BMJ Open

Prevalence of obesity in attention-deficit/hyperactivity disorder: study protocol for a systematic review and meta-analysis

Samuele Cortese,[1,2] Carlos Renato Moreira Maia,[3] Luis Augusto Rohde,[3] Carmen Morcillo-Peñalver,[1] Stephen V Faraone[4]

To cite: Cortese S, Moreira Maia CR, Rohde LA, *et al*. Prevalence of obesity in attention-deficit/hyperactivity disorder: study protocol for a systematic review and meta-analysis. *BMJ Open* 2014;**4**: e004541. doi:10.1136/bmjopen-2013-004541

► Prepublication history and additional material is available. To view please visit the journal (http://dx.doi.org/10.1136/bmjopen-2013-004541).

Received 23 November 2013
Revised 4 February 2014
Accepted 17 February 2014

[1]Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK
[2]Division of Psychiatry, Institute of Mental Health, University of Nottingham, Nottingham, UK
[3]Department of Psychiatry, Federal University of Rio Grande do Sul, Porto Alegre, Brazil
[4]Departments of Psychiatry and of Neuroscience and Physiology, State University of New York Upstate Medical University, Syracuse, New York, USA

Correspondence to
Dr Samuele Cortese;
samuele.cortese@gmail.com

ABSTRACT

Introduction: An increasing number of clinical and epidemiological studies suggest a possible association between attention-deficit/hyperactivity disorder (ADHD) and obesity/overweight. However, overall evidence is mixed. Given the public health relevance of ADHD and obesity/overweight, understanding whether and to what extent they are associated is paramount to plan intervention and prevention strategies. We describe the protocol of a systematic review and meta-analysis aimed at assessing the prevalence of obesity/overweight in individuals with ADHD versus those without ADHD.

Methods and analysis: We will include studies of any design (except case reports or case series) comparing the prevalence of obesity and/or overweight in children or adults with and without ADHD (or hyperkinetic disorder). We will search an extensive number of databases including PubMed, Ovid databases, Web of Knowledge and Thomson-Reuters databases, ERIC and CINAHL. No restrictions of language will be applied. We will also contact experts in the field for possible unpublished or in press data. Primary and additional outcomes will be the prevalence of obesity and overweight, respectively. We will combine ORs using random-effects models in STATA V.12.0. The quality of the study will be assessed primarily using the Newcastle-Ottawa Scale. Subgroup meta-analyses will be conducted according to participants' age (children vs adults) and study setting (clinical vs general population). We will explore the feasibility of conducting meta-regression analyses to assess the moderating effect of age, gender, socioeconomic status, study setting, geographic location of the study (low-income, middle-income countries vs high-income countries), definition of obesity, method to assess ADHD, psychiatric comorbidities and medication status.

Ethics and dissemination: No ethical issues are foreseen. The results will be published in a peer-reviewed journal and presented at national and international conferences of psychiatry, psychology, obesity and paediatrics.

Registration: PROSPERO-National Institute of Health Research (NIHR) Prospective Register of Systematic Reviews (CRD42013006410).

Strengths and limitations of this study

- Comprehensive search strategy.
- Search and data extraction conducted independently by two authors.
- Analytical plan including a series of meta-regression analyses to address clinically relevant questions.
- No limitations of the systematic review and meta-analysis are foreseen; limitations of single included studies will be addressed in the section 'Assessment of study quality and bias in included studies'.

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder. According to the recently published Diagnostic and Statistical Manual of Mental Disorders, fifth edition, (DSM-5),[1] ADHD is characterised by a persistent and impairing pattern of inattention and/or hyperactivity/impulsivity. Hyperkinetic disorder (HKD), defined in the International Classification of Diseases, 10th Edition (ICD-10),[2] is a narrower diagnostic category, requiring symptoms of inattention and hyperactivity/impulsivity and possibly including participants diagnosed with the combined presentation ADHD as per DSM-5.[1] A large body of evidence shows that ADHD is often comorbid with other psychiatric conditions, such as oppositional defiant disorder (ODD)/conduct disorder, specific learning disorders, mood and anxiety disorders and sleep disturbances.[3 4]

