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Physical activity, suicidal ideation, suicide attempt and death among individuals with mental or other medical disorders: A systematic review of observational studies

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ABSTRACT

A growing body of research has demonstrated the potential role for physical activity as an intervention across mental and other medical disorders. However, the association between physical activity and suicidal ideation, attempts, and deaths has not been systematically appraised in clinical samples. We conducted a PRISMA 2020-compliant systematic review searching MEDLINE, EMBASE, and PsycINFO for observational studies investigating the influence of physical activity on suicidal behavior up to December 6, 2023. Of 116 eligible full-text studies, seven (n = 141691) were included. Depression was the most frequently studied mental condition (43%, k = 3), followed by chronic pain as the most common other medical condition (29%, k = 2). Two case-control studies examined suicide attempts and found an association between physical activity and a reduced frequency of such attempts. However, in studies examining suicidal ideation (k = 3) or suicide deaths (k = 2), no consistent associations with physical activity were observed. Overall, our systematic review found that physical activity may be linked to a lower frequency of suicide attempts in non-prospective studies involving individuals with mental disorders.

1. Introduction

Individuals with mental or physical illness are at an increased risk of suicide compared to the general population (Harris and Barraclough, 1997; Jia et al., 2014). This is attributable to various factors such as functional limitations, comorbid substance use, and impediments in psychological wellbeing (Kaplan et al., 2007; Hawton et al., 2013). The presence of a mental disorder leads to a significantly higher burden of other medical disorders and vice versa (Evans et al., 2005). This overlap has led some to consider abandoning the dichotomy between mental and other medical disorders in favor of a unified terminology and appreciation of bidirectional relationships (Baker and Menken, 2001; Holt et al., 2013; Dragioti et al., 2023). The mechanisms underlying these bidirectional associations are thought to be related to numerous factors, including (but not limited to) autonomic dysregulation, dopamine circuits, unhealthy diets, and physical inactivity (Bonnet et al., 2005; Joynt et al., 2003; Zhang et al., 2021; Koch et al., 2022). Independent of comorbid medical disease, low physical activity levels are associated with increased depression and anxiety, and subsequently suicidal ideation (Ma et al., 2022; Vancampfort et al., 2018). Therefore, it is of utmost importance to address modifiable risk factors such as physical inactivity in order to bolster one's mental and physical health.

Over the last 30 years, a growing body of research has demonstrated a role of physical activity as an effective intervention across mental and other medical disorders (Sabe et al., 2022; Sallis, 2015). Numerous studies have demonstrated the benefits of physical activity on both treating and preventing mental disorders, with similar efficacy compared to pharmacological interventions (Carek et al., 2011; Dunn et al., 2005; Kim et al., 2019; Mota-Pereira et al., 2011; Recchia et al., 2022). By improving physical health outcomes, physical activity may mediate improvement in mental health outcomes, similarly reducing suicidal behaviors (Croatto et al., 2022; Fabiano et al., 2023). As a result, physical activity has been incorporated into international guidelines for the treatment of mental disorders (Marx et al., 2022; Stubbs et al., 2018).

While the role of lifestyle factors in this is not well established, higher levels of physical activity have been associated with lower rates of suicidal ideation in the general population (Vancampfort et al., 2018). Furthermore, our recent systematic review of randomized controlled trials (RCTs) found that exercise interventions significantly decreased suicide attempts compared to inactive controls in those with mental or physical illness (Fabiano et al., 2023). However, a modest sample size limited power, and no significant difference in suicidal ideation or deaths was observed. Further, the majority of RCTs in the initial systematic review were of low study quality, and often measured suicidal behaviors as adverse events rather than by direct measurement, thus introducing a high risk of bias in measurement and limiting their direct application to clinical practice. Amidst the concerning increase in both the prevalence of mental disorders and the incidence of suicides, we aimed to explore the specific influence of physical activity on suicidal behaviors. This inquiry is particularly crucial considering the known health benefits associated with exercise (Lopez et al., 2006; Mathers and Loncar, 2006; Naghavi, 2019; Sagar et al., 2020). This facilitates recognition of patient populations who may most benefit from physical activity and will allow for the provision of more targeted therapy. The evidence linking physical activity and suicidal behaviors is currently mixed. Therefore, the purpose of this systematic review is to pool data from observational studies in order to determine the association between physical activity and suicidal ideation, suicide attempts, and suicide deaths across a variety of patients with mental disorders or other medical conditions.

