

Physical Activity and Anxiety: A Systematic Review and Meta-analysis of Prospective Cohort Studies



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Context: Anxiety symptoms and disorders are highly prevalent and costly. Prospective studies suggest that physical activity may prevent anxiety development; however, this body of literature has not been reviewed comprehensively.

Evidence acquisition: Studies measuring physical activity at baseline and anxiety at a designated follow-up at least 1 year later were located using MEDLINE, PsycINFO, and CINAHL Complete through June 2018.

Evidence synthesis: Data were analyzed July–December 2018. Study quality was assessed using Q-Coh. Among studies of adults, a random-effects meta-analysis was conducted for crude and the most fully adjusted models for three outcomes: self-reported anxiety symptoms, a diagnosis of any anxiety disorder, and a diagnosis of generalized anxiety disorder. As there were few studies with diverse samples and outcome measures, findings were elaborated with a critical narrative review of all studies. Twenty-four studies (median follow-up, 4.75 years) of >80,000 unique individuals were included in the systematic review; thirteen were included in the meta-analyses. Six studies were assessed as low quality, nine as acceptable, and nine as good. From adjusted models, odds of elevated anxiety symptoms (OR=0.8742, 95% CI=0.7731, 0.9886, $n=9$), any anxiety disorder (OR=0.6626, 95% CI=0.5337, 0.8227, $n=3$), and generalized anxiety disorder specifically (OR=0.5438, 95% CI=0.3231, 0.9153, $n=3$) were significantly lower after physical activity exposure.

Conclusions: Available evidence suggests that engaging in physical activity protects against anxiety symptoms and disorders. However, notable challenges in the current evidence base include issues regarding exposure and outcome measures, consistent adjustment for putative confounders, representativeness of samples, and attrition bias, which warrant further research.

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INTRODUCTION

Anxiety disorders are consistently the most prevalent class of mental disorders in the general population¹ and are the sixth leading cause of years lived with disability.² There is robust epidemiologic and clinical evidence to support associations between anxiety disorders and chronic medical conditions, such as irritable bowel syndrome, asthma, cancer, chronic pain, and cardiovascular disease as well as associated premature mortality.^{3,4} In 2010, the 12-month prevalence of any ICD-10 anxiety disorder was 13.4% in

Europe (69.1 million people), costing more than €74 billion,⁵ and 22% for any DSM-5 anxiety disorder in the

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U.S.⁶ Findings from several national and international studies have shown the profound economic and societal impacts of anxiety disorders.^{7–9}

Frontline treatments for anxiety disorders include antidepressants, such as selective serotonin reuptake inhibitors, and cognitive behavioral therapy.^{10,11} However, selective serotonin reuptake inhibitors can have negative side effects, such as increased weight gain¹², suicidality, and aggression.¹³ Cognitive behavioral therapy has been only moderately efficacious, with the need for the identification of more-effective treatments.¹⁰ Further, the number of individuals seeking care can be low; as the symptoms associated with anxiety disorders are commonly interpreted as normal responses to social adversity, and rigorous biomedical causal models are scarce.¹⁴ Given the prevalence and individual and economic burden of anxiety disorders, and that treatments can be inadequate,^{10,12,13} strategies that facilitate the prevention of anxiety are needed.

One such strategy is physical activity (i.e., movement that is carried out by the skeletal muscles that results in energy expenditure).¹⁵ Experimental evidence has shown that exercise (i.e., planned, structured, and repetitive movement intended to improve or maintain one or more components of fitness)¹⁵ is effective in reducing anxiety symptoms in people with^{16–18} and without^{19–21} anxiety disorders, including those with chronic illnesses.²²

Whether physical activity can help prevent anxiety is less clear. Cross-sectional evidence supports inverse associations between physical activity and anxiety symptoms²³ and disorders.²⁴ However, population-based evidence of a prospective association between physical activity and incident anxiety disorders or elevated symptoms has not been synthesized.

Therefore, this review has three primary aims: (1) to synthesize the available literature, (2) to assess limitations in this research, and (3) to make recommendations for future research. As there are few studies with diverse samples and outcome measures, meta-analysis quantifies associations of physical activity with anxiety across studies of similar samples (i.e., adults versus adolescents) and outcome measures (i.e., self-reported anxiety symptoms versus a clinical diagnosis/self-reported clinical diagnosis of any, and specific, anxiety disorders). Meta-analytic findings are elaborated with a critical narrative review of all studies.

