BMJ Open

Physical activity for children and adolescents with attention deficit hyperactivity disorder: a protocol of a systematic review and meta-analysis

Marie-Louise Jensen ,[1] Ole Jakob Storebø ,[2,3] Merete Bender Bjerrum,[4,5,6] Marianne Vamosi[1]

To cite: Jensen M-L, Storebø OJ, Bjerrum MB, *et al*. Physical activity for children and adolescents with attention deficit hyperactivity disorder: a protocol of a systematic review and meta-analysis. *BMJ Open* 2024;**14**:e093241. doi:10.1136/bmjopen-2024-093241

► Prepublication history for this paper is available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-093241).

Received 03 September 2024
Accepted 22 November 2024

For numbered affiliations see end of article.

Correspondence to
Marie-Louise Jensen; marielj@ruc.dk

ABSTRACT

Introduction Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder among children and adolescents. The disorder negatively influences their academic performance and social relations, and their quality of life (QoL) is lower than that of peers without ADHD. The majority of children and adolescents with ADHD are treated with medication that potentially has an insufficient effect or frequently occurring adverse events. Physical activity is thought to alter the physiology of ADHD by affecting the same catecholaminergic system in the brain which is targeted by medication.

Methods and analysis This protocol is written in accordance with the 'Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols' guideline. Randomised clinical trials with participating children and adolescents between the ages of 3 and 18 years with a primary diagnosis of ADHD or hyperkinetic disorder will be included in the systematic review. The main objective of the review is to examine the effect of physical activity on QoL, executive functions, symptoms and functional impairment in this population. Previous systematic reviews on the effect of physical activity in children and adolescents with ADHD have several methodological and conceptual limitations. These reviews, for example, included both randomised and non-randomised clinical trials or had restrictions regarding the frequency and intensity of the physical activity interventions they included. The present review will include the newest studies in the field and follow the main principles outlined in the 'Cochrane Handbook for Systematic Reviews of Interventions'. Furthermore, it will be the first review in the field to include QoL as an outcome and to apply trial sequential analysis as part of the meta-analysis.

Ethics and dissemination As the systematic review is a secondary analysis of data from primary trials, approval from an ethics committee is not required. The results of the review will be published in a peer-reviewed scientific journal and presented at relevant conferences.

Trial registration number This protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 16 August 2024 (CRD42024576670).

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Inclusion of the newest studies in the field from a broad range of sources.
⇒ Inclusion of all types of physical activity interventions and quality of life as an outcome.
⇒ Inclusion of randomised clinical trials only.
⇒ Systematic assessments of the risk of bias in the included studies and of the certainty of the evidence in the review.
⇒ No formal user involvement.

INTRODUCTION

Description of the condition

Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder among children and adolescents, with a worldwide prevalence of about 5%.[1] Males are more often diagnosed than females, but the gender distribution varies across geographical locations, with a gender ratio ranging from 2:1 to 10:1.[2] The diagnosis is part of the Diagnostic and Statistical Manual of Mental Disorders (DSM) and International Statistical Classification of Diseases and Related Health Problems (ICD) 11 criteria,[3–8] while the corresponding symptom complex is within the group of hyperkinetic disorders in previous versions of the ICD criteria.[9 10] In this protocol, the disorder is consistently referred to as ADHD. The DSM and ICD criteria have in common that the core symptoms of impulsivity, hyperactivity and inattention should be pervasive, but also inconsistent with the developmental level of the person affected.[7 8 10] Furthermore, a deficit in executive functions, defined as, for example, the ability to organise, plan and control goal-directed behaviour, also appears to be an important component of the disorder.[11] The leading hypothesis on the pathophysiology of ADHD is that it involves a dysfunction of the

catecholamine response in the prefrontal cortex, which is the part of the brain associated with executive functions.[12]

These characteristics of the disorder negatively influence the academic performance and social relations of children and adolescents with ADHD,[13 14] and their quality of life (QoL) is lower than that of peers without ADHD.[15] Moreover, this disorder is, in many cases, comorbid with other conditions like autism spectrum disorder, anxiety, learning disabilities, conduct disorders, tics disorder or epilepsy, which complicates the treatment and care of the persons affected.[16] The exact aetiology of ADHD is unknown and controversial but is considered to be a complex interplay between environmental, psychosocial and genetic components.[17 18] Environmental factors correlated with the risk of developing ADHD include exposure to toxicants, nutrition deficiencies, events during pregnancy and birth, deprivation, stress, infection, poverty and trauma.[18] Most individuals with ADHD get diagnosed at school age, and in about 70% of cases, the symptoms persist into adolescent and adult life.[19]