ADHD is a major public health issue. Its worldwide-pooled prevalence is estimated at about 5% in school-age children.[5] Impairing symptoms of ADHD persist in adulthood in up to 65% of cases,[6] with a pooled prevalence of adulthood ADHD ~2.5%.[7] Because

of its core symptoms and comorbid disorders, ADHD imposes an enormous burden on society in terms of psychological dysfunction, adverse vocational outcomes, stress on families and societal financial costs. Average annual incremental costs of ADHD have been recently estimated at $143–$266 billion in the USA.[8] In Europe, annual national costs range between €1041 and €1529 million.[9] A recent study in the UK[10] showed that financial costs were more than four times higher in individuals when compared with those without ADHD.

While the comorbidity between ADHD and psychiatric disorders has been extensively studied, the possible association with medical conditions has received less attention. However, in recent years, it has become clear that many conditions classically thought to be nervous system disorders actually do include alterations in other physiological systems.[11] As a consequence, an increasing literature on the association between neuropsychiatric disorders and medical conditions has emerged in the past years.

As for ADHD, there has been a rising interest, in particular, on its possible association with obesity or overweight.[12] Obesity and overweight, defined in adults as a body mass index (BMI) ≥30 and ≥25 kg/m^2,[13] respectively, are a major public health issue. The prevalence of overweight (including obesity) is currently above 50% in adults[14] and 25% in children[15] in several countries. The USA, where one adult in three presents with obesity,[16] is the most affected country. The UK is the second worst affected nation: rates of overweight (including obesity) have tripled in the past three decades, reaching about 60% in adults[17] and approximately 33%[18] in children. Obesity and overweight have become a public health issue also in low-middle income countries such as the Middle East, North Africa, Latin America and the Caribbean, where obesity/overweight rates have approached those found in higher income countries.[19] Obesity/overweight is considered as one of the major causes of morbidity (including risk for cardiovascular risk, diabetes and cancer) and mortality.[16] In addition, obesity entails an enormous psychological burden including low self-esteem and social rejection.[20] The worldwide societal costs of obesity are impressive and are not likely to abate in the future. Indeed, the combined medical costs related to the treatment of obesity and associated diseases are estimated to increase in several countries, for example, by $48–$66 billion/year in the USA and by £1·9–£2 billion/year in the UK by 2030.[16]

Clinical[21] as well as epidemiological[22 23] studies have shown a significant association between ADHD and obesity/overweight in children and adults. It has been suggested that impulsivity and inattention may lead to irregular and dysregulated eating patterns and lifestyle, which in turn contribute to weight gain.[24] Alternatively, it has been hypothesised that obesity and ADHD share common underlying neurobiological abnormalities, such as dysfunctions in brain reward pathways.[24] However, results have not been consistent across studies, and some failed to find a significant association between ADHD and obesity/overweight.[25 26] It is possible that factors related to study design (eg, lack of power, cross-sectional vs longitudinal), selection bias (eg, clinical samples vs epidemiological ones) or study participants characteristics (eg, age, gender or medication status) contribute to explain the inconsistency in currently available studies. In addition, it is not clear to what extent ADHD-related and obesity-related factors, such as psychiatric comorbidities or socioeconomic status (SES), account for a possible association between these two conditions.

Given the public health impact of ADHD and obesity, systematic empirical evidence on their possible association is paramount to design intervention and preventive programmes addressing these two conditions, when they co-occur. Currently, although narrative reviews[12 24 27 28] have been published on the relationship between ADHD and obesity/overweight, to our knowledge, no systematic reviews with study quality appraisal or meta-analyses are available.

OBJECTIVES

Here, we specifically focus on the prevalence of obesity/overweight in children and adults with ADHD. We will conduct a systematic review and meta-analysis of published and unpublished studies to address the main study question: "Is the prevalence of obesity significantly higher in individuals with compared to those without ADHD?" We will also conduct meta-regression analyses to address the impact of possible confounding factors. Since the variable 'overweight' is generally less reported than 'obesity' across studies, we will explore the feasibility of conducting a separate meta-analysis on the prevalence of overweight (rather than obesity) in individuals with ADHD, as well as to evaluate the role of confounding factors on the relationship of ADHD to overweight.

