

## Health benefits, safety and cost of physical activity interventions for mental health conditions: A meta-review to inform translation efforts

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### ABSTRACT

**Background:** Mental illness is a leading cause of the global burden of disease. Physical activity (PA) can improve physical and mental health outcomes for people with mental illness, yet routine implementation of PA within standard care remains ad-hoc. The reasons for this are unclear, although the dissonance between the evidence produced in research settings and that needed in real-world environments may be key.

**Purpose:** To explore the effectiveness of PA interventions as a treatment for mental illness. We synthesised past systematic reviews and meta-analyses.

**Methods:** We conducted a systematic review of reviews from database inception to 09/2017. Reviews were included that considered any mental health condition (diagnosed via standardised criteria) and where PA interventions were a stand-alone or adjunctive treatment. Effectiveness was defined as outcomes that are important in real-world healthcare (i.e. expected clinical outcomes, intervention safety and cost).

**Results:** From 4008 hits, 33 reviews (including 155 unique studies) were included and 32 reported that PA has a positive effect on at least one main outcome of interest (symptoms of mental illness, quality of life and/or physical health). There was inconsistent reporting of adverse events and no cost data was identified. The AMSTAR quality rating suggests inconsistencies in review quality.

**Conclusions:** The research agenda must expand to report on outcomes that can support evidence translation efforts (i.e. cost and adverse events). Without such a shift, research in PA and mental health may fail to achieve translation to routine care and may have limited impact on patient outcomes.

### 1. Introduction

Mental illness represents a growing and significant burden to individuals, communities and the health system. On average, just under 30% of the population will experience a mental illness at some point in their life (Steel et al., 2014). Many people live long periods of their life affected by mental illness, as evidenced through the contribution mental illness makes to years-lived with some form of disability (i.e. disability adjusted life years) (Moussavi et al., 2007; Vigo, Thornicroft, & Atun, 2016). For example, the global cost of mental illness was

estimated at \$2.5 trillion in 2010, with this figure expected to rise to \$6 trillion by 2030 (Marquez & Saxena, 2016). Further, high-prevalence disorders (anxiety, depression, substance use) cost the Australian healthcare system \$A974 million and over \$11 billion annually when economic costs to society are included (i.e. productively loss) (Lee et al., 2017).

Mental illness is highly co-morbid with physical health problems, such as diabetes and cardiovascular disease (Vancampfort et al., 2015b, 2016). In severe and persistent mental disorders, such as schizophrenia, major depression and/or bipolar (referred to as *serious mental illness*)

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(Vancampfort, Rosenbaum, et al., 2017), the co-existence of comorbid physical illness is associated with increased mortality (Hjorthøj, Stürup, McGrath, & Nordentoft, 2017; D.; Lawrence, Hancock, & Kisely, 2013). Critically, life expectancy in this population is ~15 years less than in people without a mental illness (Hjorthøj et al., 2017; D.; Lawrence et al., 2013) primarily due to the increased prevalence of physical health conditions, such as cancer and cardiometabolic disease (Mental Health Commission of NSW, 2016).

Modifiable risk factors such as poor diet, smoking and a lack of physical activity (PA) are primary drivers of the increased cardiometabolic disease in this population (P. Smith, Mazure, & McKee, 2014; Teasdale, Samaras, Wade, Jarman, & Ward, 2017; Vancampfort, Firth, et al., 2017). As such, efforts to reduce the burden of comorbid cardiometabolic disease often focus on improving these risk factors. In particular, there is increasing international recognition of the importance of addressing physical inactivity among people with mental illness (Rosenbaum et al., 2018). Promisingly, evidence seems to suggest increasing levels of PA may have a dual effect on health outcomes for people with mental illness (Curtis et al., 2016; Schuch, Vancampfort, Richards, et al., 2016; Stubbs et al., 2017). PA not only improves physical health but can have a direct impact on mental health symptoms across the spectrum of mental illness (Rosenbaum, Tiedemann, Sherrington, Curtis, & Ward, 2014). For example, PA can improve symptoms of anxiety and depression (Schuch, Vancampfort, Richards, et al., 2016; Stubbs et al., 2017) and together with dietary interventions and life-skills training, can mitigate weight-gain associated with anti-psychotic medication (Curtis et al., 2016). This weight-gain contributes to the development of cardiometabolic disease and early mortality in this population (Álvarez-Jiménez, Hetrick, González-Blanch, Gleeson, & McGorry, 2008).