The medication most often prescribed to treat ADHD is methylphenidate which increases the availability of the catecholamines dopamine and norepinephrine in the prefrontal cortex.[20] Methylphenidate may have an effect on the symptoms of ADHD but may not have any effect on the QoL of children and adolescents with the disorder.[20 21] Furthermore, methylphenidate may have adverse events like sleeping problems, headaches, stomachaches and reduced appetite, which often lead to withdrawal of treatment.[22]

Description of the intervention

Physical activity has, compared with other non-pharmacological interventions such as behavioural therapy, neurofeedback and cognitive training, been shown to have the largest effect on cognitive difficulties in children, adolescents and adults with ADHD.[23] Physical activity is defined as 'any bodily movement produced by skeletal muscles that results in energy expenditure' with exercise being a subset of this.[24] This type of intervention is thought to alter the physiology of ADHD by increasing the levels of mainly dopamine and norepinephrine in the brain and thus affect the same catecholaminergic system which is targeted by medication.[12] Furthermore, longer term programmes of physical activity affect the resting systemic rates of catecholamine secretion, not only the acute catecholamine response.[12 25]

The importance of the review

Physical activity is a broad concept with many possible variations regarding intensity, frequency and duration, and its effects may vary across age and gender.[12] To improve the implementation of physical activity as an intervention in the treatment of ADHD, precise estimates of the effect on different outcomes are important, and so is knowledge of which compositions are the most effective. This is relevant on many levels, for example, for children with ADHD and their parents when choosing treatment strategy, for healthcare professionals recommending treatment options, for policymakers incorporating physical activity as part of treatment guidelines and for researchers constructing physical activity interventions for trials.

Several systematic reviews have been conducted on the effect of physical activity on children and adolescents with ADHD.[26–36] These reviews, however, have several methodological and conceptual limitations. Neudecker *et al* searched for studies in four databases,[27] Ng *et al* searched in two databases,[28] Xie *et al* searched in four databases,[31] Sun *et al* searched in four English and four Chinese databases[33] and Montalva-Valenzuela *et al* searched in four databases.[34] Welsch *et al* and Seiffer *et al* had certain restrictions regarding the frequency of the physical activity interventions they included,[32 35] and Seiffer *et al* had restrictions regarding the intensity.[35]

Neudecker *et al*,[27] Ng *et al*,[28] Jeyanthi *et al*,[29] Welsch *et al*[32] and Montalva-Valenzuela *et al*[34] included both randomised and non-randomised clinical trials in their reviews. Liang *et al*,[30] Xie *et al*,[31] Welsch *et al*[32] and Zhu *et al*[36] combined results from randomised clinical trials (RCTs) and non-randomised clinical trials in their meta-analyses. Neudecker *et al*,[27] Ng *et al*[28] and Xie *et al*[31] did not make a systematic assessment of the risk of bias in the studies they included. Zhu *et al*[36] were the only ones who made a systematic assessment of the certainty of the evidence in their review, but it was not possible to identify this assessment or the assessment of the risk of bias, nor did they address any of these in their conclusion. Finally, neither of the studies included QoL as an outcome. The reviews were published between 1 and 9 years ago[26–36], with the latest search being conducted in October 2022.[36]

Besides including the newest studies in the field, the present review will include studies from a broad range of sources, include all types of physical activity interventions, include QoL as an outcome, include only RCTs and conduct systematic assessments of the risk of bias in the included studies, and of the certainty of the evidence in the review.

Objectives

The main objective of this systematic review is to examine the effect of physical activity on children and adolescents with ADHD. It aims to answer the following questions:

1. What is the effect of physical activity on QoL, executive functions, symptoms and functional impairment in children and adolescents with ADHD?
2. Which types of intensity, frequency, duration and delivery of physical activity are the most effective?
3. Do the effects vary by age, gender and ADHD medication status?
4. What are the adverse events of physical activity on children and adolescents with ADHD?

METHODS

The systematic review will be conducted following the main principles outlined in the 'Cochrane Handbook for Systematic Reviews of Interventions'.[37] This protocol is written in accordance with the 'Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols' guideline.[38] The work on the protocol started on 1 May 2024, and the systematic review is scheduled to be completed on 1 February 2025.

Patient and public involvement

Neither patients nor the public were involved in developing this protocol.