METHODS

Methods for this systematic review/meta-analysis have been developed according to recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses[29] and the Meta-Analysis of Observational Studies in Epidemiology[30] statements.

Selection criteria

Study type

All original, peer-reviewed studies with a control group, independently from the design (excluding case series and case studies), will be considered. We will exclude studies without control group since, given the high heterogeneity in the prevalence of obesity according to country/geographical region, pooling the point prevalence rates of obesity without a comparison with a control group would be poorly informative and its clinical as well as public health implications would not be clear. Authors of published meeting abstracts reporting

potentially useful information will be contacted to obtain full usable data. Experts in the field will be asked to provide possible further data from studies not yet published or in press but not yet published online.

Population

ADHD: The population of interest will include children and/or adults with either: (1) a categorical diagnosis of ADHD according to the DSM (III, III-R, IV, IV-TR or 5) or HKD as per the ICD-10 or previous ICD versions; or (2) a definition of ADHD using a symptoms threshold on a validated ADHD rating scales; or (3) for adults, a positive answer to the question: "Did your doctor ever tell you that you have ADHD?") or (4) a diagnosis of ADHD recorded in medical files/registries. We will explore the feasibility of conducting subgroup analyses including only studies with a diagnosis of ADHD (or HKD) confirmed by structured/semistructured interviews. We will also evaluate the feasibility of conducting a meta-regression analysis to assess whether and to what extent different methods to diagnose ADHD influence the meta-analysis results. We will also assess whether the prevalence of obesity in individuals with ADHD differs between studies reporting a diagnosis of lifetime ADHD versus those using current diagnosis of ADHD.

We will exclude studies assessing only symptoms of ADHD, without a diagnosis. We will also exclude studies including participants with a diagnosis of minimal brain dysfunction, which would not be comparable with DSM definitions of ADHD, or with DAMP syndrome (deficit in attention, motor control and perception), since this category is controversial[31] and, additionally, deficits in motor control may impact on physical activity levels in individuals with this syndrome, consequently introducing possible bias in the estimation of the prevalence of obesity.

Comparisons: Participants without a diagnosis of ADHD, from clinical or epidemiological samples.

Age and gender: Studies including individuals of any age and of both genders will be retained. Subgroup meta-analyses will be conducted in children and adults, respectively. We will also conduct a meta-regression analysis of the moderating effect of age (childhood vs adulthood) and we will explore the feasibility of a meta-regression analysis to evaluate the impact of gender.

ADHD medication status: Studies will be included regardless of the past or current treatment of the participants with psychostimulants (which may be associated with weight loss, at least during the first month of treatment[32]). The sensitivity of meta-analytical results to medication status will be examined in a meta-analysis, if feasible, limited to psychostimulant-naïve participants. We will also explore the feasibility of conducting a meta-regression analysis to explore the moderating effect of psychostimulant treatment.

Setting: Studies including participants recruited in clinical settings or in the general population will be included. The sensitivity of meta-analytic results to different settings will be examined in two separate meta-analyses limited to studies conducted in the clinical setting or in the general population. We will also conduct a meta-regression analysis to explore the moderating effect of study setting.

Comorbidities: Studies recruiting individuals with ADHD and psychiatric comorbidities (eg, ODD or mood and anxiety disorders) will be included. We will explore the feasibility of meta-regression analyses to assess the moderating effect of psychiatric comorbidities on the prevalence of obesity/overweight in individuals with ADHD. We will exclude studies where, in addition to ADHD, the presence of a metabolic disorder or any other disorder impacting on weight (such as diabetes) is an inclusion criterion.

SES of participants and geographic location of the study: Studies will not be selected based on the SES of the participants or the geographic location where the study was conducted. We will explore the feasibility of meta-regression analyses to assess the moderating effect of SES and geographic location.