2. Methods

This systematic review adhered to the Preferred Reporting Items for

[1] Nicholas Fabiano and Arnav Gupta contributed equally to this paper.

Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021).

2.1. Ethics

Research ethics board approval was waived at the University of Ottawa for this type of research. The a priori protocol was uploaded to Open Science Framework and can be found at: https://osf.io/ct7jz/.

2.2. Search strategy and inclusion criteria

MEDLINE, EMBASE, and PsycINFO were searched on December 6, 2023 for observational studies investigating the association between physical activity (resistance, aerobic or mind-body) in participants of any age with a mental and/or medical disorders on suicidal outcomes (suicidal ideation, suicide attempts or suicide deaths) with no limits set based on date of publication or language. A librarian was involved to aid in the development of the search strategy. The search terms included exercise, physical activity, and suicide. The full search strategy is available in eTable 1. A manual search was additionally conducted on Google Scholar and in references of eligible studies, and of previous reviews. The research question and inclusion criteria were established a priori. Studies were included if they met the following criteria: (a) observational design (prospective cohort, retrospective cohort, or case-control), (b) a portion of participants had a mental and/or medical disorder (or subclinical condition), and (c) report on the effect that any type of exercise or physical activity had on suicidal ideation, suicide attempts or suicide death, regardless of other additional treatment.

2.3. Screening

Study screening was conducted on Covidence (Veritas Health Information, 2023). Five independent reviewers (AG, SW, JT, IM, SB) screened titles and full texts in duplicate, with discrepancies to be resolved by a third independent reviewer (NF).

2.4. Extraction

Four independent reviewers (SW, JT, IM, SB) extracted relevant data from the included studies into a pre-designed Microsoft Excel spreadsheet. All extractions were done in duplicate with discrepancies resolved by consensus. The primary outcomes were suicidal ideation, suicide attempts, and suicide deaths. The maximally adjusted effect sizes (continuous and binary) with corresponding 95% confidence intervals (95% CI) were extracted. In cases where the 95% confidence interval was not reported, the p-value was extracted to estimate the 95% CI. Details of the physical activity or exercise (frequency, intensity, type, and time [FITT]), exercise instructor (expert [physical educators, physiotherapists or exercise physiologists] or not) and compliance with international physical activity guidelines (150 min per week of at least moderate or 75 min per week of vigorous physical activity) were extracted. Information such as study design (cohort, case-control), first author, year of publication, country, time window, mental/other medical condition, diagnostic criteria, sample size, suicide ideation assessment tool, and demographic data (age, sex, ethnicity) were also extracted.

2.5. Quality assessment

The NIH Study Quality Assessment Tools were used to assess the quality of included studies (Study Quality Assessment Tools, 2022). Four independent reviewers (SW, JT, IM, SB) assessed each criterion of the checklist in duplicate with discrepancies resolved by consensus. For cohort (prospective or retrospective) studies, the following scores were

Table 1
Patient and Study Characteristics.

Study	Study Type	Country	Sample Size	Mean Age	% Females	Condition	Exercise Details	Number of Patients in Exercise Group	Control Details	Number of Patients in Control Group
Meerwijk 2022	PC	USA	66,257	27.8	7.8	Chronic pain	Exercise therapy (covers a wide range of therapeutic procedures that include, among others, treadmill, isokinetic exercise, lumbar stabilization, stretching, strengthening, neuromuscular re-education, gait training, and aquatic exercise)	37 310	No exercise therapy	28 947
Mukamal 2007	PC	USA	46,755	54.4	0.0	High BMI (>30)	Active (≥6.33 MET-hr/week)	NR	Inactive (<6.33 MET-hr/week)	NR
Perera 2018	CC	Canada	281	44.9	50.5	Post-Suicide-Attempt	Mild to strenuous physical activity during leisure time	208	Sedentary during leisure time	62
Simon 2004	CC	USA	666	Mean NR (range 13-34)	54.4	Depression, Hopelessness, Alcoholism or any Medical Condition	Running, calisthenics, golf, gardening, or walking for exercise > =1x/week	508	No running, calisthenics, golf, gardening, or walking for exercise (0x/week)	156
Kang 2013	PC	South Korea	1204	72.2	58.0	Depression, anxiety, insomnia, or any chronic medical illness	Physically Active	852	Physically Inactive	352
Kikuchi 2009	PC	Japan	26,481	59.6	0.0	Chronic pain	Self-reported walking duration ≥ 1 hr/day	10 298	Self-reported walking duration < 1 hr/day	10 785
Perez 2022	PC	USA	47	30.0	72.3	Major depressive disorder	Moderate-to-vigorous, light standing/ambulatory physical activity based on accelerometer/inclinometer for 7 days	NR	Sedentary behaviors based on accelerometer/ inclinometer for 7 days	NR