EVIDENCE ACQUISITION

A systematic review and a meta-analysis were conducted in accordance with established guidelines for conduct and reporting.^{25,26} The protocol was not registered but satisfied contemporary standards.²⁷

Data Sources and Searches

The searches were conducted by two authors (CMcD and MPH) using MEDLINE, PsycINFO, and CINAHL Complete. Articles published from database inception to June 2018 that contained the following terms within their title, abstract, or keywords:

1. at least one term of *physical activity, leisure time, exercise, or sport**;
2. one of *anxiety, generalized anxiety disorder (GAD), panic, phobia*;
3. and one of *association, follow-up, risk factor, protect*, causal*, onset, prospective, cohort, or longitudinal* were located.

Supplemental searches using combinations of these key terms and of articles citing and cited by included studies and relevant review articles were performed manually in Google Scholar.

Study Selection

Inclusion criteria included the following: (1) peer-reviewed prospective cohort studies; (2) physical activity measured at baseline by single or multiple questions assessing participation in exercise, sports, or frequency, time, or distance of physical activity, as meeting public health guidelines for moderate or vigorous physical activity, or a validated measure that estimated total volume (i.e., frequency X time X intensity) or Metabolic Equivalent of Task; and (3) anxiety symptoms or disorder subsequently measured at a defined follow-up assessment by self-reported physician diagnosis, clinical diagnosis, diagnosis using diagnostic interviews (e.g., instruments using DSM²⁸ or ICD²⁹ criteria), or established cut offs or continuous scores of anxiety screening instruments. Articles were excluded if they satisfied one of the following criteria: (1) included a sample solely of people with elevated anxiety symptoms or an anxiety disorder at baseline; (2) had an outcome of diagnosed obsessive-compulsive disorder or post-traumatic stress disorder, which are not currently defined as an anxiety disorder;²⁸ (3) used an ill-defined measure of physical activity exposure;³⁰ and (4) had a follow-up period from baseline <1 year, as <1 year was not considered a sufficient time frame for physical activity to exert a meaningful protective influence against elevated anxiety symptoms and incident anxiety disorders. Studies that met these criteria but reported statistics that could not be converted to ORs were not included in the analyses but were included in a critical narrative review. Located studies were managed in EndNote, version X7. [Figure 1](#) provides a flowchart of article inclusion and exclusion.

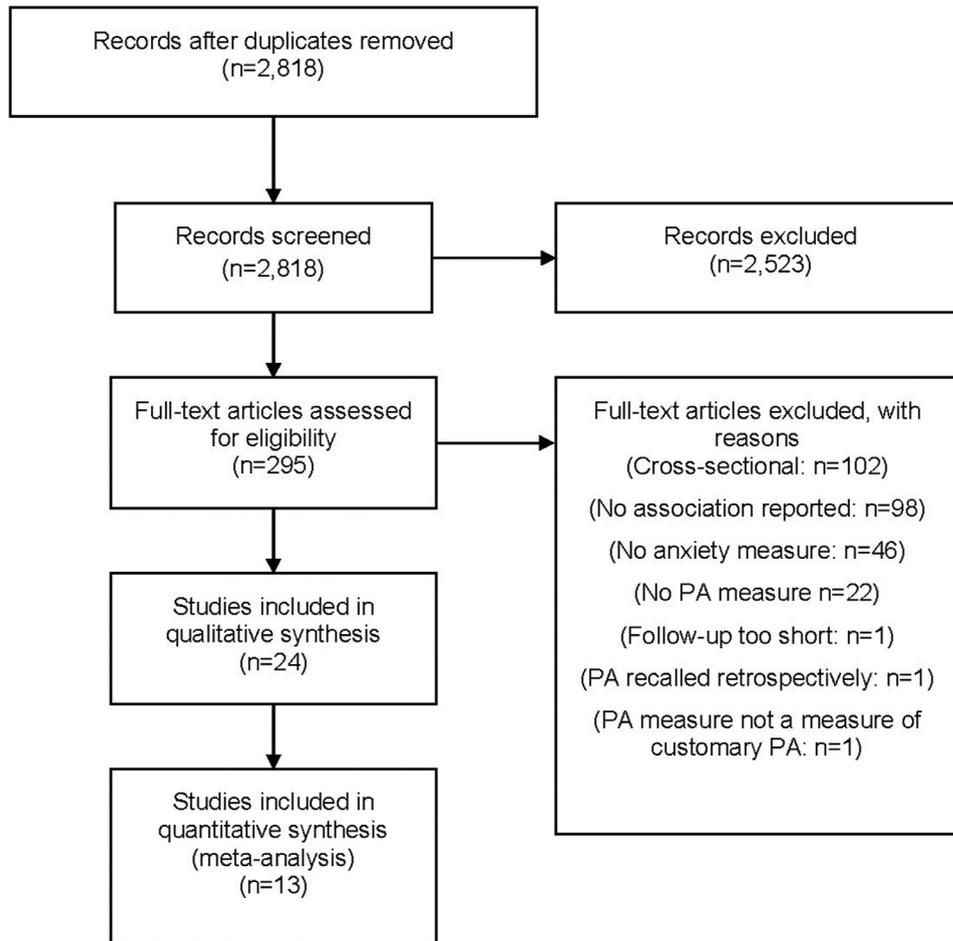


Figure 1. Flow chart of article inclusion and exclusion.
PA, physical activity.