Outcome

Primary outcome: The primary outcome will be the point prevalence of obesity in individuals with ADHD versus matched comparisons without ADHD. As in a recent meta-analysis,[33] obesity will be defined either (1) on the basis of self-report (ie, positive answer to the question: "Do you have obesity?") or as diagnosis reported in medical files/registries or (2) as a body mass index (BMI) (obtained by self-reported or directly measured height and weight) above a preset value. In adults, the preset value will be BMI $\geq$30 kg/m^2, as per the definition adopted by the WHO.[34] In children, there is no consensus on the definition of obesity.[35] While some authors have used BMI >95th or >98th centile for age and sex (based on national normative data), others have relied on centile curves that pass through the points of 30 kg/m^2, consistent with the definition in adults.[36] We will explore the feasibility of conducting meta-regression analyses to assess the impact of different obesity definitions in children.

Authors of studies reporting height and weight, or BMI, but not obesity rates of individuals with and without ADHD, will be contacted and asked to provide data on the prevalence of obesity based on the following definitions: adults: BMI $\geq$30 kg/m^2; children: both BMI >95th or >98th centile for age and sex (based on national normative data).

Additional outcome: We will explore the feasibility of conducting all the analyses replacing obesity with overweight, defined either: (1) on the basis of self-report (ie, positive answer to the question: "Are you overweight?") or (2) as a condition reported in medical files/registries; or (3) as a BMI (obtained by self-reported or measured height and weight) $\geq$25 kg/m^2 in adults and above 85th centile in children.

Search methods for identification of studies

Electronic searches

The strategy for the electronic search has been developed with the assistance of librarians from the New York University Medical Library, New York City, New York, USA.

Electronic searches will be performed in the following databases:

PubMed	
Ovid databases:	Ovid MEDLINE
	Biological Abstracts
	EMBASE Classic+EMBASE
	PsycINFO
Web of Knowledge and Thomas Reuters databases:	BIOSIS Previews
	Inspec
	Science Citation Index Expanded (SCI-Expanded)
	Social Sciences Citation Index (SSCI)
	Arts & Humanities Citation Index (A&HCI)
	Conference Proceedings Citation Index–Science (CPCI-S)
	Conference Proceedings Citation Index–Social Sciences and Humanities (CPCI–SSH)
	CABI: CAB Abstracts and Global Health
	Food Science and Technology Abstracts (FSTA)
ERIC	
CINAHL	

No language or period of publication limitations will be applied. If needed, a professional translator will be contacted.

The search terms and syntax for PubMed will be as follows:

> (ADHD OR adhd OR attention deficit disorder with hyperactivity OR minimal brain disorders OR syndrome hyperkinetic OR hyperkinetic syndrome OR hyperactivity disorder OR hyperactive child syndrome OR childhood hyperkinetic syndrome OR attention deficit hyperactivity disorders OR attention deficit hyperactivity disorder OR adhd attention deficit hyperactivity disorder OR adhd OR overactive child syndrome OR attention deficit hyperkinetic disorder OR hyperkinetic disorder OR attention deficit disorder hyperactivity OR attention deficit disorders hyperactivity OR child attention deficit disorder OR hyperkinetic syndromes OR syndromes hyperkinetic OR hyperkinetic syndrome childhood) AND (Obes* OR Overweight OR BMI OR Body Mass Index OR Quetelet's index OR Body size OR Adiposity)

Specific search terms and syntax for the other databases are reported in online supplementary appendix 1.

Searching other resources

Manual searches will include scanning of reference lists of relevant papers retrieved, specialist journals (such as the *Journal of the American Academy of Child and Adolescent Psychiatry, Journal of Child Psychology and Psychiatry, European Child and Adolescent Psychiatry, the American Journal of Psychiatry, International Journal of Obesity, Obesity and Pediatrics*) and conference proceedings (such as the annual meeting of *the American Academy of Child and Adolescent Psychiatry* and the *International Congress on Obesity*). Authors of abstracts reporting data on height and weight, but not on obesity rates in individuals with and without ADHD, will be contacted and asked to provide, where possible, data on obesity rates derived by height and weight. We will also contact members of the *European Network for Hyperkinetic Disorders* (Eunethydis), an international network of researchers in the field of ADHD from Europe and other continents, and ask them to provide any unpublished data on the prevalence of obesity in individuals with ADHD.