Abbreviations: case control (CC), prospective cohort (PC), not reported (NR), body mass index (BMI), metabolic equivalent of task (MET)

used: 0–5 (poor), 6–10 (fair), 11–14 (good). For case-control studies, the following scores were used: 0–4 (poor), 5–8 (fair), 9–12 (good).

3. Results

3.1. Study and participant characteristics

The search identified 1505 studies, and after removing 437 duplicates, 1068 studies were screened. One hundred sixteen full-texts were reviewed of which 109 were excluded; reasons for exclusion are illustrated in Fig. 1**, with the list of excluded studies and reasons for exclusion in the** supplementary materials. ***Seven*** studies met eligibility for extraction, all of which were published between 2004 and 2022.

Study characteristics and exercise details are summarized in Table 1**. Five** studies (71%) were prospective cohorts, while two studies (29%) were case-control studies. They most commonly originated from the United States (57%, k = 4). Depression was the most commonly included mental disorder (43%, k = 3), and chronic pain was the most

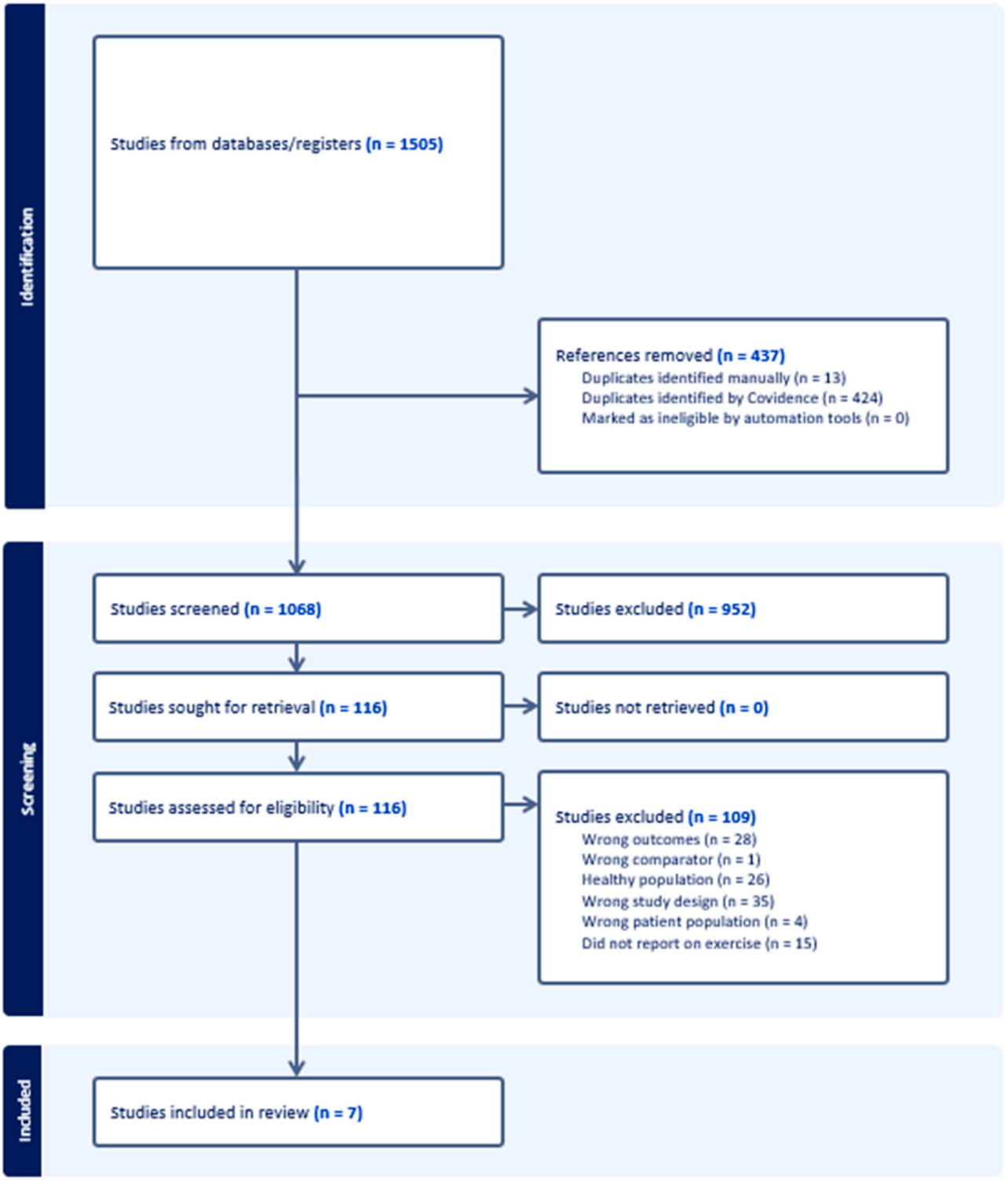

Fig. 1. PRISMA Diagram.

commonly included other medical condition (29%, k = 2). Aerobic exercise was the most commonly assessed type of exercise (43%, k = 3); no studies commented on muscle strengthening exercises. Finally, the most common control group was physically inactive or sedentary individuals (43%, k = 3).

Participant characteristics are summarized in Table 1. Altogether, 141,691 participants were included in the studies captured by this systematic review. Females represented 4.5% (n = 6384) of this sample, and the mean age was 32.0 years. Among the 3 studies that reported ethnicity, individuals were most commonly White (n = 41 370; 61.5%).

3.2. Suicidal Ideation

Three studies (n = 67,508) analyzed suicidal ideation (Meerwijk et al., 2022; Kang et al., 2014; Perez et al., 2022). In Meerwijk and colleagues' (2022) prospective cohort study composed of 66 257 active duty soldiers with chronic pain, those who regularly exercised (n = 37 310) generally showed non-significant differences in suicidal ideation compared to controls