Mechanisms linking physical activity with psychiatric symptoms across the lifespan: a protocol for a systematic review

Phuong Thuy Nguyen Ho, Tram Ha Pham Bich, Thao Tong, Wichor M Bramer, Amy Hofman, David Revalids Lubans, Meike W Vernooij, Maria Rodriguez-Ayllon

ABSTRACT

Introduction Persistent psychiatric symptomatology during childhood and adolescence predicts vulnerability to experience mental illness in adulthood. Physical activity is well-known to provide mental health benefits across the lifespan. However, the underlying mechanisms linking physical activity and psychiatric symptoms remain underexplored. In this context, we aim to systematically synthesise evidence focused on the mechanisms through which physical activity might reduce psychiatric symptoms across all ages.

Methods and analysis With the aid of a biomedical information specialist, we will develop a systematic search strategy based on the predetermined research question in the following electronic databases: MEDLINE, Embase, Web of Science, Cochrane and PsycINFO. Two independent reviewers will screen and select studies, extract data and assess the risk of bias. In case of inability to reach a consensus, a third person will be consulted. We will not apply any language restriction, and we will perform a qualitative synthesis of our findings as we anticipate that studies are scarce and heterogeneous.

Ethics and dissemination Only data that have already been published will be included. Then, ethical approval is not required. Findings will be published in a peer-reviewed journal and presented at conferences. Additionally, we will communicate our findings to healthcare providers and other sections of society (eg, through regular channels, including social media).

PROSPERO registration number CRD42021239440.

INTRODUCTION

Persistent psychiatric symptomatology in childhood and adolescence predicts vulnerability to experience mental illness later in life. For instance, it is known that individuals with mental illness have a decreased life expectancy of 10–15 years and a lower quality of life than individuals from the general population. Psychiatric symptoms are typically grouped into two broad categories (ie, internalising/emotional and externalising/behavioural). Specifically, the externalising problems include a variety of disinhibited/externally focused behavioural symptoms such as conduct problems, rule-breaking behaviour, attention-deficit/hyperactivity problems. On the contrary, the internalising disorder include a variety of overinhibited/internally focused symptoms, such as depression, anxiety or somatic symptoms. Several risk factors for psychiatric symptoms have been well established in childhood (eg, poverty and social disadvantage) and adulthood (eg, level of education and physical illness). However, less is known about the protective factors (eg, physical activity) that might contribute to decreasing both child and adult psychopathology.

There is a growing body of literature suggesting that physical activity has a small-to-moderate positive effect on psychiatric symptoms in children and adolescents and in adults and older adults. However, most of the studies have focused on exploring the effect size of the association or effect in terms
of dose-response, while the mechanisms underlying this relationship or effect remain underexplored. In 2016, Lubans et al. published a systematic review of the mechanisms linking physical activity and psychiatric symptoms in children and adolescents. They proposed a conceptual model, which postulated three distinct yet intertwined potential groups of mechanisms (ie, neurobiological, psychosocial and behavioural mechanisms). In brief, they identified a lack of available evidence for the specific mechanisms responsible for the effect of physical activity on mental and cognitive health in young people. Additionally, they only included intervention studies, and although this type of design can provide evidence for cause and effect, observational studies can also provide complementary information, particularly when there is a lack of evidence on the topic.

In adults, only narrative reviews, mainly focused on cognition and depression, have explored the potential mechanisms that might link physical activity with psychiatric symptoms in adulthood. For instance, Stillman et al. suggested that physical activity might reduce depression and anxiety via psychosocial pathways (eg, mood). Additionally, Kandola et al. presented a conceptual framework of the key biological and psychosocial mechanisms underlying the relationship between physical activity and depressive symptoms in adults. However, no previous systematic reviews have been performed to synthesise the existing evidence in adults.

Understanding the mechanisms linking physical activity with psychiatric symptoms may help to explain, predict and intervene more effectively, which could stimulate the identification of cost-efficient alternative therapies for preventing and treating mental illness at all ages. To establish this evidence-based, it is imperative to synthesise and update all relevant literature mapping the mechanisms through which physical activity reduces psychiatric symptoms across the lifespan.

**Objective**

We aim to conduct a systematic review to explore the underlying mechanisms linking physical activity with psychiatric symptoms in humans of all ages.

**Review questions**

How does physical activity affect/associate with psychiatric symptoms via psychosocial, neurobiological and behavioural pathways across the lifespan?

**METHODS**

The present protocol follows the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) for Protocols guideline for systematic review and meta-analysis protocols. We will perform the search in March 2022, and we are planning to finish the systematic review in June 2022.

**Patient and public involvement**

Patients and the public were not involved in the design, development, conduct, reporting or dissemination of this study.

**Eligibility criteria**

We will include studies based on predefined criteria as summarised in Table 1 and the text.