IDENTIFICATION AND SELECTION OF STUDIES

Studies identified with electronic and manual searches will be listed with citation, titles and abstracts in Endnote (Microsoft, Redmond, Washington, USA); duplicates will be excluded using the Endnote function 'remove duplicates'. The eligibility process will be conducted in two separate stages:

1. Two authors (SC and CRMM) will independently screen title and abstracts of all non-duplicated papers and will exclude those not pertinent. A final list will be agreed with discrepancies resolved by consensus between the two authors. When consensus is not reached, a third author (CM-P) will act as arbitrator. If any doubt about inclusion exists, the article will proceed to the next stage.
2. The full-text version of the articles passing stage 1 screening will be downloaded and assessed for eligibility by two authors (SC and CRMM), independently. Discrepancies will be resolved by consensus between the two authors and, if needed, a third author (CM-P) will act as arbitrator.

Data from multiple reports of the same study will be linked together. With regard to prospective studies, we will consider data at baseline. Where required, we will contact the corresponding author to inquire on study eligibility.

DATA EXTRACTION

Two researchers (SC and CRMM) will independently perform data extraction; any discrepancies will be resolved by consensus between the two authors. If this is not possible, another author (CM-P) will make a judgement on the data entered and act as an arbitrator.

Data will be extracted and inserted in an Excel sheet. The following data will be extracted:

1. Publication detail: year and language of publication, country where the study was conducted;
2. Design: type of study (cross-sectional, case–control, cohort, etc); study temporality (prospective, retrospective); patient enrolment (consecutive, non-consecutive); setting (clinical vs epidemiological population study);
3. Study participants details: number, mean age (SD), gender distribution, SES and ethnicity of participants with and without ADHD; characteristics of participants without ADHD (healthy comparisons, comparisons with psychiatric disorders other than ADHD, other); psychiatric comorbidities of individuals with and without ADHD (type and prevalence); method to establish the diagnosis of ADHD (self-reported diagnosis, diagnosis recorded in medical files/registry, structured or semistructured interview according to DSM (III, III-R, IV and IV-TR) or ICD (ICD-10 or previous versions) criteria); medication status of individuals with and without ADHD (type of medication and percentage of treated participants, during and prior to the study);
4. Outcome measure: method used to define obesity/overweight (self-reported diagnosis, diagnosis in medical file/registry, cut-off in BMI calculated from self-reported or measured height and weight); prevalence (unadjusted and, if reported, adjusted) of obesity and, if reported, of overweight in individuals with and without ADHD;
5. Covariates included in the adjusted (by the study authors) ORs effect sizes of obesity prevalence, such as SES and psychiatric comorbidities.

ASSESSMENT OF STUDY QUALITY AND BIAS IN INCLUDED STUDIES

The same two authors (SC and CRMM) will independently perform the assessment of study quality and bias in included studies. Currently, there is no consensus on rating methods and appropriateness of quality assessment in meta-analyses of observational studies.[37] We will use primarily the Newcastle-Ottawa Scale[38] which has been recommended by the Cochrane collaboration.[39] We will also use the rating system proposed by Paulson and Bazemore[40] and adopted in recent meta-analyses of observational studies[41]. This approach rates studies on a scale of 0–10, assigning two points each for: (1) description of the sampling method; (2) presence of clearly stated inclusion criteria; (3) assessment of baseline demographic characteristics; (4) assessment of ethnic diversity and (5) comprehensive descriptions of outcomes. Any discrepancies in the rating of study quality and bias will be resolved by consensus between the two authors. If this is not possible, another author (CM-P) will make a judgement on rating and act as an arbitrator.

DATA SYNTHESIS

We will present a narrative synthesis and a quantitative meta-analysis of the prevalence of obesity/overweight in participants with and without ADHD.