who did not exercise (Meerwijk et al., 2022). When stratified by the number of exercise therapy visits, participants who participated in 4–5 (HR = 0.85, 95%CI 0.74–0.97, $p < 0.05$), 8–9 (HR = 0.83, 95%CI 0.70–0.97, $p < 0.05$), and > 9 total visits (HR = 0.85, 95%CI 0.76–0.95, $p < 0.01$) were significantly associated with reduced suicidal ideation. In Kang and colleagues' (2013) prospective cohort consisting of 1204 patients with chronic mental illnesses (e.g., depression, anxiety), physical inactivity was not associated with a significant difference in incidence of suicidal ideation (OR = 1.09, 95%CI 0.61–1.94) (Kang et al., 2014). In Perez and colleagues' (2022) prospective cohort consisting of 47 participants with major depressive disorder, physical activity level (light standing, light ambulatory and moderate-to-vigorous physical activity) over 7 days as measured by accelerometer/inclinometer was not significantly associated with suicidal ideation (Perez et al., 2022). However, when restricted to the cohort of participants in a major depressive episode (n = 38), light ambulatory physical activity reduced the risk of low (OR = 0.910, 95% CI 0.84–0.98, p = 0.018) and moderate/high (OR = 0.92, 95% CI 0.85–1.00, p = 0.036) suicidal ideation.

3.3. Suicide attempts

Two studies (n = 947) analyzed suicide attempts (Perera et al., 2018; Simon et al., 2004). In Perera and colleagues' (2018) case-control study composed of 281 patients admitted to a psychiatric inpatient unit, cases who had a history of suicide attempts were significantly less likely to engage in mild (OR = 0.12, 95%CI 0.04–0.39, $p < 0.001$) or moderate/intense exercise (OR = 0.15, 95%CI 0.05–0.48, $p = 0.001$) compared to those without (Perera et al., 2018). Simon and colleagues (2004) conducted a case-control study consisting of 153 individuals with depression, hopelessness, alcoholism or any serious medical condition, with near lethal suicide attempts, and 513 controls randomly selected from the same catchment area. They found that having had no physical activity was associated with a greater odds of suicide attempts (OR = 6.06, 95%CI 2.83–12.95, *p*-value NR) (Simon et al., 2004).

