neuman 2005[190]	No usable outcomes
N'Goran 2015[183]	No usable outcomes
Niemczyk 2015[191]	Inadequate ADHD diagnosis
Nierenberg 2005[192]	Inappropriate population
Nolan 2001[193]	No usable outcomes
Norwich 2002[194]	No usable outcomes
Nylander 2015[195]	Inadequate ADHD diagnosis
O'Callaghan 1996[196]	Inadequate ADHD diagnosis
Odlaug 2013[198]	No usable outcomes
Oerlemans 2016[199]	Inappropriate population
Ofovwe 2006[200]	No usable outcomes
O'Shea 2013[197]	Review
Osman 2015[201]	No usable outcomes
Ottman 2011[202]	Inadequate ADHD diagnosis
Panevska 2014[204]	No usable outcomes
Pastor 2002[206]	Inadequate ADHD diagnosis
Pastor 2008[207]	Inadequate ADHD diagnosis
Pastor 2015[205]	Inadequate ADHD diagnosis
Peterson 2001[208]	No usable outcomes
Petresco 2014[209]	No usable outcomes
Pheula 2011[210]	No usable outcomes
Phillips 2014[211]	Inadequate ADHD diagnosis
Pierrehumbert 2006[212]	No usable outcomes
Pineda 2003[214]	Inappropriate population
Pineda 1999[213]	No usable outcomes
Pinto 2016[215]	Inadequate ADHD diagnosis
Ponde 2007[216]	No usable outcomes
Rastam 2013[217]	Inappropriate population
Ray 2009[218]	No usable outcomes
Reich 1993[219]	No usable outcomes
Rey 1994[220]	Inappropriate population
Reyes 2013[221]	No usable outcomes
Richa 2014[222]	No usable outcomes
Ristovska 2013[223]	No usable outcomes
Roberts 2009[224]	No usable outcomes
Roberts 2007[226]	No usable outcomes
Rodgers 2015[227]	Inadequate ADHD diagnosis
Rojo-Moreno 2015[228]	No usable outcomes
Rosler 2004[230]	Inappropriate population
Rowland 2001[232]	No usable outcomes
Rowland 2015[231]	No usable outcomes

Reference	Reason for exclusion
Ruhl 2009[233]	No usable outcomes
Runfola 2014[234]	No usable outcomes
Russ 2012[235]	Inadequate ADHD diagnosis
Russell 2014[236]	No usable outcomes
Safavi 2016[237]	No usable outcomes
Sagiv 2013[238]	Inadequate ADHD diagnosis
Salazar 2015[239]	No usable outcomes
Sanchez 2011[242]	No usable outcomes
Sanchez 2014[241]	No usable outcomes
Sanchez-Gistau 2015[240]	No usable outcomes
Sarkhel 2006[243]	No usable outcomes
Sawyer 2007[244]	No usable outcomes
Schneider 2006[245]	Inadequate ADHD diagnosis
Sciberras 2014[246]	No usable outcomes
Segenreich 2015[247]	No usable outcomes
Seitz 2013[248]	No usable outcomes
Singh 2013[249]	Inadequate ADHD diagnosis
Sivertsen 2015[250]	No usable outcomes
Smalley 2007[251]	No usable outcomes
Smidts 2007[252]	No usable outcomes
Snowling 2006[253]	No usable outcomes
Soma 2009[254]	Inadequate ADHD diagnosis
Sonneville 2015[255]	No usable outcomes
Spencer 1998[256]	No usable outcomes
Sprich 2000[257]	No usable outcomes
Stampoltzis 2012[258]	No usable outcomes
Steinsbekk 2015[259]	No usable outcomes
Stevens 2016[260]	Inadequate ADHD diagnosis
Strang-Karlsson 2008[262]	No usable outcomes
Subchartanan 2015[263]	No usable outcomes
Suren 2012[264]	Inadequate ADHD diagnosis
Takahashi 2016[265]	Inadequate ADHD diagnosis
Tashakori 2011[266]	No usable outcomes
Termine 2006[267]	No usable outcomes
Thabet 2010[268]	No usable outcomes
Thompson 1996[269]	No usable outcomes
Tibu 2016[270]	No usable outcomes
Tsao 2017[271]	No usable outcomes
Turkyilmaz 2012[272]	No usable outcomes
Turner 2002[273]	No usable outcomes
Umar 2015[274]	No usable outcomes
Van Damme 2015[275]	No usable outcomes
Velez-Galarraga 2016[277]	No usable outcomes
Venkata 2013[278]	No usable outcomes
Verhulst 1997[279]	No usable outcomes

Reference	Reason for exclusion
Vingilis 2015[280]	No usable outcomes
Vitola 2016[281]	No usable outcomes
Voigt 2006[282]	Inadequate ADHD diagnosis
Wang 2016[284]	Inadequate ADHD diagnosis
Wang 2017[283]	No usable outcomes
Wong 1992[285]	No usable outcomes
Wu 2013[287]	Inappropriate population
Yahia 2014[288]	Inappropriate population
Yau 2013[289]	No usable outcomes
Zorlu 2015[290]	No usable outcomes
Zucker 2015[291]	No usable outcomes
Zwirs 2007[292]	No usable outcomes

I.2 Excluded health economic studies

None.