Coupled with calls for integrated physical and mental healthcare (National Mental Health Commission, 2016; Naylor et al., 2016; Rodgers et al., 2018; Vancampfort, Stubbs, Ward, Teasdale, & Rosenbaum, 2015c), it is reasonable that PA is viewed as a promising intervention to help address the mental ill-health disease burden. However, widespread uptake of PA as part of routine care for people with a mental illness is sub-optimal (Lederman et al., 2017; Pratt et al., 2016; Vancampfort et al., 2015c). This is despite the evidenced-base moving to a stage where government and non-government organisations have endorsed the role of PA in mental health treatment (Mental Health Commission of NSW, 2016; National Institute for Health and Care Excellence (NICE), 2014; Ravindran et al., 2016; The Royal Australian and New Zealand College of Psychiatrists, 2015).

The reasons for poor uptake of PA as part of routine treatment in mental health care are not clear. Although more broadly, the uptake of evidenced-based interventions in routine practice is widely recognised as being complex, problematic and slow (Balas & Boren, 2000; Brownson, Colditz, & Proctor, 2012). Consequently, new fields of research have evolved, dedicated solely to bridging the gap between research and practice (Eccles & Mittman, 2006). For example, implementation and dissemination scientists have consistently identified factors associated with the intervention, the people using the intervention, the setting that hosts the intervention and broader environmental influences that contribute to this gap (implementation) (Durlak & DuPre, 2008). This information is coupled with strategies that actively help to spread effective interventions, so that population-wide benefits are achieved (dissemination) (Rabin, Brownson, Haire-Joshu, Kreuter, & Weaver, 2008). Notably, implementation and dissemination should be predicated on the evidence base of the intervention of interest, wherein only interventions of proven effectiveness should be considered for wider use (Brownson et al., 2012; Frieden, 2013). Further, because there are more effective interventions than can reasonably be funded (Frieden, 2013), consideration of clinical impacts alone is insufficient to demand change (Baltussen & Niessen, 2006; Lavis, Davies, Gruen, Walshe, & Farquhar, 2006). Many factors are often considered when decisions are made to invest in an intervention,

including but not limited to; clinical effectiveness, cost-effectiveness, burden of disease analysis and potential harms (Baltussen & Niessen, 2006; Lavis et al., 2006).

Systematic reviews and meta-analyses are typically viewed as the most appropriate method to summarise an interventions' effectiveness (Centre for Reviews and Dissemination, 2009; Mulrow, 1994) primarily because they are considered comprehensive and reliable summaries of "what works". However, there is growing acknowledgement that traditional methods used by researchers to synthesise a body of evidence are incongruent with the needs of end-users (Greenhalgh & Russell, 2006; Murthy et al., 2012; Tricco et al., 2015). For example, most systematic reviews are designed to critically analyse the evidence for a specific question (Moher, Liberati, Tetzlaff, Altman, & The Prisma Group, 2009). They often focus on a discrete sample, outcome/s or disease-type in order to be comprehensive and manageable. Unfortunately, this approach can be incongruent with the needs of decision makers aiming to inform practice in complex health organisations and environments.

Acknowledging these challenges, researchers are exploring strategies (Lavis et al., 2005; Murthy et al., 2012; Tricco et al., 2015) and adapting existing methodologies (Cochrane Library, 2014; V.; Smith, Devane, Begley, & Clarke, 2011) to enhance evidence use in healthcare (Anderson et al., 2013; Petticrew et al., 2013; V.; Smith et al., 2011). There is no single methodology that is best suited to achieving this aim, however a systematic review of reviews is one adaptation (Aromataris et al., 2015). Reviews of reviews are used to consolidate the results of individual systematic reviews into one document. The benefit of this method is the ability to comprehensively summarise the evidence-base and offer generalised conclusions (Cochrane Library, 2014) to better inform decision making needs (Aromataris et al., 2015; V.; Smith et al., 2011).