Data Extraction

Data on geographic location, follow-up timeframe, number of participants included in analyses, participants' age and sex, anxiety measure, study design, physical activity measure, and physical activity dose were extracted into SPSS, version 21 by two authors (CMcD and BRG). Discrepancies were resolved by consultation between both authors. For studies included in the meta-analysis, ORs and 95% CIs or relevant data to be converted to ORs as detailed below were extracted. The OR for the largest physical activity dose in each study was selected. Multiple ORs from individual studies were included if there was no overlap in populations (i.e., associations for male and female participants were reported separately).³¹ For adjusted associations, the OR or relevant association from the fully adjusted model was extracted.

OR Calculations

When ORs and 95% CIs were not reported, they were independently calculated by two authors (CMcD and

MPH) where possible. Discrepancies were resolved by consultation between both authors. ORs and 95% CIs were calculated from 2×2 tables,³¹ or converted from standardized regression weights^{32–34} and Pearson correlation coefficients³⁵ using standard procedures.³⁶ When associations were reported with the highest or middle physical activity group as the reference group, ORs for the lowest physical activity group were inverted.^{32,37–40}

Study Quality

Two authors (CMcD and BRG) used the Q-Coh⁴¹ to independently assess study quality. Discrepancies were resolved by consultation between both authors. This tool assesses seven domains (representativeness of the sample, comparability of the groups at the beginning of the study, quality of the exposure measure, maintenance of the comparability during the follow-up time, quality of the outcome measure, attrition, and statistical analyses). These domains are derived from the extended classification of biases (i.e., selection bias, performance bias,

detection bias, and attrition bias) and are consistent with the Grade Working Group (www.gradeworkinggroup.org/). The studies were rated as good (risk of bias in zero to one domain), acceptable (risk of bias in two domains), or low (risk of bias in three or more domains). This scale has previously displayed good inter-rater reliability.^{41,42}

Data Analysis

Data were analyzed from July to December 2018. Only two studies examined adolescents and were excluded from analyses. Analyses of AORs were run separately for outcomes of (1) elevated self-reported anxiety symptoms; (2) incident diagnosis/self-reported diagnosis of any anxiety disorder (i.e., a diagnosis of any DSM²⁸ or ICD²⁹ anxiety disorder, including GAD); and (3) incident diagnosis of GAD specifically (there were insufficient data to run analyses for other specific anxiety disorders). Analyses of crude ORs were run for studies using self-reported anxiety symptoms as the outcome. The logarithm of each OR was computed, weighted by its inverse variance before analyses, and the results were converted back to ORs for presentation. DerSimonian and Laird's inverse of variance random effects models were used with macros (*MeanES*) to aggregate the mean logOR.^{43,44} Heterogeneity was quantified with *Q* statistic and *I*².⁴⁵ Heterogeneity was indicated if *Q*_{Total} reached a significance level of *p*<0.05.⁴⁴ Analyses were conducted for both crude and adjusted logORs separately.

EVIDENCE SYNTHESIS

Study Characteristics

The study characteristics are reported in [Appendix Table 1](#) (available online). More than 80,000 unique individuals from 24 studies (median follow-up, 4.75 years) were included in this review (median *N*=2,120, IQR=1,161, 4,526). The three largest studies used data from Waves 1–2³⁹ and Waves 2–3^{31,46} of the Nord-Trøndelag Health Study (HUNT) study. The median age was 43.7 (25.6–48.4) years, with just two studies focusing exclusively on children or adolescents.^{47,48} The median proportion of female participants was 54.5% (49%–61%). The studies were conducted in North America (*n*=2), Europe (*n*=18), Australia (*n*=2), and Asia (*n*=2). All studies used a self-report measure of physical activity assessed at baseline alone (*n*=18) or as change over time (*n*=6). The outcomes were anxiety symptoms (*n*=8), a screening level for anxiety symptoms indicative of a disorder (*n*=10), self-reported diagnosis of anxiety disorder (*n*=1), and diagnosis of an anxiety disorder (*n*=5). The quality of six studies was assessed as low, nine as acceptable, and nine as good ([Appendix Table 2](#), available online). Agreement was good in all inferences evaluating the different domains of

quality (κ =0.61–1.00, all *p*<0.01), with initial agreement on 95.2% domains achieved. Agreement for the overall assessment of quality was very good (κ =0.91), with initial agreement on 94.4% studies achieved.