3.4. Suicide deaths

Two studies (n = 73 236) analyzed suicide mortality (Kikuchi et al., 2009; Mukamal, 2007). In Mukamal and colleagues' (2007) prospective cohort study composed of 46 755 individuals with obesity, higher intensity of exercise (up to 41.99 MET-hr per week) was not significantly associated with reduced risk of suicide deaths compared to inactive individuals (defined as <6.33 MET-hr per week) (Mukamal, 2007). In Kikuchi and colleagues' (2009) prospective cohort study consisting of 26 481 individuals with chronic pain, self-reported walking duration was not significantly associated with suicide deaths, irrespective of pain intensity (Kikuchi et al., 2009).

3.5. Quality assessment

The NIH quality assessments are available in Table 2–4. Overall, 86% (k = 6) of the studies were rated as good quality, 14% (k = 1) of the studies were rated as fair quality. The most common limitation was lack of blinding to exposure or outcomes (k = 4, 57%).

4. Discussion

In this review, we sought to examine the association between physical activity and suicide-related behaviors and ideation in people with long-term health conditions. Seven observational studies were included, of fair to good quality. Due to significant methodological heterogeneity, quantitative synthesis through meta-analyses of outcomes such as suicidal ideation, suicide attempts and suicide deaths was not possible. The two studies which examined suicide attempts both found physical activity to be associated with less frequent attempts. Both of these studies utilized a case-control design and were not prospective. In the studies examining suicidal ideation and/or suicide deaths, no consistent associations with physical activity were observed.

For the three studies which examined suicidal ideation, associations with physical activity were inconsistent (Meerwijk et al., 2022; Kang et al., 2014; Perez et al., 2022). In a 2-year prospective cohort of elderly Korean adults with comorbid mental and physical illness, Kang and colleagues (2013) found no association between physical inactivity and suicidal ideation as measured by the Geriatric Mental State diagnostic schedule (GMS B3) (Kang et al., 2014). The presence of suicidal ideation was evaluated at baseline and subsequently at a 2-year follow-up. No significant changes in suicidal ideation were observed for either the subgroup with suicidal ideation at baseline or the other without suicidal ideation. Along with this, a prospective cohort of active duty army soldiers with chronic pain who subsequently enrolled in the Veterans Health Administration (VHA) by Meerwijk and colleagues (2022) found inconsistent associations between exercise therapy exposure and suicidal ideation, as determined by ICD-9 and ICD-10 diagnoses recorded in the VHA healthcare records (Meerwijk et al., 2022). Subgroup analyses were conducted based on number of exercise therapy visits and generally found that greater attendance to exercise therapy (greater frequency of exercise) was associated with statistically significant decreases in suicidal ideation, whereas < 3 visits did not show a significant association. Further, a prospective cohort by Perez and colleagues (2022) found that physical activity levels as measured by accelerometer/inclinometer were not associated with suicidal ideation in those with major depressive disorder (Perez et al., 2022). However, when analyzing solely the subgroup experiencing a major depressive episode, there were very modest reductions in suicidal ideation only for light ambulatory, but not for moderate-to-vigorous physical activity based on intensity. Our previous meta-analysis of randomized controlled trials (RCTs) similarly did not demonstrate a significant change in suicidal ideation (as quantified by standardized scales or as a binary outcome) following exercise intervention (Fabiano et al., 2023). However, a meta-analysis of cross-sectional studies by Vancamport and colleagues (2018) concluded that increased levels of physical activity were associated with lower suicidal ideation in the general population (Vancampfort et al., 2018). Given the cross-sectional nature of these meta-analyzed studies, one must acknowledge their vulnerability to confounding variables such as the adoption of other healthy lifestyle habits alongside physical activity which have been shown to independently reduce suicidal ideation (Tucker et al., 2014; Goodwin and Marusic, 2008). Further, physical activity is often conducted within a group setting offering social support to those who regularly partake (Wankel and Berger, 1990). This social support has been shown to independently reduce suicidal ideation, irrespective of the presence of physical activity (Miller et al., 2015). Therefore, the relationship between physical activity and suicidal ideation requires further research which adequately controls for confounding variables to accurately

Table 2
Summary of Study Results.