### Table 1 Inclusion criteria based on PICOS strategy

<table>
<thead>
<tr>
<th>PICOS</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>1. All ages across the lifespan: infancy and toddlerhood (birth to age 2), preschoolers (2–5 years), children (6–11 years), adolescents (12–18 years), young and middle adults (18–65 years), late adulthood (+65 years).</td>
<td>1. Studies including individuals with physical or psychological disorders diagnosed by medical records.</td>
</tr>
<tr>
<td></td>
<td>2. Human studies.</td>
<td>2. Elite athletes.</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>1. Observational studies, which explored the mechanisms through which physical activity is associated with psychiatric symptoms.</td>
<td>3. Animal studies.</td>
</tr>
<tr>
<td></td>
<td>2. Studies examining the mechanisms through which physical activity has a positive effect on psychiatric symptoms.</td>
<td></td>
</tr>
<tr>
<td><strong>Comparison</strong></td>
<td>1. Not applicable.</td>
<td></td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>1. The subscales of internalising symptoms (ie, depression, anxiety, somatic symptoms) and externalising symptoms (ie, conduct problems, rule-breaking behaviour, attention-deficit/hyperactivity problems).</td>
<td>1. Conference proceedings and other types of grey literature.</td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>1. Intervention studies (randomised controlled trials, non-randomised controlled trials, prospective longitudinal studies and cross-sectional studies).</td>
<td>2. Narrative reviews, systematic reviews or meta-analyses.</td>
</tr>
</tbody>
</table>

MET, metabolic equivalent of task.
Population
We will include human studies including participants of all ages. Studies including individuals with physical or psychological disorders diagnosed by medical records, elite athletes and animals will be excluded.

Intervention
We will include all observational studies, which have explored the mechanisms through which physical activity is associated with psychiatric symptoms. Intervention studies examining the mechanisms through which physical activity affects psychiatric symptoms will be also included. Studies in which physical fitness (ie, capacity to perform physical activity, which refers to a full range of physiological and psychological qualities), or sedentary behaviour (ie, any waking behaviour characterised by an energy expenditure ≤1.5 METs, while in a sitting, reclining or lying posture) are the independent variables instead of physical activity (ie, any bodily movement produced by skeletal muscle that results in energy expenditure) will be excluded. Additionally, multiple health behaviour intervention studies (eg, co-interventions such as a dietary programme combined with physical activity) will be excluded because they preclude drawing conclusions on the isolated effect of physical activity or sedentary behaviour on psychiatric symptoms.

Outcomes
We will include the subscales of internalising (ie, depression, anxiety, somatic symptoms) and externalising (ie, conduct problems, rule-breaking behaviour, attention-deficit/hyperactivity problems) disorders.

Study designs
Intervention studies (randomised controlled trials (RCTs), non-RCTs, prospective longitudinal and cross-sectional studies will be included. We will not include conference proceedings and other types of grey literature since risk of bias for these studies cannot be adequately assessed.21

Potential mechanisms
Studies will be included if they explored the role of any potential neurobiological, psychosocial or behavioural mechanisms in the relationship between physical activity and psychiatric symptoms. We will refer to the variables used to explore the potential mechanisms as ‘mediating variables’, but we will include any study exploring the mechanisms linking physical activity and psychiatric symptoms and not only those that used a mediation analysis.

Further restrictions
No language and publication date restriction will be applied. All databases will be searched from their date of inception, and we will include every study that meets the above-mentioned criteria regardless of the language.

Search strategy for identifying relevant studies
With the assistance of a biomedical information specialist, we will develop a systematic search strategy based on the predetermined research question in the following electronic databases: MEDLINE Ovid, Embase.com, Web of Science Core Collection, Cochrane CENTRAL register of Trials and PsycINFO Ovid. First, we will search for potentially relevant studies based on a search strategy that is the combination of Medical Subject Headings terms for Medline and Emtree terms for Embase and free text search. Our research team, including a librarian who is specialised in search strategy development, has developed this search strategy. Search terms are personalised to each database (see online supplemental appendix). Search terms include four parts: (1) terms to identify our independent variable (ie, physical activity); (2) terms to identify our mechanisms (ie, neurobiological, psychosocial, behavioural mechanisms); (3) terms to identify our outcome (ie, psychiatric symptoms) and (4) terms to exclude articles that match our exclusion criteria. An additional search for studies will be performed by screening reference lists of included studies and their citations through Google Scholar. Third, we will contact experts in the field to identify additional studies that may have been missed and any relevant ongoing or unpublished studies.

Study records
Data management
First, we will extract all studies identified by the different sources into an EndNote Library. Second, we will use a published method that uses this software to automatically eliminate the duplicate studies.22 In our final report, we will note the number of duplicates in the PRISMA flow diagram (figure 1).