Self-Reported Anxiety Symptoms

All crude ORs (*k*=6, *n*=5) were <1.00, indicating that physical activity was associated with lower odds of self-reported anxiety symptoms.^{31,34,49–51} The mean crude OR was 0.8436 (95% CI=0.7638, 0.9317, *Q*_{Total (5)}=7.5913, *p*=0.1802; *I*²=47.31%, 95% CI=12.95%, 68.11%).

All AORs (*k*=9, *n*=9) were <1.00.^{23,32–34,37,38,40,49,51} The mean AOR was 0.8742 (95% CI=0.7731, 0.9886, *Q*_{Total (8)}=13.6364, *p*=0.0917; *I*²=48.67%, 95% CI=23.10%, 65.73%). [Figure 2](#) shows a forest plot of the distribution of AORs. These findings are supported by four^{52–55} of the five⁴⁶ other adult studies and both the adolescent papers^{47,48} that measured anxiety symptoms but could not be included in analyses.

Diagnosis of Any Anxiety Disorder

All AORs (*k*=3, *n*=3) were <1.00.^{56–58} The mean OR was 0.6626 (95% CI=0.5337, 0.8227, *Q*_{Total (2)}=2.7218, *p*=0.2564; *I*²=62.26%, 95% CI=23.30%, 82.40%). [Figure 3](#) shows a forest plot of the distribution of ORs. These findings were supported by one⁵⁹ of the two⁶⁰ other studies to examine a diagnosis of any anxiety disorder.

Diagnosis of Generalized Anxiety Disorder

All AORs (*k*=3, *n*=3) were <1.00.^{57,58,61} The mean OR was 0.5438 (95% CI=0.3231, 0.9153; *Q*_{Total (2)}=0.5991, *p*=0.7412; *I*²=0.00%). [Figure 4](#) shows a forest plot of the distribution of ORs. Both studies that examined associations of physical activity with panic, agoraphobia, social phobia, and specific phobia also indicated inverse associations for these outcomes.^{57,58}

Physical Activity Dose–Response

There were insufficient data to quantitatively assess a dose–response, and the findings appeared to be mixed. Six studies^{32,37,38,51,56,61} that used a physical activity measure of volume (i.e., a product of time engaged in physical activity and its intensity) reported findings for more than one level of physical activity. Of these, three studies^{32,56,61} supported lower odds for increased dose of physical activity. Among the six studies^{31,39,46,57–59} that measured a single parameter of physical activity, two^{57,59} reported stronger associations for increased amounts of physical activity. Three^{56,57,61} of the four studies^{56–58,61} that measured some sort of dose–response and used a diagnosis/self-reported diagnosis of an anxiety disorder found stronger associations with increased amounts of physical activity.

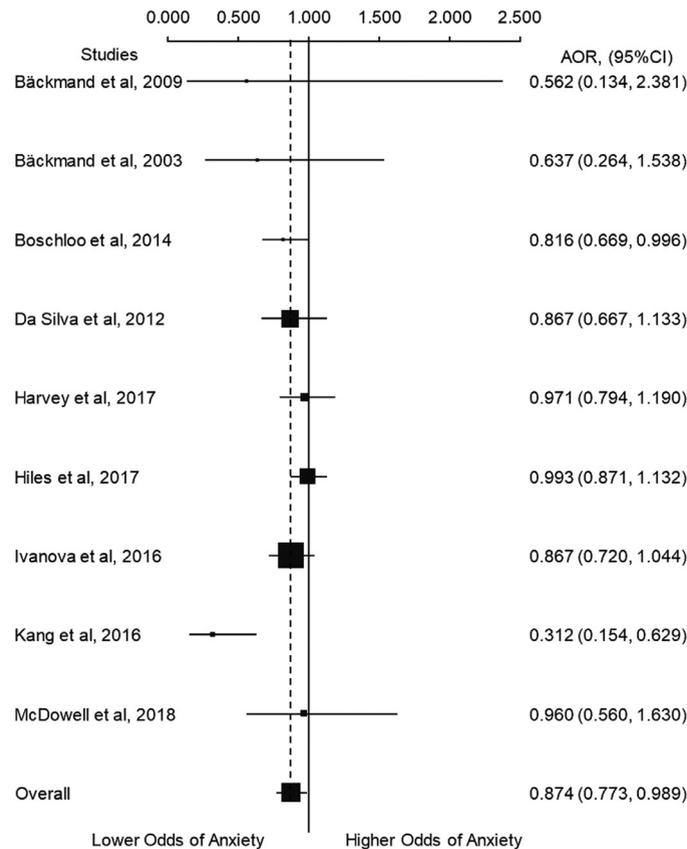


Figure 2. Forest plot of the distribution of AORs and 95% CIs for anxiety symptoms.