Study	Suicide Ideation	Suicide Attempts	Suicide Deaths
Meerwijk 2022	No Exercise Therapy: Reference1 visit: HR = 1.02 (95%CI 0.91-1.15)2–3 visits: HR = 0.9 (95%CI 0.79-1.01) 4–5 visits: HR = 0.85 (95%CI 0.74-0.97)6–7 visits: HR = 0.98 (95%CI 0.85-1.13) 8–9 visits: HR = 0.83 (95%CI 0.70-0.97)> 9 visits: HR = 0.85 (95%CI 0.76-0.95)	NR	NR
Mukamal 2007	NR	NR	< 6.33 MET-hr/week: Reference6.33-14.49 MET-hr/week: HR = 0.82 (95%CI 0.46-1.45)14.50-25.08 MET-hr/week: HR = 0.86 (95%CI 0.48-1.52) 25.09-41.98 MET-hr/week: HR = 0.83 (95% CI 0.46-1.49) > 41.99 MET-hr/week: HR= 1.01 (95%CI 0.61-1.68)
Perera 2018	NR	Psychiatric inpatient with history of SA, likelihood to engage in mild PA vs sedentary: OR = 0.35(95%CI 0.16-0.76)Psychiatric inpatient, no history of SA, likelihood to engage in mild PA vs sedentary: OR = 0.56(95% CI0.24-1.30) Community control, no history of SA, likelihood to engage in mild PA vs sedentary: OR = 0.12(95% CI0.04-0.39) Psychiatric inpatient with history of SA, likelihood to engage in moderate/ strenuous PA vs sedentary: OR = 0.42 (95% CI0.19-0.95) Psychiatric inpatient, no history of SA, likelihood to engage in moderate/ strenuous PA vs sedentary: OR = 0.96 (95% CI0.38-2.45) Community control, no history of SA, likelihood to engage in moderate/ strenuous PA vs sedentary:OR = 0.15 (95% CI0.05-0.48)	NR
Simon 2004	NR	Primary PA: ReferenceNo primary physical activity: OR = 6.06 (95%CI 2.83-12.95)	NR
Kang 2013	Inactive (those who initially did not have SI but developed SI in follow-up): OR = 1.09 (95%CI 0.61-1.94)	NR	NR
Kikuchi 2009	NR	NR	*Walking < 1 h/day*No pain: HR = ReferenceVery mild pain: HR = 1.69 (95% CI 0.52-5.53)Mild pain: HR = 3.02 (95% CI0.95-9.6)Severe pain: HR = 4.47 (95% CI 1.30-15.35)*Walking ≥ 1 h/day* No pain: HR = ReferenceVery mild pain: HR = 1.11 (95% CI 0.40-3.04)Mild pain: HR = 1.86 (95% CI0.68-5.08)Severe pain: HR = 2.12 (95% CI 0.67-6.74)
Perez 2022	Participants with MDD and risk of low SI: Light standing PA: OR = 1.01 (95%CI 1.00-1.03) Light ambulatory PA: OR = 0.96 (95%CI 0.92-1.01) Moderate-to-vigorous PA: OR = 1.01 (95%CI 0.94-1.08) Participants with MDD and risk of moderate/high SI: Light standing PA: OR = 1.01 (95%CI 1.00-1.03) Light ambulatory PA: OR = 0.98 (95%CI 0.94-1.02) Moderate-to-vigorous PA: OR = 1.02 (95%CI 0.96-1.08) Participants currently experiencing a MDE and risk of low SI: Light standing PA: OR = 1.03 (95%CI 1.00-1.06) Light ambulatory PA: OR = 0.910 (95%CI 0.84-0.98) Moderate-to-vigorous PA: OR	NR	*NR*

(*continued on next page*)

Table 2 (*continued*)

Study	Suicide Ideation	Suicide Attempts	Suicide Deaths
	= 1.07 (95%CI 0.95-1.20) Participants currently experiencing a MDE and risk of moderate/high SI: Light standing PA: OR = 1.03 (95%CI 1.00-1.06) Light ambulatory PA: OR = 0.92 (95% CI 0.85-1.00) Moderate-to-vigorous PA: OR = 1.12 (95%CI 0.99-1.26)		

Abbreviations: not reported (NR), odds ratio (OR), hazard ratio (HR), suicide attempt (SA), major depressive disorder (MDD), major depressive episode (MDE), suicidal ideation (SI), physical activity (PA)

assess this association.