STATISTICAL ANALYSIS

Calculation of individual study estimates of the prevalence of obesity/overweight in individuals with ADHD versus those without ADHD

We will first calculate (or obtain by the study authors) the prevalence of obesity/overweight in individuals with and without ADHD from studies that do not report such prevalence but where data on weight and height for each participant have been collected. The prevalence of obesity and overweight in adults will be calculated as the percentage of participants with BMI ≥30 and ≥25 kg/m^2, respectively. The prevalence of obesity and overweight in children will be expressed as the percentage of participants with age-adjusted and gender-adjusted BMI z scores (calculated based on national normative samples) ≥2 and ≥1, respectively, which correspond to 95th and 85th centile, respectively. Given the lack of consensus in the field on the definition of paediatric obesity, we will repeat analyses considering also BMI z score ≥2.5 (which corresponds to the 98th BMI centile).

The SE and 95% CI of these proportions will then be determined.

Pooled estimates of the prevalence of obesity/overweight in individuals with versus those without ADHD

All analyses will be performed using STATA V.12.0.[42] The prevalence of obesity in participants with and without ADHD from each study will be converted to OR effect size, with ORs above 1 reflecting increased likelihood of obesity in individuals with ADHD versus those without ADHD. Heterogeneity between studies will be tested with Cochran's Q test[43] and with I^2 values. The general interpretation of I^2 values is[39]:

- 0–40%: might not be important
- 30–60%: may represent moderate heterogeneity
- 50–90%: may represent substantial heterogeneity
- 75–100%: considerable heterogeneity.

Meta-analyses of unadjusted and, where available, adjusted ORs (by the study authors, to control for confounding variables) will be carried out using random effects models, which include sampling and study-level errors. If available, adjusted risk estimates will be extracted and analysed. If available, RR and HR will be extracted and addressed in parallel analyses. We will assess the presence of publication bias visually by funnel plot[44] and formally by its direct statistical analogue, Begg's adjusted rank correlation test,[45] using the *metabias* program applied in STATA. If publication bias is detected, we will adjust for this using Duval Tweedie's method[46] in STATA. We will also assess, if feasible, the moderating role of gender, age, study setting, geographic location of the

study, SES, method to assess ADHD, definition of obesity/overweight, psychiatric comorbidities and medication status through meta-regression using the *metareg* program applied in STATA. The stability of the results and the influence of studies will be tested using a leave-one-study-out sensitivity analysis,[47] using the *metainf* program applied in STATA.

Contributors SC conceived the study and drafted the protocol. CRMM, LAR, CM-P and SVF assisted in protocol design. SC and CRMM conducted the scoping searches. All authors read and approved the final version of the manuscript.

Competing interests SC has served as scientific consultant for Shire Pharmaceuticals from June 2009 to December 2010. He has received support to attend meetings from Eli Lilly and Co in 2008 and from Shire in 2009–2010. There are no further conflicts of interest. CRMM has served as speaker to Novartis, receives financial research support from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), developed educational material to Novartis, and received travel awards from the Health Technology Assessment Institute (IATS), Universidade Federal do Rio Grande do Sul (UFRGS), and travel and registration support to the 4th World Congress on ADHD from the World Federation of ADHD. LAR was on the speakers' bureau/advisory board and/or acted as consultant for Eli-Lilly, Janssen-Cilag, Novartis and Shire in the last three years. The ADHD and Juvenile Bipolar Disorder Outpatient Programmes chaired by him received unrestricted educational and research support from the following pharmaceutical companies in the past 3 years: Eli-Lilly, Janssen-Cilag, Novartis and Shire. SVF received consulting income, travel expenses and/or research support from Akili Interactive Labs, Alcobra, VAYA Pharma and SynapDx and research support from the National Institutes of Health (NIH). His institution is seeking a patent for the use of sodium–hydrogen exchange inhibitors in the treatment of ADHD. In previous years, he received consulting fees or was on Advisory Boards or participated in continuing medical education programmes sponsored by: Shire, Alcobra, Otsuka, McNeil, Janssen, Novartis, Pfizer and Eli Lilly. SVF receives royalties from books published by Guilford Press: *Straight Talk about Your Child's Mental Health* and Oxford University Press: *Schizophrenia: The Facts*.