DISCUSSION

To the authors' knowledge, this is the first systematic review and meta-analysis of longitudinal associations between physical activity and anxiety. All crude and adjusted associations included in the current meta-analyses indicated inverse associations between physical activity and subsequent anxiety, but just four of 15 (two crude and two adjusted), two of three, and two of three ORs reached statistical significance for anxiety symptoms, any anxiety disorder, and GAD outcomes, respectively. Nonetheless, a small, significant, cumulative association between physical activity and anxiety symptoms was observed (OR=0.8742, 95% CI=0.7731, 0.9886). The studies that were not included in the meta-analysis also reported small, inverse associations between physical activity and anxiety symptoms.^{52–55} Although analyses included only three studies within each category, stronger associations between physical activity and reduced odds of a subsequent diagnosis of any anxiety disorder (OR=0.6626, 95% CI=0.5337, 0.8227) and a subsequent diagnosis of GAD specifically (OR=0.5438, 95% CI=0.3231, 0.9153) were also found. A moderate degree of heterogeneity was found for outcomes of self-reported

anxiety symptoms and a diagnosis of any anxiety disorder; however, the small number of studies included in analyses precluded any meaningful attempt to provide quantitative examination (i.e., meta-regression analysis) of potential sources of variability. The present findings are promising but based on a relatively small body of literature. Consequently, there is currently insufficient quantitative evidence to justify firm conclusions regarding the protective effect of physical activity for subsequent anxiety.

Further, critical appraisal of this body of literature included assessment of study quality using the Q-Coh to assess seven domains derived from the extended classification of biases.⁴¹ Although the Q-Coh again demonstrated good inter-rater reliability,^{41,42} it remains less popular than other tools such as the Newcastle-Ottawa Scale, which has questionable reliability and validity.⁶² The studies included here were collectively of moderate quality (i.e., 75% acceptable or good), although the quality of six studies was assessed as low. The most pertinent issues were exposure and outcome measures, adjustment for putative confounders, including controlling for baseline anxiety severity, representativeness of samples, and attrition bias.

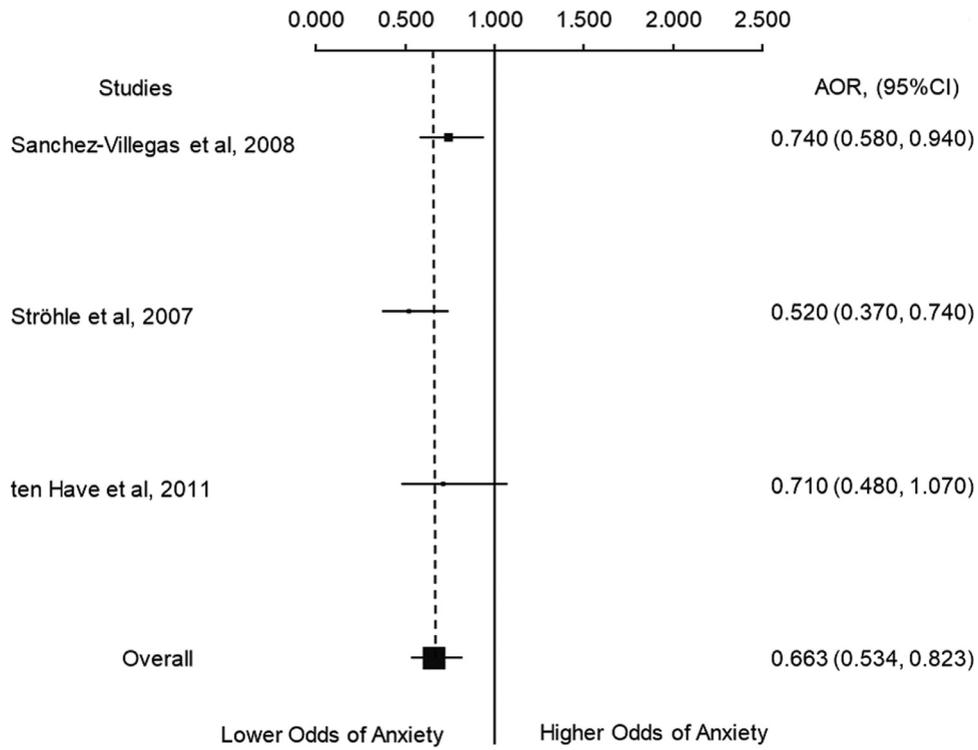


Figure 3. Forest plot of the distribution of ORs and 95% CIs for any anxiety disorder.