Physical activity was associated with a lower risk of suicide attempts in both included studies (Perera et al., 2018; Simon et al., 2004). Specifically, in a case-control study of psychiatric inpatients compared to community controls admitted to hospital, Perera and colleagues (2018) concluded that those who attempted suicide had a decreased likelihood of being physically active than their controls without suicide attempts. Physical activity was measured by the International Physical Activity Questionnaire and the decreased odds were observed for mild, moderate and strenuous physical activity (Perera et al., 2018). Similarly, in a case-control study of individuals with nearly lethal suicide attempts compared to community controls recruited by telephone, Simon and colleagues (2004) found that those that attempted suicide were less likely than controls to report involvement in physical activity in the past month (Simon et al., 2004). This association was maintained by sub-analysis based on intensity, frequency, and duration of physical activity. These findings are in keeping with our previous meta-analysis of RCTs, where individuals with mental or physical illness randomized to exercise had significantly fewer suicide attempts compared to inactive controls (Fabiano et al., 2023). The inconsistent association of physical activity with less frequent suicide attempts, but not with suicidal ideation, can be rationalized through the ideation-to-action framework which states that suicidal ideation and suicide attempts are two distinct processes with specific influential factors (Klonsky and May, 2015). Therefore, since most suicide attempts are characterized by emotional impulsivity which physical activity has been demonstrated to reduce, we posit that higher levels of physical activity lead to a lower number of suicide attempts (Lopez-Castroman et al., 2016; Javelle et al., 2022; Cerrillo-Urbina et al., 2015). With this in mind, physical activity may prove to be an effective measure of suicide attempt reduction in those with chronic conditions which place them at elevate risk such as borderline personality disorder (BPD), however further research is required in this area, particularly distinguishing between exercise type, volume and intensity (Brodsky et al., 2006).

There was no association found between physical activity and risk of death by suicide in both studies included within this review (Kikuchi et al., 2009; Mukamal, 2007). In a prospective cohort study of men free of cancer, Mukamal and colleagues (2007) concluded that physical activity (irrespective of intensity) was not associated with reduced risk of suicide death compared to inactive controls, but instead was inversely related to body mass index (BMI) (Mukamal, 2007). Similarly, in a prospective cohort study of Japanese men with chronic pain, Kikuchi and colleagues (2009) found no association between self-reported walking and suicide deaths, however suicide was significantly higher in subjects with more pain (Kikuchi et al., 2009). This is in keeping with

Table 3
NIH Quality Assessment for Cohort Studies.

Study	Meerwijk 2022	Mukamal 2007	Kang 2013	Kikuchi 2009	Perez 2022
1. Was the research question or objective in this paper clearly stated?	✓	✓	✓	✓	✓
2. Was the study population clearly specified and defined?	✓	✓	✓	✓	✓
3. Was the participation rate of eligible persons at least 50%?	✓	✓	✓	✓	✓
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓	✓	✓	✓	✓
5. Was a sample size justification, power description, or variance and effect estimates provided?	***X***	✓	✓	✓	***X***
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓	✓	✓	✓	✓
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓	✓	✓	✓	✓
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	✓	✓	✓	✓	✓
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓	✓	***X***	✓	✓
10. Was the exposure (s) assessed more	✓	✓	✓	***X***	***X***

(*continued on next page*)

Table 3 (*continued*)

Study	Meerwijk 2022	Mukamal 2007	Kang 2013	Kikuchi 2009	Perez 2022
than once over time?					
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓	✓	✓	✓	✓
12. Were the outcome assessors blinded to the exposure status of participants?	***X***	✓	***X***	?	?
13. Was loss to follow-up after baseline 20% or less?	✓	✓	***X***	✓	✓
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure (s) and outcome(s)?	✓	✓	✓	✓	✓
Total	12/14	14/14	11/14	12/14	12/14

Legend: Yes (✓), No (***X***), Unclear (?)

Table 4
NIH Quality Assessment for Case-Control Studies.