Eligibility criteria

Participants

Children and adolescents between the ages of 3 and 18 years with a primary diagnosis of ADHD or hyperkinetic disorder, with or without psychiatric comorbidities. The diagnosis should be made by a healthcare professional according to the DSM-III,[39] DSM-III-R,[3] DSM-IV,[4] DSM-IV-TR,[5] DSM-5,[6] DSM-5-TR,[7] ICD-9,[9] ICD-10[10] or ICD-11.[8] Studies will be included in which 75% of the participants are between 3 and 18 years of age and the mean age of the study population is within this range. Studies including participants with severe physical illness or an IQ below 70 will be excluded.

Interventions

Studies will be included in which the participants in the intervention group received any type of physical activity intervention as previously defined. It may be delivered in any setting and be of any mode of delivery, and there are no upper or lower limits on the duration of the intervention. Studies of physical activity as a part of an intervention, for example, in combination with diet restrictions and/or health-promoting conversations, will be excluded if the effect of the physical activity cannot be discerned from the available data. Furthermore, studies that examine the total effect of physical activity in combination with medical treatment will also be excluded. The exceptions are studies that use physical activity as an additional treatment, and in which the main intervention is evenly distributed between the two groups.

Comparisons

Studies will be included in which physical activity is compared with no intervention, treatment as usual, another non-pharmacological intervention or medical treatment in children and/or adolescents with ADHD. As the aim of the review is to evaluate the effect of physical activity as well as to compare the effect of different physical activity interventions, studies will also be included that compare the intervention with a different variation of physical activity.

Outcomes

Data on QoL, executive functions, symptoms, functional impairment and adverse events will be extracted preintervention, postintervention and at the longest available follow-up. As the concepts of QoL and health-related quality of life (HRQoL) are often used interchangeably,[40] data on HRQoL will also be extracted. The outcomes can be self-reported by the children or adolescents themselves or by proxy (eg, parent, caregiver, clinician and/or teacher).

Types of studies

RCTs, including cluster-randomised trials. Only reports in English, German, Danish, Swedish and Norwegian will be included, but a list of possible relevant studies in other languages will be provided along with a list of relevant ongoing studies.

Information sources

A research librarian with experience in the search for healthcare literature for systematic reviews was consulted with regard to the choice of databases, terms and search strategy. The literature search will be conducted by M-LJ in the following electronic bibliographic databases and trial registers:

- Cochrane Central Register of Controlled Trials; Cochrane Library (latest issue).
- MEDLINE; Ovid (1946 to current).
- Embase; Ovid (1974 to current).
- PsycINFO; Ovid (1806 to current).
- CINAHL; EBSCOhost (1937 to current).
- Education Resources Information Center; EBSCOhost (1966 to current).
- Web of Science; Clarivate (1900 to current).
- ClinicalTrials.gov.
- WHO International Clinical Trials Registry Platform.
- ProQuest Dissertations & Theses Citation Index (1637 to current).
- medRxiv.
- PsyArXiv.
- bioRxiv.

A citation search and search for related articles will be conducted as relevant studies are identified, and the reference lists of these studies and previous reviews will be checked.

Search strategy

The search terms are based on the results from the preliminary searches, as well as a search for spelling variants, synonyms and acronyms. Both controlled vocabulary specific for each database and free-text terms will be included in the search. The terms are related to the study population, the condition, the intervention, and the study type. To avoid overlooking important data on studies reported in several reports, these will not be excluded based on outcomes. Because of this, search terms related to outcomes are not included in the search. The search filters developed by Cochrane for identifying randomised trials in MEDLINE and Embase will be applied respectively.[41] The search strategy for MEDLINE is attached as online supplemental appendix 1. This strategy will be

adapted to the remaining databases to account for variations in the controlled vocabulary, proximity operators, truncation, etc. The search will be conducted with no restrictions on publication year, type or status.

Study records

Selection process

The citations identified through the systematic search will be exported to the review software Covidence,[42] where duplicates will be removed. According to the 'Cochrane Handbook for Systematic Reviews of Interventions', it is not mandatory that titles and abstracts of identified citations are screened by more than one person.[37] However, to strengthen the validity of the review, the inter-rater reliability between M-LJ and MV will be tested. 10% of the titles and abstracts will be screened independently by the two, and a kappa coefficient will be calculated. If it exceeds 0.95, the remaining part of the titles and abstracts will be screened by M-LJ in order to remove reports that are obviously not relevant. The full-text reports will be searched in the latest version of the citation to account for any corrections or retractions. These will be screened independently by M-LJ and MV who will decide which studies to include based on the eligibility criteria. Any lack of agreement between the two parties will be resolved through discussion and if a consensus is not reached, through arbitration by OJS. Multiple records of the same study will be identified and linked by comparing trial registration numbers, author names, locations, interventions, sample sizes and outcomes. A list of excluded studies will be provided along with the reasons for exclusion, and the selection process will be depicted in a flow diagram.[43]

Data collection process

A standardised data extraction form will be created in Covidence[42] by M-LJ, piloted by M-LJ and MV in two of the included studies, and revised if necessary. Data will be extracted independently by M-LJ and MV. Any lack of agreement between the two parties will be resolved through discussion and if a consensus is not reached, through arbitration by OJS. Data from multiple reports of the same study will be extracted directly into a single data form.