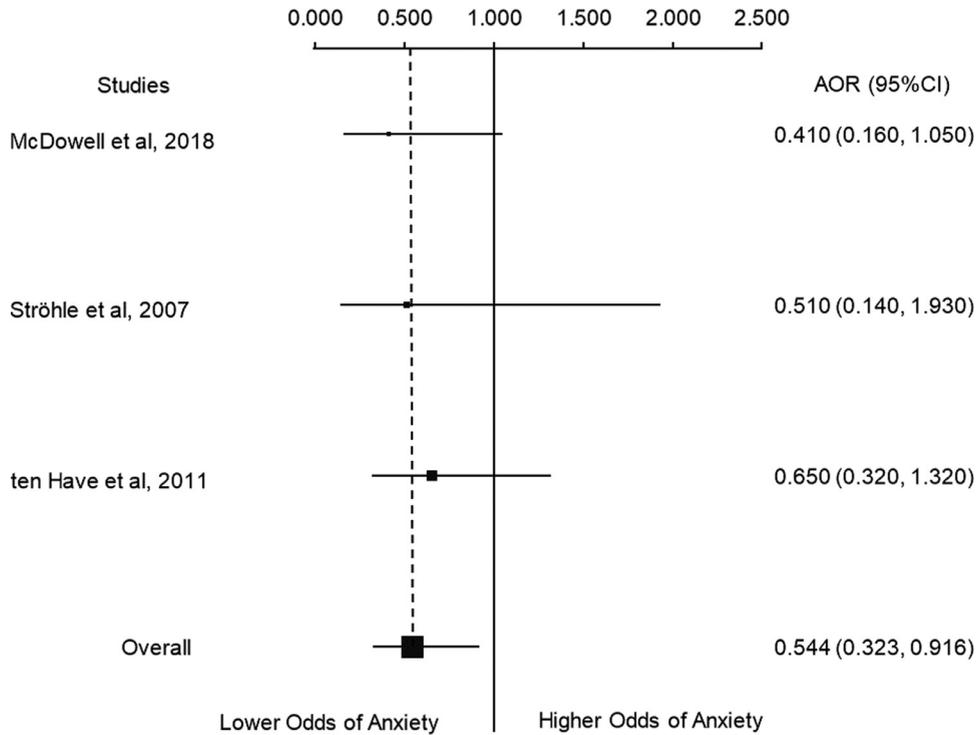


Figure 4. Forest plot of the distribution of ORs and 95% CIs for generalized anxiety disorder.

Physical Activity Exposure Measures

Several methods are available to assess physical activity. Generally, device-measured physical activity demonstrates less variability in properties of methodologic effectiveness than self-report measures.⁶³ Self-report measures may also be susceptible to over-reporting, potentially resulting from misclassification of sedentary or light activity as moderate, or overestimation of activity duration^{63,64}; however, differences between self-report and device-measured physical activity may be partially attributable to conceptual differences.⁶⁵ For example, accelerometer-based monitors quantify acceleration at a fixed point of the body (e.g., hip, wrist, and thigh) over short periods determined by the device settings, whereas self-report instruments measure reported time periods of longer duration engaged in specific behaviors, many of which are non-continuous in nature.⁶⁵ Therefore on occasion, it may be preferable to use self-report instruments; for example, assessing adherence to physical activity guidelines, which were developed based on epidemiologic relationships between self-reported physical activity and health outcomes. All studies included in the current review used self-report measures of physical activity, of which 13 used a measure that assessed physical activity volume.^{32,33,37,38,47,50–53,55,56,60,61} If physical activity exposure does indeed reduce odds of anxiety and, as expected, over-reporting of physical activity occurred, misclassification would underestimate the magnitude of this reduction as inactive people who were classified as active would have increased likelihood of anxiety.

The common study design of included studies largely limited physical activity exposure to a single measure of physical activity at baseline. No studies regularly tracked physical activity levels in a cohort across time, which would reduce the risk of misclassification bias.⁶⁶ Just six studies^{33,37,38,47,48,53} assessed physical activity more than once to permit an estimate of change in exposure across follow-up. Of these, five studies^{33,37,38,47,53} used a physical activity measure that could capture volume, but only three also adequately controlled for putative confounders.^{33,37,38} Two of these studies supported inverse associations between change in physical activity exposure and anxiety.^{33,38} Additional research is needed to more rigorously quantify associations between change in physical activity exposure and anxiety. The influence of cardiorespiratory fitness, an objective surrogate measure of physical activity exposure, and maintenance of fitness over time on anxiety is not well-known. One study reported a significant, inverse association between cardiorespiratory fitness and development of any anxiety

disorder over a 4.5-year follow-up (RR=0.69, 95% CI=0.50, 0.95).⁶⁰ However, this study did not fully address residual confounding and only used a single measure of cardiorespiratory fitness. The maintenance of fitness over 10–12 years has been associated with lower odds of depression complaints made to a physician;⁶⁷ but similar associations have not been examined for anxiety outcomes.