In the mental health field this methodology has been used to determine the efficacy of pharmacological versus non-pharmacological interventions for the treatment of major depression (Gartlehner et al., 2017), to investigate the effects of exercise on depressive symptoms in older people (Catalan-Matamoros, Gomez-Conesa, Stubbs, & Vancampfort, 2016) and to determine the effectiveness of drug and physical treatments in mild to moderate or severe depression (Cipriani, Barbui, Butler, Hatcher, & Geddes, 2011). This methodology is used here to explore the *effectiveness* of PA as a treatment for mental illness. Pointedly, we defined effectiveness as more than just the expected clinical outcomes given earlier acknowledgement of the many factors that can influence adoption of a new intervention (Baltussen & Niessen, 2006; Lavis et al., 2006). As such, effectiveness is defined as: 1) what are the main clinical outcomes expected of the intervention (i.e. changes in mental health symptoms, physical health metrics such as cardiorespiratory risk and/or quality of life); 2) is the intervention safe (i.e. reporting on adverse events); and 3) what are the costs associated with the intervention. We selected cost and adverse events over other factors because they become particularly important when considering the ongoing challenges healthcare systems face in providing safe (Leape et al., 2009), evidence-based care in fiscally demanding environments (Garber et al., 2014; Papanicolaos, Woskie, & Jha, 2018). For example, the USA has a higher healthcare spending than other high income countries with no resulting improvement to health outcomes (Schneider, Sarnak, Squires, Shah, & Doty, 2017). As such, efforts to maximise efficiencies (through optimising health at the lowest possible cost) is a priority (Garber et al., 2014). Recent studies in mental health have collectively explored these three constructs (Arnberg, Linton, Hultcrantz, Heintz, & Jonsson, 2014; Jonsson et al., 2016), reflecting this priority. Further internationally, cost and safety feature across many guiding documents designed to improve the delivery of evidence-based care (Agency for Healthcare Research and Quality, 2018; Department of Health, 2018; National Institute for Health and Care Excellence (NICE), 2018). Finally, we purposely included both physical and mental health outcomes as a main intervention effect, to address

calls from the sector to adopt integrated care practices (National Mental Health Commission, 2016; Naylor et al., 2016; Rebar, Stanton, & Rosenbaum, 2017; Vancampfort et al., 2015c).

This review of reviews aims to:

- 1) Summarise the current literature on the effectiveness of PA interventions as a treatment for mental health conditions.
- 2) Synthesise past systematic reviews and meta-analyses to improve practical application and inform healthcare decisions.
- 3) Identify gaps in the evidence base and provide recommendations for priority research, to support evidence-translation efforts.

## 2. Method

### 2.1. Protocol and registration

This systematic review was registered with the PROSPERO database (CRD42017065789). The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009). An electronic data-base search was conducted from earliest record to September 2017 using Medline, Cochrane Central Register of Systematic Reviews, Web of Science, Sport Discus, CINAHL, Scopus, PsycINFO. The search strategy is provided in Supplemental Table 1. The reference lists of other relevant systematic review of reviews (Catalan-Matamoros et al., 2016; Cipriani et al., 2011; Daley, 2008; Gartlehner et al., 2017) were also hand-searched. One reviewer (LC) developed the data extraction spreadsheet that was reviewed and agreed to by two separate reviewers (EZ and PC). Two reviewers completed the abstract and title search, full text review and data extraction (LC and OL). Disagreements were mediated through discussion and where a decision was unable to be reached, a third reviewer was available to adjudicate (SR).

### 2.2. Inclusion criteria

Reviews were included if they met the following criteria:

- 1) Participants had a diagnosed mental health condition (excluding eating disorders) according to a standardised diagnostic criterion (i.e. DSM – V, ICD-10). Any mental health diagnosis was considered, for example; major depressive disorder, schizophrenia, anxiety disorders
- 2) Participants were over 18 years old
- 3) PA and/or exercise was used as either a stand-alone or adjunctive treatment for the mental health condition and not as a preventative strategy. We did not differentiate between studies that explored exercise as a stand-alone treatment or adjunctive treatment because in pragmatic trials it would be unlikely that usual care would be withheld to explore the stand-alone effects of exercise. However, efficacy studies may have ability to do this in for example settings where access to evidence-based treatment is limited.
- 4) PA and/or exercise was a primary variable of interest in the study and data on the effects of PA could be extracted from the included study
- 5) Study type was systematic reviews and/or meta-analyses
- 6) The review had to report on at least one of the outcomes of interest listed below and/or any cost data (i.e. cost-effectiveness analysis, cost consequence analysis)
  - a. Quality of life
  - b. Mental health symptoms (i.e. using a validated measure)
  - c. A physical health metric (i.e. cardio-respiratory risk, body mass index)
  - d. Adverse events
- 7) A comparator condition (i.e. usual care) was listed in the review