Data items

Data will be extracted in the following categories:

- Administration: first author, publication year, geographical location, funding source, potential conflicts of interest.
- Study methods: design, statistical analysis.
- Participants: setting, sample size, diagnostic criteria, mean age, gender distribution, medication status.
- Intervention: components, frequency, duration, delivery, staff qualifications, equipment, definition of control.
- Outcomes: name of scale, self- or proxy-report, timing of measurement.
- Results: data for each group/subgroup for each outcome, between-group estimates, key conclusions.

The most detailed numerical data will be extracted, preferably in the form of 2×2 tables or means and SD, but otherwise effect estimates, CIs, p values, etc. Due to the possible long term effect of PA[12 25] and the consequent risk of carry-over effects, only first-period data from cross-over trials will be used.

Outcomes and prioritisation

There is no relevant core outcome set for individuals with ADHD available from either the Core Outcome Measures in Effectiveness Trials Initiative[44] or the International Consortium for Health Outcomes Measurement.[45] Researchers reviewing outcomes for this group underline the importance of moving beyond symptoms in the evaluation of the effects of treatment options, for example, examining QoL, executive functions and functional impairment.[46] In this review, QoL, executive functions, symptoms and functional impairment should be measured with validated instruments, whereas both systematic and spontaneous reports of adverse events will be included.

Primary outcomes

1. QoL can be considered the most important goal of care,[47] because of the chronic nature of the disorder.[48] Examples of scales include, but are not limited to:
   - The Child Health and Illness Profile (CHIP-CE, CHIP-AE)[49 50]; The Child Health Questionnaire[51]; The Pediatric Quality of Life Inventory 4.0[52]; Kidscreen-27.[53]
2. Executive functions are a composite concept with no unambiguous definition. All outcomes considered representative of executive functions by the review authors, for example, reaction time or inhibitory control, will be extracted. Examples of scales include, but are not limited to:
   - Stroop Task[54]; Stop-Signal Test[54]; The Behavior Rating Inventory of Executive Function[55]; The Brown Attention-Deficit Disorder Scales.[56]

Secondary outcomes

1. ADHD symptoms. Examples of scales include, but are not limited to:
   - ADHD Rating Scale[57]; Connors' Rating Scales - revised[58]; The Swanson, Nolan, and Pelham Teacher and Parent Rating Scale[59]; The Strengths and Weaknesses of ADHD Symptoms and Normal Behavior.[60]
2. Functional impairment. Examples of scales include, but are not limited to:
   - The Columbia Impairment Scale[61]; The Academic Performance Rating Scale[62]; The Social Skills Improvement System[63]; The Impairment Rating Scale[64]; The Weiss Functional Impairment Scale.[65]
3. Adverse events are defined as unfavourable outcomes caused by the physical activity intervention. As stomachaches and reduced appetite are suspected to be

adverse events of ADHD medication, an unintended weight loss could be a potential adverse event of physical activity.

Risk of bias in individual studies

The risk of bias in the studies will be assessed using the 'Cochrane Risk of Bias Tool for Randomized Controlled Trials version 2' (RoB2).[37] The RoB2 consists of five domains that uncover systematic errors due to (1) the randomisation process; (2) deviations from the intended interventions; (3) missing outcome data; (4) measurement of the outcome; and (5) selection of the reported outcome.[37] Data will be extracted from the included studies to facilitate this assessment, and for each outcome, the domains will be given an independent judgement of 'high risk of bias', 'low risk of bias' or 'some concerns'.[37] The risk of bias assessment will be conducted independently by M-LJ and MV. Any lack of agreement between the two parties will be resolved through discussion and if a consensus is not reached, through arbitration by OJS. Studies with any level of risk of bias will be retained in the analysis.

Data synthesis

Summary measures and methods of handling and combining data

A meta-analysis will be conducted using Cochrane RevMan Web software,[66] if data from the included studies are available in a usable format or can be obtained from the authors. To combine findings related to outcomes with dichotomous data, risk ratios with a 95% CI will be computed. For continuous outcomes, mean differences between the two groups will be compared and presented with a 95% CI. Attempts will be made to obtain missing data by contacting the study authors.