In addition to inconsistent physical activity measures, although analyses aggregated the associations reported for the greatest physical activity dose in each study, inconsistent doses across studies may explain some of the observed heterogeneity if the association between physical activity and anxiety does indeed vary according to physical activity dose. Identifying whether associations are dose-dependent is fundamentally important to guide recommendations for clinical practice and public health policy, but also for satisfying evidentiary criteria for a causal association between physical activity exposure and anxiety outcomes. One³² of seven,^{31,32,37–39,46,51} two^{56,57} of three,^{56–58} and two^{57,61} of three^{57,58,61} studies that examined a dose–response (i.e., included three or more levels of physical activity) reported lower odds of anxiety symptoms, any diagnosed anxiety disorder, and GAD, respectively, for increased amounts of physical activity. Of these 11 studies that assessed a dose–response, six^{32,37,38,51,56,61} used a physical activity measure that considered volume. However, different measures of exposure were used and criteria for classification into dose categories were not equivalent across studies. Just two studies reported associations for comparable dose categories (International Physical Activity Questionnaire categories),^{32,51} making it difficult for future meta-analyses to accurately convert the findings to a standard estimate of physical activity volume at each level.

Physical activity can occur in many modes and domains that may have different associations with anxiety or confound physical activity volume as derived from self-reported measures.^{60,68} For example, light-intensity physical activities or walking may have enhanced practicality and accessibility compared with other forms of physical activity; however, the association between these activities and anxiety is unclear. A recent scoping review highlighted the potential importance of walking for mental health,⁶⁹ but just one study⁵⁹ included here examined walking and another study³¹ examined light-intensity physical activity (i.e., not sweating or being out of breath). In unadjusted analyses, walking ≥ 105 minutes/week compared with <105 minutes/week was nonsignificantly, inversely associated with the onset of any anxiety disorder

(OR=0.72, 95% CI=0.38, 1.37).⁵⁹ In adjusted analyses, compared with women who engaged in no light-intensity physical activity, those who engaged in <1 hour, 1–2 hours, or ≥3 hours/week were nonsignificantly less likely to develop anxiety (RRs=0.83, 0.91). No inverse associations were observed among men (RRs=0.99, 1.13); however, adjusted models differed between male and female participants as BMI was omitted from the female model owing to substantially higher *p*-values when it was included.³¹

Measurement of Anxiety Outcomes

The rigor and quality of the conceptualization and assessment of anxiety was varied. All studies included here used validated measures of anxiety except one study,⁴⁸ which assessed two items rated on a Likert scale. Only five studies^{57–61} used a standardized diagnosis of an anxiety disorder, and another study⁵⁶ used self-reported physician diagnosis of an anxiety disorder to measure incident anxiety. Despite the high quality of these outcome measures, only half of these studies used high-quality measures of physical activity exposure (i.e., volume and MET hours).^{51,56,60} Additionally, though the symptom profiles of anxiety disorders share commonalities, they are a heterogeneous class of disorders with differing symptoms that may be more or less sensitive to physical activity exposure. Here, this resulted in clear heterogeneity in the assessment of anxiety symptoms and disorders. For example, the studies included here sampled diverse disorder groups, with three reporting associations for GAD^{57,58,61} and two for panic, agoraphobia, social phobia, and specific phobia, specifically.^{57,58} The studies that measured anxiety symptoms most commonly used the anxiety subscale of the Hospital Anxiety and Depression Scale.⁷⁰ However, four of these studies used a cut off score of ≥8 to classify anxiety caseness,^{31,39,46,51} two used a cut off score of ≥11,^{52,55} and one used a continuous measure of symptoms.⁵³ Three studies classified anxiety caseness as scores in the top decile of their respective inventory.^{37,38,49} There may also be important differences regarding outcome measures used among the included groups. Anxiety symptom expression can differ based on age,^{71,72} such that older adults may report more somatic symptoms.^{51,73} Given that the Hospital Anxiety and Depression Scale was the most frequently used assessment of symptoms in the included studies and is largely focused on cognitive symptoms, it is plausible that additional risk of bias resulted from differences in responses to the Hospital Anxiety and Depression Scale across age groups.