Reviews were not restricted to a defined setting (i.e. in-patient

versus out-patient setting). Due to the broad nature of reviews of reviews any comparator was accepted (i.e. care as usual, wait-list control, active control, pharmacological interventions). This approach is in line with explanatory literature for reporting of systematic reviews (Shamseer et al., 2015). All reviews that met the definition of PA as defined by the World Health Organisation – “any bodily movement produced by skeletal muscles that requires energy expenditure” (World Health Organization, 2017) were included. Exercise is a sub-set of PA and is defined as “planned physical activity with bodily movements that are structured and repetitive, performed for the purpose of improving or maintaining physical fitness” (Department of Health, 2017). All forms of PA and exercise were included (i.e. yoga, tai chi, aerobic exercise, resistance training and/or combinations of exercise).

### 2.3. Exclusion criteria

Reviews were limited to human studies that were published in English. Reviews were excluded if only PA and/or exercise education/advice was provided and was not accompanied by an active intervention.

### 2.4. Quality assessment

The quality of included reviews was assessed using the AMSTAR (Assessing Methodological Quality of Systematic Reviews) tool (Shea et al., 2009). A score of < 4 points indicates low quality, 4–7 points indicate medium quality and 8–11 points are considered high quality (Sharif, Sharif, Ali, & Ahmed, 2013). To assess the quality of individual studies included within a systematic review, we relied on the ratings supplied by the original review authors (Supplemental Table 2). The AMSTAR rating of included reviews is provided in Supplemental Table 3.

### 2.5. Data analysis

Quantitative data was reported in Supplemental Table 2 (Summary of the Results). This approach is consistent with protocol recommendations outlined in the Cochrane Handbook (The Cochrane Collaboration, 2011) and a systematic review of reviews methods paper (V. Smith et al., 2011). The effect size of the intervention are reported, where 0.2 represents a small effect, 0.5 a moderate effect, and 0.8 a large effect (Cohen, 1988). Heterogeneity of included reviews was reported using the  $I_2$  statistic. High heterogeneity was represented by  $I_2 \geq 75\%$ , moderate heterogeneity by  $I_2 = 50\%$  and low heterogeneity by  $I_2 \leq 25\%$  (Higgins & Thompson, 2002). A meta-analysis was not planned for this systematic review of reviews. Due to anticipated differences in populations, outcomes and interventions we present data in a narrative summary.

## 3. Results

### 3.1. Search results

7050 studies were retrieved from the database search and were exported to Endnote (X8) for deduplication. After deduplication, the remaining 4098 articles were imported into Covidence for screening. A second deduplication was completed on importing to Covidence. 4008 articles remained for title and abstract screening with zero additional studies identified through hand-screening. After screening, a total of 33 reviews met the inclusion criteria (Fig. 1). Supplemental Table 4 provides a list of excluded studies and the rationale for exclusion.

Eleven reviews included people with a depression diagnosis (Blake, Mo, Malik, & Thomas, 2009; Cramer, Anheyer, Lauche, & Dobos, 2017; Eriksson & Gard, 2011; Heinzl, Lawrence, Kallies, Rapp, & Heissel, 2015; Krogh, Nordentoft, Sterne, & Lawlor, 2011; Kvam, Kleppe, Nordhus, & Hovland, 2016; Schuch, Vancampfort, Richards, et al.,