Study	Perera 2018	Simon 2004
1. Was the research question or objective in this paper clearly stated and appropriate?	✓	✓
2. Was the study population clearly specified and defined?	✓	✓
3. Did the authors include a sample size justification?	✓	***X***
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	✓	✓
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	✓	✓
6. Were the cases clearly defined and differentiated from controls?	✓	✓
7. If less than 100% of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?	***X***	✓
8. Was there use of concurrent controls?	?	?
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	✓	✓
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?	✓	✓
11. Were the assessors of exposure/risk blinded to the case or control status of participants?	✓	***X***
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?	***X***	?
Total	9/12	8/12

Legend: Yes (✓), No (***X***), Unclear (?)

our previous meta-analysis of RCTs where no difference in suicide deaths were observed between those exercising compared to inactive controls (Fabiano et al., 2023). It is clear that regular physical activity has numerous multi-system benefits such as reduced cardiovascular mortality, reduction in chronic pain, increased physical function, and improved quality of sleep, however may not directly reduce suicide-related mortality (Strasser, 2013; Gordon and Bloxham, 2016; Sullivan Bisson et al., 2019). It is important to consider however that both studies which analyzed suicide deaths in this systematic review included exclusively male participants (Kikuchi et al., 2009; Mukamal, 2007). Research has demonstrated that although males make less suicide attempts than females, their attempts are of higher lethality (Prediction of Lethality in Suicide Attempts, 2019). This may impact our results if the association is moderated by sex, gender, or attempt severity.

4.1. Strengths

There were numerous strengths of this study. Firstly, reporting bias was minimized through the production of an a priori protocol. Our search was conducted across various databases and included gray literature to minimize publication bias. All screening and extraction were conducted in duplicate which ensured accuracy and integrity of our data. Although solely including observational studies, we excluded those with cross-sectional designs due to their inability to discern temporal relations and significant vulnerabilities to the effects of confounding. Lastly, as literature focusing on the relationship between physical activity and mental health has been of increasing interest over recent years, this systematic review benefits from having the most current information available.

4.2. Limitations

The main limitation of this study is the small number of studies included and their heterogeneity, which did not allow for conducting a meta-analysis. Foremost, meta-analyses of outcomes variables such as suicidal ideation, suicide attempts and suicide deaths was not possible due to significant methodological heterogeneity among included studies. Moreover, we did not include RCTs in the current review but was conducted separately (Fabiano et al., 2023), which challenges inferences about causality between exposure and outcome given potential for confounding in observational studies, including medication (Ilzarbe and Vieta, 2023). Also, in the studies we extracted data from, we found that details regarding physical activity or exercise were often not adequately reported. For instance, no study commented on muscle strengthening exercises nor provided further details on exercise intensity or volume. We recommend that future research on this topic more clearly and consistently detail physical activity, specifically following the FITT parameters to allow for an operational definition of physical activity that could then be compared between studies. Further, to achieve more complete and robust evidence, higher quality and additional observational studies investigating this topic are essential. These observational studies should particularly focus on blinding to exposure and outcome, which was the most common limitation found on our quality assessment. As the majority of studies in this review focused on depression or chronic pain, future studies should aim to explore the influence of physical activity in a variety of mental or other medical conditions to get a more comprehensive overview. Thus, we are aware of the potential bias in the review process, as we may have overlooked certain studies which did not explicitly fall in but may have reported relevant findings. Thus there is a possibility that at initial search, some studies might have been omitted and thus could not be extracted from the studies identified within the initial search. The generalizability of our findings is also of concern since there was an extreme underrepresentation of female participants (4.5%) and no physical disorders beyond chronic pain. While some studies utilized prospective cohort

designs, the case-control studies involved retrospective estimations of physical activity, which may be prone to bias. We cannot rule out differential misclassification based on case vs. control status.

5. Conclusions

Overall, our systematic review found that physical activity was associated with decreased suicide attempts in those with mental disorders. However, we found no association between physical activity and suicidal ideation among patients with mental disorders or suicide deaths among patients with physical disorders. Results are consistent with evidence from trials. Due to the observational character of the included study, we cannot conclude anything about the direction of the associations, and we cannot exclude that a common underlying variable can explain the findings. The association with suicide attempts but not suicidal ideation might be due to physical activity-induced reductions in impulsivity preceding suicide attempts. Future research across a variety of mental disorders and other medical conditions which adequately control for confounding variables known to influence the association and between physical activity and suicidal behaviors are required to better understand this relationship, quantify the physiological mechanisms, and identify the minimal clinically-important difference for physical activity and suicidal behaviors.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neubiorev.2024.105547.

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