Inconsistent Adjustment for Putative Confounders

Inconsistent adjustment for putative confounders, representativeness of samples and diversity in key sample characteristics, and attrition bias are also key sources of bias in this body of literature. Reporting of the assessment of and adjustment for putative confounders was poor, including failure to control baseline anxiety, and few studies directly tested whether participant characteristics, such as age, gender, race/ethnicity, medical condition, or psychoactive medication use, modified the association between physical activity exposure and anxiety. Six studies^{34,35,37,38,46–48} failed to control for baseline anxiety, either in their study design or analyses. Varying symptom scores remain within each binary outcome group formed from screening tests and also when cases are diagnosed. Because the low physical activity groups will be expected to have higher symptoms at baseline, failure to adjust for baseline anxiety symptoms risks reverse causation. The diverse sample groups that were included, and the resultant heterogeneity across participant characteristics, likely explain some of the heterogeneity observed in analyses, but also question the representativeness of the samples. The samples from studies with an outcome of self-reported symptoms included younger and older adults, former elite male athletes and military personnel, and patient groups. Similarly, studies with an outcome of any anxiety disorder sampled populations of university graduates, adolescents and young adults, and adults from the general population. It is plausible that physical activity exposures, and the factors that influence physical activity behavior, differ between these groups. Similarly, just two included studies examined children or adolescents alone,^{47,48} both at high risk of bias, and one with young adults⁵⁷ that was also the only study in this population to use a diagnosis of anxiety disorders as the outcome. Only two studies reported results separately for men and women,^{31,46} and one study reported results separately for people with and without visual impairment.⁴⁶ Important information including participants' race/ethnicity and illnesses were reported in three^{34,47,49} and seven^{31,32,40,46,55,56,58} studies, respectively. Additionally, the length of follow-up assessments varied from 1 to 16 years. One study with a follow-up of <1 year was excluded from the current study; it reported inverse associations between physical activity and anxiety throughout pregnancy, consistent with the current findings.⁷⁴ Moreover, few studies fully accounted for participants lost to follow-up, particularly potential differences in attrition between exposure groups.

Biological Plausibility

Experimental evidence has demonstrated the benefits of exercise alone and or as an additive to other treatments

for obsessive–compulsive disorder,¹⁸ panic disorder,¹⁶ GAD,¹⁷ and anxiety symptoms.^{19,21,22} The available evidence has provided some support for the biological plausibility of the association between physical activity and reduced anxiety. People with GAD⁷⁵ and social phobia⁷⁶ display decreased hippocampal volumes, while there is an increasing body of literature demonstrating that exercise can improve hippocampal functioning⁷⁷ and volume.⁷⁸ A comprehensive narrative review concluded that inflammation, oxidative and nitrogen stress, and subsequent alteration of neurotrophins, neurogenesis, and neuroplasticity are likely to play a role in the pathogenesis of anxiety disorders, and physical activity is known to influence the same pathways.⁷⁹

Implications for Future Research

Future research would benefit from corroborating self-reported physical activity exposure with device-based assessments, and in selecting the physical activity measure used, one should consider not only its feasibility and practicality, but also its methodologic effectiveness.⁶³ In addition, at a minimum, future research should examine a consistent set of dose categories. As the WHO promotes engaging in ≥ 150 minutes of moderate, ≥ 75 minutes of vigorous, or an equivalent combination of moderate-to-vigorous activity per week for health, and ≥ 300 minutes of moderate, ≥ 150 minutes of vigorous, or an equivalent combination for additional health benefits,⁸⁰ these would be logical categories to examine. Whether any potential dose–response association is linear, curvilinear, or a threshold, also warrants investigation. Further research on associations between different modes and domains of physical activity and anxiety is also required. Although walking activity is not always of light intensity (e.g., incline walking), given its potential enhanced convenience and availability, more rigorous investigation of the role of device-assessed lighter-intensity walking activity in total physical activity exposure and associations with anxiety is needed. Given the clear heterogeneity in the assessment of anxiety symptoms and disorders, comprehensive assessment approaches that corroborate standardized diagnostic interviews or self-reported physician diagnosis of an anxiety disorder with self-report diagnostic screeners and measures of symptom severity are warranted. Methodologically, more rigorous consideration of the influence of sample characteristics, differences in putative confounders between age groups, and the appropriateness of specific self-report measures of anxiety symptoms across age groups is needed. Additionally, the median age of onset of anxiety disorders is typically in adolescence or early adulthood; for example, the anxiety disorders with the earliest and latest median age of

onset are phobias and separation anxiety disorder (age 15–17 years) and GAD (age 23–30 years), respectively.⁶ Thus, future research focused on younger population groups is imperative.

CONCLUSIONS

Despite the notable challenges in the current evidence base, including issues regarding exposure and outcome measures, consistent assessment of and adjustment for putative confounders, representativeness of samples, and attrition bias, the available evidence suggests that physical activity may protect against anxiety symptoms and disorders. This manuscript highlights these potential protective benefits and the key areas in which there is a need for further research.

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SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at <https://doi.org/10.1016/j.amepre.2019.05.012>.

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