Ethics approval No ethical issues are foreseen since ethical approval has been obtained for each study that will be included in the systematic review/meta-analysis. The results of this study will be published in a peer-reviewed journal and will also be presented at national and international meetings in the fields of (child) psychiatry, psychology, paediatrics and obesity.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. American Psychiatric Association. *Diagnostic and statistical manual of mental disorder*. 5th edn. American Psychiatric Publishing, 2013.
2. World Health Organization. *The ICD-10 classification of mental and behavioral disorders: clinical descriptions and diagnostic guidelines 1992; diagnostic criteria for research 1993*. Geneva: WHO, 1992.
3. Biederman J, Faraone SV. Attention-deficit hyperactivity disorder. *Lancet* 2005;366:237–48.
4. Cortese S, Brown TE, Corkum P, *et al*. Assessment and management of sleep problems in youths with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2013;52:784–96.
5. Polanczyk G, de Lima MS, Horta BL, *et al*. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *Am J Psychiatry* 2007;164:942–8.
6. Faraone SV, Biederman J, Mick E. The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. *Psychol Med* 2006;36:159–65.
7. Simon V, Czobor P, Balint S, *et al*. Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. *Br J Psychiatry* 2009;194:204–11.
8. Doshi JA, Hodgkins P, Kahle J, *et al*. Economic impact of childhood and adult attention-deficit/hyperactivity disorder in the United States. *J Am Acad Child Adolesc Psychiatry* 2012;51:990–1002.
9. Le Hoa H, Hodgkins P, Postma MJ, *et al*. Economic impact of childhood/adolescent ADHD in a European setting: the Netherlands as a reference case. *Eur Child Adolesc Psychiatry* 2013. doi:10.1007/s00787-013-0477-8 [epub ahead of print].
10. Holden SE, Jenkins-Jones S, Poole CD, *et al*. The prevalence and incidence, resource use and financial costs of treating people with attention deficit/hyperactivity disorder (ADHD) in the United Kingdom (1998 to 2010). *Child Adolesc Psychiatry Ment Health* 2013;7:34.
11. Qureshi IA, Mehler MF. Towards a 'systems'-level understanding of the nervous system and its disorders. *Trends Neurosci* 2013;36:674–84.
12. Cortese S, Vincenzi B. Obesity and ADHD. Clinical and neurobiological implications. *Curr Top Behav Neurosci* 2012;9:199–218.
13. Haslam DW, James WP. Obesity. *Lancet* 2005;366:1197–209.
14. International Obesity Taskforce. http://www.iaso.org/iotf/obesity/ (accessed 22 Nov 2013).
15. Wang Y, Lobstein T. Worldwide trends in childhood overweight and obesity. *Int J Pediatr Obes* 2006;1:11–25.
16. Wang YC, McPherson K, Marsh T, *et al*. Health and economic burden of the projected obesity trends in the USA and the UK. *Lancet* 2011;378:815–25.
17. National Health Service. 2012. https://catalogue.ic.nhs.uk/publications/public-health/obesity/obes-phys-acti-diet-eng-2012/obes-phys-acti-diet-eng-2012-rep.pdf (accessed 22 Nov 2013).
18. National Health Service. 2012. https://catalogue.ic.nhs.uk/publications/public-health/obesity/nati-chil-meas-prog-eng-2010–2011/nati-chil-meas-prog-eng-2010–2011-rep1.pdf (accessed 22 Nov 2013).
19. Popkin BM, Slining MM. New dynamics in global obesity facing low- and middle-income countries. *Obes Rev* 2013;14(Suppl 2):11–20.
20. Young-Hyman D, Tanofsky-Kraff M, Yanovski SZ, *et al*. Psychological status and weight-related distress in overweight or at-risk-for-overweight children. *Obesity (Silver Spring)* 2006;14:2249–58.
21. Gungor S, Celiloglu OS, Raif SG, *et al*. Malnutrition and obesity in children with ADHD. *J Atten Disord* 2013. doi:10.1177/1087054713478465 [epub ahead of print].
22. Pagoto SL, Curtin C, Lemon SC, *et al*. Association between adult attention deficit/hyperactivity disorder and obesity in the US population. *Obesity (Silver Spring)* 2009;17:539–44.
23. Waring ME, Lapane KL. Overweight in children and adolescents in relation to attention-deficit/hyperactivity disorder: results from a national sample. *Pediatrics* 2008;122:e1–6.
24. Cortese S, Morcillo Penavler C. Comorbidity between ADHD and obesity: exploring shared mechanisms and clinical implications. *Postgrad Med* 2010;122:88–96.
25. Byrd HC, Curtin C, Anderson SE. Attention-deficit/hyperactivity disorder and obesity in US males and females, age 8–15 years: National Health and Nutrition Examination Survey 2001–2004. *Pediatr Obes* 2013;8:445–53.
26. Dubnov-Raz G, Perry A, Berger I. Body mass index of children with attention-deficit/hyperactivity disorder. *J Child Neurol* 2011;26:302–8.
27. Cortese S, Angriman M, Maffeis C, *et al*. Attention-deficit/hyperactivity disorder (ADHD) and obesity: a systematic review of the literature. *Crit Rev Food Sci Nutr* 2008;48:524–37.
28. Davis C. Attention-deficit/hyperactivity disorder: associations with overeating and obesity. *Curr Psychiatry Rep* 2010;12:389–95.
29. Liberati A, Altman DG, Tetzlaff J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;339:b2700.
30. Stroup DF, Berlin JA, Morton SC, *et al*. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12.
31. Brante T. More on data destruction and research misconduct in Sweden. BMJ E-letter. 2004. http://www.bmj.com/rapid-response/2011/10/30/more-data-destruction-and-research-misconduct-sweden
32. Cortese S, Holtmann M, Banaschewski T, *et al*. Practitioner review: current best practice in the management of adverse events during