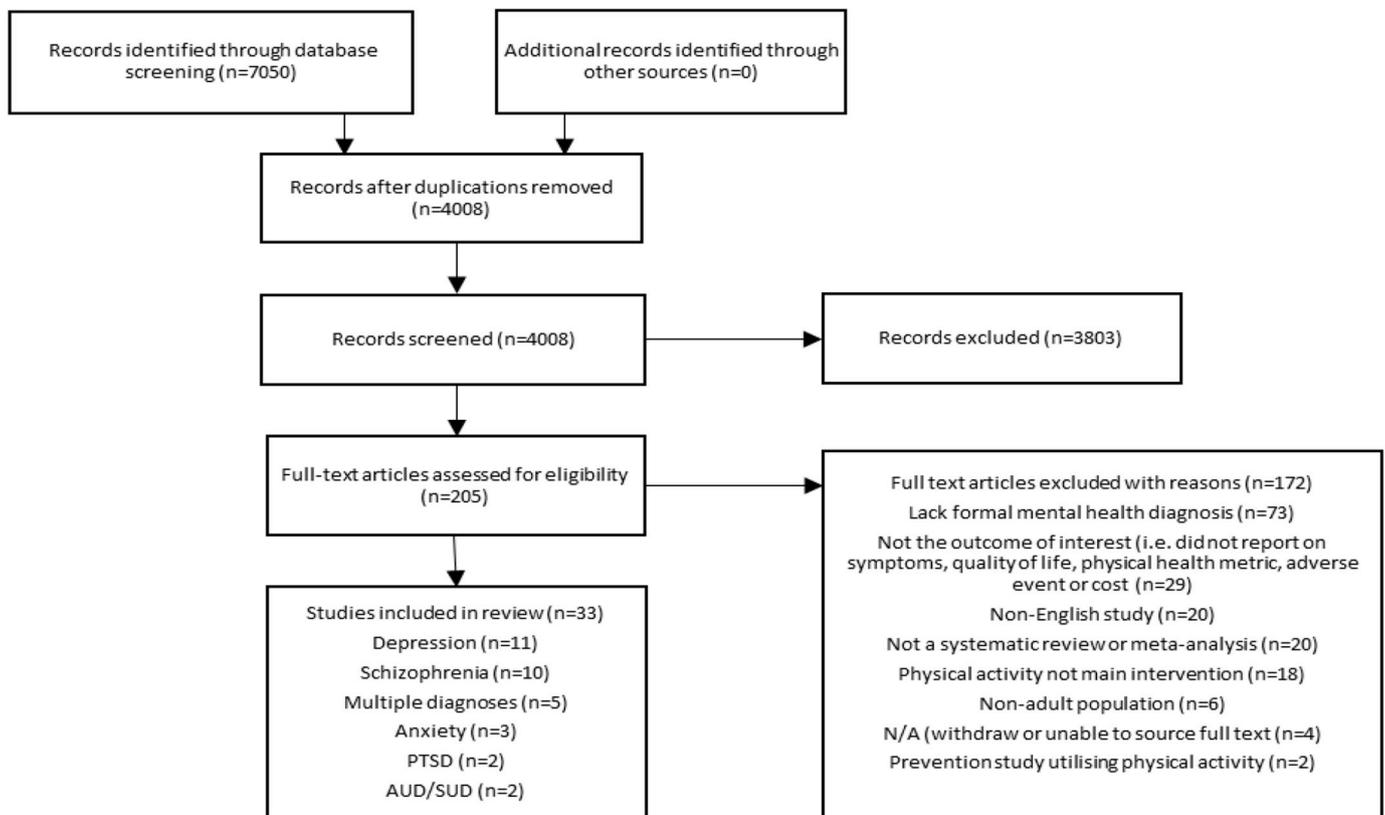


Fig. 1. Prisma flowchart.

2016c; Schuch et al., 2016b; Schuch et al., 2016c; Stubbs, Rosenbaum, Vancampfort, Ward, & Schuch, 2016; Sukhato et al., 2017), ten reviews included people with a schizophrenia diagnosis (Dauwan, Begemann, Heringa, & Sommer, 2016; Firth, Cotter, Elliott, French, & Yung, 2015; Keller-Varady et al., 2017; Martin, Beard, Clissold, Andraos, & Currey, 2017; Soundy, Roskell, Stubbs, Probst, & Vancampfort, 2015; Vancampfort et al., 2012; Vancampfort et al., 2015a; Vancampfort et al., 2015; Vera-Garcia, Mayoral-Cleries, Vancampfort, Stubbs, & Cuesta-Vargas, 2015; Zheng et al., 2016), five reviews included people with any mental health diagnosis (Klatte, Pabst, Beelmann, & Rosendahl, 2016; Rosenbaum, Newby, Steel, Andrews, & Ward, 2015a; Rosenbaum et al., 2014; Stanton & Happell, 2014; Vancampfort, Rosenbaum, et al., 2017) according to a recognised diagnostic criteria (for the purpose of this paper we used the term “multiple diagnoses” to describe reviews that included populations with different mental health diagnoses), three reviews included people with a diagnosis of anxiety disorder (Bartley, Hay, & Bloch, 2013; Jayakody, Gunadasa, & Hosker, 2014; Stubbs et al., 2017), two reviews included people with a post-traumatic stress disorder diagnosis (PTSD) (S. Lawrence, De Silva, & Henley, 2010; Rosenbaum et al., 2015) and two reviews included people with a diagnosis of alcohol use disorder (AUD)/substance use disorder (SUD) (Hallgren, Vancampfort, Giesen, Lundin, & Stubbs, 2017; Wang, Wang, Wang, Li, & Zhou, 2014). Full details of the included reviews are summarised in Supplemental Table 5.