In expectation of high clinical heterogeneity due to different physical activity interventions, the analysis will be conducted using a random effects model with a fixed-effects analysis as a sensitivity check.[37] In the likely event that different measurement scales were used to measure the same content, standardised mean differences will be used.[37] Furthermore, the recommendations by Thorlund *et al* for presenting pooled estimates of continuous QoL data[67] will be followed. Intention-to-treat data will be prioritised but observed cases data will be accepted. Clinical heterogeneity will be evaluated using the 'Clinical Diversity In Meta-analysis' tool.[68] Statistical heterogeneity will be assessed using I^2 and χ^2 tests, with values of I^2 over 50% and $p<0.1$ of χ^2 indicating substantial heterogeneity.[37] If heterogeneity is substantial, a narrative description in text and tables will be provided.

Due to high clinical heterogeneity, the number of trials included in the meta-analyses is expectedly low. To account for this insufficient statistical power, trial sequential analysis will be conducted in order to control both type 1 and type 2 errors in the primary outcomes.[69] The significance threshold will be adjusted to account for multiple comparisons using the method outlined by Jakobsen *et al*.[70] The diversity-adjusted required information size (DARIS) will be calculated[69 71] based on the minimal relevant difference of the physical activity intervention on specific scales of QoL and executive functions. To be able to assess statistical inference, trial sequential monitoring boundaries will be constructed.[69] If these are not crossed before the DARIS, it indicates that further trials of physical activity may be needed to detect or reject an effect of the intervention.[70] The results from the trial sequential analysis will be used in The Grading of Recommendations Assessment, Development and Evaluation (GRADE) as the rating for imprecision.[70]

Additional analyses

Heterogeneity will be further explored through subgroup analysis based on the following characteristics:

1. Population:
   - Age (3–6 years of age, 7–12 years of age, 13–18 years of age).
   - Gender (male vs female).
   - Medication status (medicated vs non-medicated).
2. Intervention
   - Intensity (very light/light intensity: <63% of maximum heart rate; moderate intensity: 64–76% of maximum heart rate; hard/very hard intensity: >76% of maximum heart rate).[72]
   - Frequency (≤2 times per week vs >2 times per week).
   - Duration of session (≤45 min vs >45 min).
   - Duration of intervention (<6 weeks, 6–12 weeks, >12 weeks).
   - Provider (professional trainer vs non-professional trainer).
   - Delivery (individual vs group-based).
   - Type of control-group (no intervention, treatment as usual, another non-pharmacological intervention, medical treatment, another physical activity intervention).

The heterogeneity of the frequency and duration of the interventions in the included studies is expectedly high. Some interventions may, for example, involve one session per week, while others may require several sessions per week, each perhaps with varying durations. These differences could impact the effect estimates, which is why the importance of frequency and duration will be explored through subgroup analyses.

Meta-biases

Egger's test[73] for small study effects will be conducted and funnel plots will be provided to assess potential publication bias in the meta-analysis, if there are more than 10 studies included in the analysis. To assess potential outcome reporting bias, available protocols of the included RCTs published before the study was conducted, will be identified. Outcomes reported in the protocols will be compared with the outcomes reported in the published report. If a protocol is unavailable, outcomes reported in the methods and results sections of the published report will be compared.

Confidence in cumulative evidence

The GRADE[37] will be used to assess the confidence in the body of evidence for each outcome. The assessment is based on five domains: (1) risk of bias; (2) inconsistency; (3) indirectness; (4) imprecision; and (5) publication bias.[37] Based on the assessment, the certainty of the evidence will either be downgraded one or two levels or not be downgraded. The GRADE assessment will be conducted independently by M-LJ and MV. Any lack of agreement between the two parties will be resolved through discussion and if a consensus is not reached, through arbitration by OJS.

ETHICS AND DISSEMINATION

As the systematic review is a secondary analysis of data from primary trials, approval from an ethics committee is not required. The results of the review will be published in a peer-reviewed scientific journal and presented at relevant conferences.

Author affiliations
[1]Roskilde University, Roskilde, Denmark
[2]Research Director of Center of Evidence-Based Psychiatry, Psychiatric Research Unit, Region Zealand, Denmark
[3]Department of Psychology, Faculty of Health Science, University of Southern Denmark, Odense, Denmark
[4]Research Unit of Nursing and Healthcare, Institute of Public Health, Health, Aarhus University, Aarhus, Denmark
[5]The Centre of Clinical Guidelines - Danish National Clearinghouse, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark
[6]Director of The Danish Centre of Systematic Reviews - A JBI Centre of Excellence, The University of Adelaide, Adelaide, South Australia, Australia

Contributors M-LJ is the guarantor of this protocol and has drafted the manuscript. She is responsible for documenting any future amendments to the protocol. OJS contributed to the development of the selection criteria, search strategy and data extraction criteria. He provided critical revision and final approval of the protocol. MBB contributed to the development of the selection criteria, search strategy and data extraction criteria. She provided critical revision and final approval of the protocol. MV contributed to the development of the selection criteria, search strategy and data extraction criteria. She provided critical revision and final approval of the protocol.