treatment with ADHD medications in children and adolescents. *J Child Psychol Psychiatry* 2013;54:227–46.
33. Danese A, Tan M. Childhood maltreatment and obesity: systematic review and meta-analysis. *Mol Psychiatry* 2013. doi:10.1038/mp.2013.54 [epub ahead of print].
34. World Health Organization. http://www.who.int/mediacentre/factsheets/fs311/en/ (accessed 22 Nov 2013).
35. Rolland-Cachera MF. Childhood obesity: current definitions and recommendations for their use. *Int J Pediatr Obes* 2011;6:325–31.
36. Sweeting HN. Measurement and definitions of obesity in childhood and adolescence: a field guide for the uninitiated. *Nutr J* 2007;6:32.
37. Juni P, Witschi A, Bloch R, *et al*. The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA* 1999;282:1054–60.
38. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm (accessed 22 Nov 2013).
39. Cochrane Handbook for Systematic Reviews of Interventions. 2012. http://www.cochrane-handbook.org (accessed 22 Nov 2013).
40. Paulson JF, Bazemore SD. Prenatal and postpartum depression in fathers and its association with maternal depression: a meta-analysis. *JAMA* 2010;303:1961–9.
41. Bonoldi I, Simeone E, Rocchetti M, *et al*. Prevalence of self-reported childhood abuse in psychosis: a meta-analysis of retrospective studies. *Psychiatry Res* 2013;210:8–15.
42. Stata Corporation. *Statistical Software: Release 11.0*. College Station, TX: Stata Corporation, 2009.
43. Cochran WG. The comparison of percentages in matched samples. *Biometrika* 1950;37:256–66.
44. Egger M, Davey SG, Schneider M, *et al*. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
45. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994;50:1088–101.
46. Duval S, Tweddie R. A nonparametric “trim and fill” method of accounting for publication bias in meta-analysis. *J Am Stat Assoc* 2000;95:89–98.
47. Normand SL. Meta-analysis: formulating, evaluating, combining, and reporting. *Stat Med* 1999;18:321–59.