### 3.2. Characteristics of included reviews

Supplemental Table 5 summarises the characteristics of included reviews. The total participant numbers and primary outcomes of the included reviews are summarised in Supplemental Table 6. The assessment tools used to measure clinical outcomes (i.e. changes in mental health symptoms and quality of life) varied across reviews. Further, studies included within the reviews also used different assessment tools to measure changes in clinical outcomes.

### 3.3. Quality of the included reviews

Supplemental Table 2 reports the AMSTAR rating of the included reviews. The quality of included reviews varied from low to high (Low quality rating  $n = 1$ , Medium quality rating  $n = 24$ , High quality rating  $n = 7$ , NA  $n = 1$ ). The principal areas where reviews were downgraded included: not registering ‘a priori’ design, failing to provide a list of excluded studies and not listing conflicts of interest for the included studies. Importantly, the quality of the systematic review is not indicative of the quality of included studies. Taken together, the quality of included studies as reported by the authors of the systematic reviews is mixed (Supplemental Table 2).

### 3.4. Individual studies

Individual studies may be reported more than once in reviews of reviews which can introduce bias in reporting of results. The solution is to unpack each of the included studies, however this defeats the purpose of conducting a review of reviews. To balance the possible over-estimation of treatment effects by reporting individual studies more than once, Table 1 provides a study count of duplicate studies.

## 4. Depression

### 4.1. Symptoms of mental illness

Eight (Blake et al., 2009; Eriksson & Gard, 2011; Heinzel et al., 2015; Krogh et al., 2011; Kvam et al., 2016; Schuch, Vancampfort, Richards, et al., 2016c; Schuch et al., 2016b; Sukhato et al., 2017) of the nine identified reviews reported a positive effect favouring PA to reduce symptoms of depression. The magnitude of this effect ranged from small to large, somewhat dependent upon the methodological approach (Supplemental Table 2). For example, reviews where the methodology included another form of PA in the comparison group

**Table 1**  
Duplicate study count.

	Total number of studies included in review	Number of studies that are duplicated in another review	Number of included studies that are not duplicated anywhere else in this review
Blake (2009)	11	10	1
Cramer (2017)	8	0	8
Eriksson (2011)	8	6	2
Heinzel (2015)	18	14	4
Kvam (2016)	23	18	5
Krogh (2011)	13	12	1
Schuch, 2016(a)	25	19	6
Sukhato (2017)	17	4	13
Schuch, 2016(b)	6	5	1
Schuch, 2016(c)	8	0	0
Stubbs (2016)	7	4	3
Dauwan (2016)	29	27	2
Keller-Varady (2017)	6	6	0
Firth (2015)	17	15	2
Martin (2017)	7	6	1
Vancampfort (2015)	11	9	2
Vancampfort, 2015(a)	7	2	5
Vancampfort (2012)	3	3	0
Zheng (2016)	6	1	5
Vera-Garcia (2015)	13	11	2
Soundy (2015)	10	3	7
Rosenbaum (2014)	39	16	23
Klatte (2016)	25	8	17
Rosenbaum, 2015(a)	2	0	2
Vancampfort (2017)	23	18	5
Stanton (2014)	8	4	4
Rosenbaum (2015)	4	0	4
Lawrence (2010)	0	0	0
Bartley (2013)	7	2	5
Jayakody (2014)	8	2	6
Stubbs (2017)	6	2	4
Bartley (2013)	7	2	5
Jayakody (2014)	8	2	6
<b>Total</b>		<b>155</b>	

(Cramer et al., 2017), or where PA was used as a stand-alone treatment and compared to established treatment protocols. Methodological issues that impact upon the effect size in depression and PA systematic reviews and meta-analyses have previously been reported (Ekkekakis, 2015). Consistent with this literature, the one review that reported inconclusive results for the effect of yoga interventions (Cramer et al., 2017) on major depressive disorders included an active control group, comprising a home-based walking program with telephone counselling. Further, Kvam and colleagues (Kvam et al., 2016) found exercise (i.e. aerobic and anaerobic) was an effective intervention (moderate/large effect) when compared to no treatment, usual care and when used in conjunction with anti-depressant medication. However, no effect and a small, non-significant effect was observed when compared as a stand-alone treatment to anti-depressants and psychological care, respectively (Kvam et al., 2016). This suggests that PA could be considered as part of a suite of interventions designed to address symptoms of depression.