Selection process
First, two independent researchers (PTNH and TPBH) will screen titles and the abstracts for eligibility. When disagreements emerge between the two independent
Table 2 Summary of research investigating the mechanisms linking physical activity with psychiatric symptoms (n=?)

<table>
<thead>
<tr>
<th>Authors, year (country)</th>
<th>N sample</th>
<th>Design; target population</th>
<th>Independent variable (instrument)</th>
<th>Mediating variable (instrument)</th>
<th>Dependent variable (instrument)</th>
<th>Statistical analysis; software</th>
<th>Confounders</th>
<th>Main findings</th>
</tr>
</thead>
</table>

The Risk of bias and quality of the evidence

In case overlapping populations are analysed in multiple studies, we will include according to the following hierarchy the study that (1) has the lowest risk of bias, or (2) incorporates the largest sample size. In the case when a study reports multiple effect estimates for overlapping populations, we will select according to the following hierarchy: (1) the most adjusted model, (2) the closest time-point to the end of the intervention or (3) the largest treatment group. Findings from observational and intervention studies will be rated using the method first employed by Sallis et al.20 and more recently by Lubans et al.21 and Rodriguez-Ayllon et al.9 If 0%–33% of studies reported a statistically significant mediation (eg, self-esteem) between the independent (eg, physical activity) and dependent variable (eg, depressive symptoms), the result will be classified as no association (Ø); if 34%–59% of studies reported a significant mediation, or if fewer than four studies reported on the outcome, the result will be classified as being inconsistent/uncertain (?) and if ≥60% of studies found a statistically significant mediation, the result will be classified as significant (√).

Data synthesis and analysis

Risk of bias and quality of the evidence

The risk of bias will be evaluated independently by two researchers (PTNH and TT) and disagreements were solved in a consensus meeting with the third researcher (MR-A). The risk of bias will be evaluated using the Joanna Briggs Institute Critical Appraisal Tool for Systematic Reviews (https://jbi.global/critical-appraisal-tools). This tool has already been used by other authors in the field.23 24 In brief, this tool includes four specific checklists depending on the study design (ie, cross-sectional studies, longitudinal studies, RCTs and non-RCTs). There are four possible answers for each category: ‘yes’ (criterion met), ‘no’ (criterion not met), ‘unclear’ or ‘not applicable’. The specific tools include: 8 items for cross-sectional studies, 11 items for longitudinal studies, 9 items for non-RCTs and 13 items for RCTs. Studies will be categorised as ‘high risk’ or ‘low risk’. Specifically, the studies will be considered as ‘low risk’ if at least 75% of the applicable items are scored as ‘yes’ (criterion met). In contrast, articles will be considered ‘high risk’ when <75% of the applicable items were scored as ‘yes’. This classification has been previously employed by Molina-Garcia et al.25

Lastly, the Grading of Recommendations Assessment, Development and Evaluation framework will be used to assess the quality of the evidence across studies.

Data extraction process

Two researchers (PTNH and TT) will independently extract data from the included studies to a customised data extraction form developed a priori that has been solved in a consensus meeting with the same third researcher (MR-A). This tool has already been used by other authors in the field.23 24 In brief, this tool includes four specific checklists depending on the study design (ie, cross-sectional studies, longitudinal studies, RCTs and non-RCTs). There are four possible answers for each category: ‘yes’ (criterion met), ‘no’ (criterion not met), ‘unclear’ or ‘not applicable’. The specific tools include: 8 items for cross-sectional studies, 11 items for longitudinal studies, 9 items for non-RCTs and 13 items for RCTs. Studies will be categorised as ‘high risk’ or ‘low risk’. Specifically, the studies will be considered as ‘low risk’ if at least 75% of the applicable items are scored as ‘yes’ (criterion met). In contrast, articles will be considered ‘high risk’ when <75% of the applicable items were scored as ‘yes’. This classification has been previously employed by Molina-Garcia et al.25

Lastly, the Grading of Recommendations Assessment, Development and Evaluation framework will be used to assess the quality of the evidence across studies.

Table 2 Summary of research investigating the mechanisms linking physical activity with psychiatric symptoms (n=?)

<table>
<thead>
<tr>
<th>Authors, year (country)</th>
<th>N sample</th>
<th>Design; target population</th>
<th>Independent variable (instrument)</th>
<th>Mediating variable (instrument)</th>
<th>Dependent variable (instrument)</th>
<th>Statistical analysis; software</th>
<th>Confounders</th>
<th>Main findings</th>
</tr>
</thead>
</table>
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.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs
Phuong Thuy Nguyen Ho http://orcid.org/0000-0003-3082-9285
Tram Ha Pham Bich http://orcid.org/0000-0002-1106-6094
Wichor M Bramer http://orcid.org/0000-0003-2681-9180
David Revalds Lubans http://orcid.org/0000-0000-0000-0000
Tram Ha Pham Bich http://orcid.org/0000-0002-1106-6094

REFERENCES