Funding The protocol and the systematic review are a part of a PhD-project funded by The Faculty of Health Sciences (Health), Aarhus University and The Novo Nordisk Foundation (grant number NNF23OC0087338). Roskilde University acts as the sponsor. Aarhus University, The Novo Nordisk Foundation and Roskilde University, as funding institutions/sponsors, are not involved in any aspects of developing this protocol or conducting the systematic review.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Marie-Louise Jensen http://orcid.org/0009-0007-7093-1440
Ole Jakob Storebø http://orcid.org/0000-0003-0204-7745

REFERENCES

1 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.
2 Mowlem FD, Rosenqvist MA, Martin J, *et al*. Sex differences in predicting ADHD clinical diagnosis and pharmacological treatment. *Eur Child Adolesc Psychiatry* 2019;28:481–9.
3 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 3rd revised edn. American psychiatric Association, 1987.
4 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th edn. American psychiatric Association, 1994.
5 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th text revision edn. American psychiatric Association, 2000.
6 American psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th edn. American psychiatric Association, 2013.
7 American psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th text revision edn. American psychiatric Association, 2022.
8 World Health Organization. *International Statistical Classification of Diseases and Related Health Problems*. 11th edn. World Health Organization, 2019.
9 World Health Organization. *International Statistical Classification of Diseases and Related Health Problems*. 9th edn. World Health Organization, 1977.
10 World Health Organization. *International Statistical Classification of Diseases and Related Health Problems*. 10th edn. World Health Organization, 1993.
11 Willcutt EG, Doyle AE, Nigg JT, *et al*. Validity of the executive function theory of attention-deficit/hyperactivity disorder: a meta-analytic review. *Biol Psychiatry* 2005;57:1336–46.
12 Wigal SB, Emmerson N, Gehricke J-G, *et al*. Exercise: applications to childhood ADHD. *J Atten Disord* 2013;17:279–90.
13 Daley D, Birchwood J. ADHD and academic performance: why does ADHD impact on academic performance and what can be done to support ADHD children in the classroom? *Child Care Health Dev* 2010;36:455–64.
14 Bagwell CL, Molina BSG, Pelham WE JR, *et al*. Attention-Deficit Hyperactivity Disorder and Problems in Peer Relations: Predictions From Childhood to Adolescence. *J Am Acad Child Adolesc Psychiatry* 2001;40:1285–92.
15 Wanni Arachchige Dona S, Badloe N, Sciberras E, *et al*. The Impact of Childhood Attention-Deficit/Hyperactivity Disorder (ADHD) on Children's Health-Related Quality of Life: A Systematic Review and Meta-Analysis. *J Atten Disord* 2023;27:598–611.
16 Radmanovic MB, Burgic SS. Comorbidities in children and adolescents with adhd. In: Kumperscak HD, ed. *ADHD. From Etiology to Comorbidity*. 2020.
17 Thapar A, Cooper M, Eyre O, *et al*. Practitioner Review: What have we learnt about the causes of ADHD? *Child Psychology Psychiatry* 2013;54:3–16.
18 Faraone SV, Banaschewski T, Coghill D, *et al*. The World Federation of ADHD International Consensus Statement: 208 Evidence-based conclusions about the disorder. *Neurosci & Biobehav Rev* 2021;128:789–818.
19 Cherkasova M, Sulla EM, Dalena KL, *et al*. Developmental Course of Attention Deficit Hyperactivity Disorder and its Predictors. *J Can Acad Child Adolesc Psychiatry* 2012;22:47–54.
20 Storebø OJ, Storm MRO, Pereira Ribeiro J, *et al*. Methylphenidate for children and adolescents with attention deficit hyperactivity disorder (ADHD). *Cochrane Database Syst Rev* 2023;3:CD009885.
21 Cortese S, Adamo N, Del Giovane C, *et al*. Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder

in children, adolescents, and adults: a systematic review and network meta-analysis. *Lancet Psychiatry* 2018;5:727–38.
22 Storebø OJ, Pedersen N, Ramstad E, *et al*. Methylphenidate for attention deficit hyperactivity disorder (ADHD) in children and adolescents - assessment of adverse events in non-randomised studies. *Cochrane Database Syst Rev* 2018;5:CD012069.
23 Lambez B, Harwood-Gross A, Golumbic EZ, *et al*. Non-pharmacological interventions for cognitive difficulties in ADHD: A systematic review and meta-analysis. *J Psychiatr Res* 2020;120:40–55.
24 Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 1985;100:126–31.
25 Zouhal H, Jacob C, Delamarche P, *et al*. Catecholamines and the Effects of Exercise. *Tran and Gen Sports Med* 2008;38:401–23.
26 Cerrillo-Urbina AJ, García-Hermoso A, Sánchez-López M, *et al*. The effects of physical exercise in children with attention deficit hyperactivity disorder: a systematic review and meta-analysis of randomized control trials. *Child Care Health Dev* 2015;41:779–88.
27 Neudecker C, Mewes N, Reimers AK, *et al*. Exercise Interventions in Children and Adolescents With ADHD: A Systematic Review. *J Atten Disord* 2019;23:307–24.
28 Ng QX, Ho CYX, Chan HW, *et al*. Managing childhood and adolescent attention-deficit/hyperactivity disorder (ADHD) with exercise: A systematic review. *Complement Ther Med* 2017;34:123–8.
29 S J, Arumugam N, Parasher RK. Effect of physical exercises on attention, motor skill and physical fitness in children with attention deficit hyperactivity disorder: a systematic review. *ADHD Atten Def Hyp Disord* 2019;11:125–37.
30 Liang X, Li R, Wong SHS, *et al*. The impact of exercise interventions concerning executive functions of children and adolescents with attention-deficit/hyperactive disorder: a systematic review and meta-analysis. *Int J Behav Nutr Phys Act* 2021;18:68.
31 Xie Y, Gao X, Song Y, *et al*. Effectiveness of Physical Activity Intervention on ADHD Symptoms: A Systematic Review and Meta-Analysis. *Front Psychiatry* 2021;12.
32 Welsch L, Alliott O, Kelly P, *et al*. The effect of physical activity interventions on executive functions in children with ADHD: A systematic review and meta-analysis. *Ment Health Phys Act* 2021;20:100379.
33 Sun W, Yu M, Zhou X. Effects of physical exercise on attention deficit and other major symptoms in children with ADHD: A meta-analysis. *Psychiatry Res* 2022;311:114509.
34 Montalva-Valenzuela F, Andrades-Ramírez O, Castillo-Paredes A. Effects of Physical Activity, Exercise and Sport on Executive Function in Young People with Attention Deficit Hyperactivity Disorder: A Systematic Review. *EJIHPE* 2022;12:61–76.
35 Seiffer B, Hautzinger M, Ulrich R, *et al*. The Efficacy of Physical Activity for Children with Attention Deficit Hyperactivity Disorder: A Meta-Analysis of Randomized Controlled Trials. *J Atten Disord* 2022;26:656–73.
36 Zhu F, Zhu X, Bi X, *et al*. Comparative effectiveness of various physical exercise interventions on executive functions and related symptoms in children and adolescents with attention deficit hyperactivity disorder: A systematic review and network meta-analysis. *Front Public Health* 2023;11:1133727.
37 Higgins JPT, Thomas J, Chandler J, eds. Cochrane Handbook for Systematic Reviews of Interventions. Chichester, UK: John Wiley & Sons, 2019.
38 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
39 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 3rd edn. American psychiatric Association, 1980.
40 Karimi M, Brazier J. Health, Health-Related Quality of Life, and Quality of Life: What is the Difference? *Pharmacoeconomics* 2016;34:645–9.
41 Lefebvre C, Glanville J, Briscoe S, *et al*. Technical supplement to chapter 4: searching for and selecting studies. In: Higgins JPT, Thomas J, Chandler J, et al, eds. *Cochrane Handbook for Systematic Reviews of Interventions, Version 6*. Cochrane, 2019.
42 Covidence. Available: www.covidence.org [Accessed 01 Aug 2024].
43 Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
44 COMET initiative. Available: www.comet-initiative.org [Accessed 01 Aug 2024].
45 ICHOM. Available: www.ichom.org [Accessed 01 Aug 2024].