#### 4.2. Exercise program variables (i.e. type, intensity, supervision)

Systematic reviews of depression have progressed from reporting the efficacy of PA interventions to exploring the modality, frequency and intensity of PA interventions that produce the largest treatment

effect. Two reviews (Blake et al., 2009; Krogh et al., 2011) explored whether the short-term positive effects of PA interventions were sustained over longer durations when follow-up data was collected. Both these reviews (Blake et al., 2009; Krogh et al., 2011) demonstrated PA had a significant, positive short-term impact on depressive symptoms, however the long-term effects of PA interventions were inconclusive. One review (Krogh et al., 2011) reported that the positive effects of PA ceased when the program ceased and no long-term effects on symptoms of depression were observed (follow-up duration varied from 9 months to 26 months) (Krogh et al., 2011). The second review (Blake et al., 2009) reported inconsistent results and also highlighted a dearth of long-term follow-up in studies (Blake et al., 2009). Three reviews (Heinzel et al., 2015; Schuch, Vancampfort, Richards, et al., 2016c; Schuch et al., 2016c) reported a moderate to large effect favouring exercise modalities that were supervised and incorporated aerobic, resistance training or mixed modalities. Two reviews (Schuch, Vancampfort, Richards, et al., 2016c; Schuch et al., 2016c) reported on the intensity of exercise and reported a larger effect size favouring exercise for moderate to-vigorous exercise. Two reviews (Schuch, Vancampfort, Richards, et al., 2016c; Schuch et al., 2016c) suggest that PA conducted in group or non-group environments appear to be effective. However, for older adults, better treatment effects were observed when the exercise was conducted in a group setting (Schuch et al., 2016c). Two reviews (Kvam et al., 2016; Sukhato et al., 2017) reported a significant effect favouring PA interventions when combined with standard treatment (i.e. anti-depressants). Finally, two reviews (Heinzel et al., 2015; Sukhato et al., 2017) explored the efficacy of home-based exercise. One review demonstrated a moderate/large, significant effect favouring home exercise only when combined with psychological treatment (Sukhato et al., 2017) and non-significant finding for home-based exercise interventions alone. The second study reported no effect for home-based exercise (Heinzel et al., 2015). It is difficult to elucidate details from the reviews about the type of home-based intervention and the level of supervision and whether this may have contributed to these findings. While Heinzel et al. (Heinzel et al., 2015) report that the level of supervision of their included studies was mixed (i.e. unsupervised home program and weekly supervision of a home program by a trained nurse), Sukhato and colleagues (Sukhato et al., 2017) do not describe the level of supervision of their included exercise studies. It is unclear whether the contact from a therapist in the combined treatment group contributed to the positive findings in that home program.

#### 4.3. Quality of life

One review (Schuch et al., 2016b) reported a significant, moderate effect favouring PA in the total (SMD = 0.39, 95% CI = 0.47 to 0.74,  $p = 0.002$ ), physical (SMD = 0.53, 95%CI = 0.22 to 0.84) and psychological (SMD = 0.53, 95%CI = 0.22 to 0.85,  $p < 0.001$ ) quality of life domains. The same study reported a small, non-significant effect favouring PA in the social (SMD = 0.28, 95%CI = -0.13 to 0.71,  $p = 0.18$ ) and environmental (SMD = 0.36, 95%CI = -0.12 to 0.85,  $p = 0.14$ ) domains.

#### 4.4. Physical health metric

One review (Stubbs et al., 2016) reported a significant, moderate effect favouring PA to improve cardio-respiratory fitness in people with depression (Hedges  $g = 0.64$ , 95% CI = -0.32 to 0.96,  $p < 0.001$ ).

#### 4.5. Adverse events and cost

No adverse events were found in the three reviews (Cramer et al., 2017; Heinzel et al., 2015; Sukhato et al., 2017) that reported this outcome. No cost data was reported in the included reviews.