46 Epstein JN, Weiss MD. Assessing treatment outcomes in attention-deficit/hyperactivity disorder: a narrative review. *Prim Care Companion CNS Disord* 2012;14:PCC.11r01336.
47 Fayers PM, Machin D. *Quality of Life*. West Sussex, UK: John Wiley & Sons, 2016.
48 Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management. ADHD: Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. *Pediatrics* 2011;128:1007–22.
49 Riley AW, Forrest CB, Rebok GW, *et al*. The Child Report Form of the CHIP-Child Edition: reliability and validity. *Med Care* 2004;42:221–31.
50 Starfield B, Riley AW, Green BF, *et al*. The adolescent child health and illness profile. A population-based measure of health. *Med Care* 1995;33:553–66.
51 Landgraf JM, Ware JE, Abetz L. *Child Health Questionnaire (CHQ): A User's Manual*. New England Medical Center: Health Institute, 1996.
52 Varni JW, Seid M, Rode CA. The PedsQL: measurement model for the pediatric quality of life inventory. *Med Care* 1999;37:126–39.
53 Ravens-Sieberer U, Gosch A, Rajmil L, *et al*. KIDSCREEN-52 quality-of-life measure for children and adolescents. *Expert Rev Pharmacoecon Outcomes Res* 2005;5:353–64.
54 Strauss E, Sherman EMS, Spreen O. *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary*. New York, USA: Oxford University Press, 2006.
55 Gioia GA, Isquith PK, Guy SC, *et al*. TEST REVIEW Behavior Rating Inventory of Executive Function. *Child Neuropsychol* 2000;6:235–8.
56 Brown TE. *Brown Attention-Deficit Hyperactivity Disorder Scales for Adolescents and Adults*. San Antonio, TX: The Psychological Corporation, Harcourt Assessment, 2001.
57 DuPaul GJ, Power TJ, Anastopoulos AD, *et al*. *ADHD Rating Scale-IV: Checklists, Norms, and Clinical Interpretation*. New York, NY: Guilford Press, 1998.
58 Conners CK. *Conners' Rating Scales - Revised (CRS-R): Technical Manual*. North Tonawanda, NY: Multi-Health Systems, 2001.
59 Swanson JM. *School-Based Assessment and Interventions for ADD Students*. Irvine, CA: K.C. Publishing, 1992.
60 Swanson J, Deutsch C, Cantwell D, *et al*. Genes and attention-deficit hyperactivity disorder. *Clin Neurosci Res* 2001;1:207–16.
61 Bird HR, Shaffer D, Fisher P, *et al*. The Columbia Impairment Scale (CIS): Pilot findings on a measure of global impairment for children and adolescents. *Int J Methods Psychiatr Res* 1993;3:167–76.
62 DuPaul GJ, Rapport MD, Perriello LM. Teacher Ratings of Academic Skills: The Development of the Academic Performance Rating Scale. *School Psych Rev* 1991;20:284–300.
63 Gresham FM, Elliott SN. *Social Skills Improvement System: Rating Scales*. Bloomington, MN: Pearson Assessments, 2008.
64 Fabiano GA, Pelham, Jr. WE, Waschbusch DA, *et al*. A Practical Measure of Impairment: Psychometric Properties of the Impairment Rating Scale in Samples of Children With Attention Deficit Hyperactivity Disorder and Two School-Based Samples. *J Clin Child Adolesc Psychol* 2006;35:369–85.
65 Canadian ADHD Resource Alliance. *Canadian ADHD practice guidelines*. Toronto, CA: CADDRA; 2006.
66 Cochrane RevMan. Available: https://revman.cochrane.org/ [Accessed 01 Aug 2024].
67 Thorlund K, Walter SD, Johnston BC, *et al*. Pooling health-related quality of life outcomes in meta-analysis—a tutorial and review of methods for enhancing interpretability. *Res Synth Methods* 2011;2:188–203.
68 Barbateskovic M, Koster TM, Eck RJ, *et al*. A new tool to assess Clinical Diversity In Meta-analyses (CDIM) of interventions. *J Clin Epidemiol* 2021;135:29–41.
69 Wetterslev J, Jakobsen JC, Gluud C. Trial Sequential Analysis in systematic reviews with meta-analysis. *BMC Med Res Methodol* 2017;17:39.
70 Jakobsen JC, Wetterslev J, Winkel P, *et al*. Thresholds for statistical and clinical significance in systematic reviews with meta-analytic methods. *BMC Med Res Methodol* 2014;14:120.
71 Wetterslev J, Thorlund K, Brok J, *et al*. Estimating required information size by quantifying diversity in random-effects model meta-analyses. *BMC Med Res Methodol* 2009;9:86.
72 Liguori G. *ACSM's Guidelines for Exercise Testing and Prescription*. Philadelphia, PA: Wolter Kluwer Health, 2021.
73 Egger M, Davey Smith G, Schneider M, *et al*. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.