## 5. Schizophrenia

### 5.1. Symptoms of mental illness

All eight reviews examining changes in mental health symptoms in people diagnosed with schizophrenia reported a positive effect favouring PA. The positive effects appear subject to moderators associated with the PA intervention. Keller-Varady and colleagues (Keller-Varady et al., 2017) reported the positive effects favouring PA included interventions that combined both aerobic and strength training. Firth et al. (Firth et al., 2015) reported a greater treatment effect when low-intensity PA interventions were removed from the analysis and only moderate to high intensity PA interventions were included. Zheng and colleagues (Zheng et al., 2016) reported Tai Chi was only effective in reducing negative symptoms and had no effect on positive symptoms. Conversely, another review (Vera-Garcia et al., 2015) reported that Tai Chi was not effective in reducing negative symptoms. However, only one included study was used to establish this result.

### 5.2. Quality of life

Four (Dauwan et al., 2016; Soundy et al., 2015; Vancampfort et al., 2012; Vera-Garcia et al., 2015) of the five reviews that reported on quality of life, found a positive effect favouring PA, in at least one quality of life domain. Firth et al. (Firth et al., 2015) reported inconclusive results; two of the included studies in his review, using at least 120 min of moderate to high intensity exercise, reported positive changes in quality of life outcomes and two other included studies found no change. Vera-Garcia and colleagues (Vera-Garcia et al., 2015) reported the positive effects of PA on quality of life outcomes were limited to aerobic PA and/or strength training, but no change was observed for high intensity PA.

### 5.3. Physical health

Physical health outcomes (measured via changes in cardio-respiratory fitness) responded favourably to PA interventions by improving, however the effect size and significance of these results varied across reviews. Vancampfort et al. (Vancampfort et al., 2015) reported a significant, small/moderate effect size favouring exercise to improve cardio-respiratory fitness in a meta-analysis of seven studies (Hedges  $g = 0.40$ , 95%CI = 0.16 to 0.64,  $p = 0.001$ ). Martin and colleagues (Martin et al., 2017) reported a non-significant, small effect favouring exercise in their systematic review of three studies. The three studies that were included in Martin et al. (Martin et al., 2017), reported that the aerobic intervention was completed twice per week and they had a drop-out rate of 35%, which may have contributed to the non-significant findings. Firth et al. (Firth et al., 2015), reported a positive change in maximal exercise capacity ( $VO_2$ ) in seven included primary studies, with the change in three of these studies demonstrating clinically meaningful improvements. That is, the increase in  $VO_2$  translates to a 15% reduction in cardiovascular disease risk and a 20% reduction in mortality (Firth et al., 2015). Firth et al. (Firth et al., 2015) review also completed a meta-analysis investigating the effects of an exercise intervention on body mass index (BMI) and found exercise did not significantly reduce BMI (mean difference =  $-0.98$  kg, 95% CI =  $-3.17$  to  $-1.22$ ). Thus, the beneficial effects of exercise (i.e. reduced cardiovascular disease risk and mortality and reduced psychiatric symptomatology), appear to occur independent of changes to BMI.

### 5.4. Adverse events and cost

No adverse events were found in the five reviews (Firth et al., 2015; Vancampfort et al., 2012, 2015a; Vera-Garcia et al., 2015; Zheng et al., 2016) that reported this outcome. No cost data was reported in the included reviews.

## 6. Multiple diagnoses (includes populations with different mental health diagnoses within the included review)

### 6.1. Symptoms of mental illness

Three reviews (Klatte et al., 2016; Rosenbaum et al., 2014, 2015a) explored the effect of PA interventions on reducing symptoms of depression in people with a mental illness, where the population included people with different diagnoses. All three reviews reported positive effects favouring PA interventions. Of these, two reviews (Klatte et al., 2016; Rosenbaum et al., 2014) reported moderate to large effect sizes favouring the PA interventions. One of these reviews (Rosenbaum et al., 2014) was able to show that the effect size was larger in interventions where the PA protocol met American College Sports Medicine (ACSM) guidelines, compared to PA interventions that did not meet ACSM guidelines. However, the authors reported caution in interpreting this result, given the difference was no longer present when a subgroup of higher quality studies was examined.

### 6.2. Quality of life

Two reviews (Klatte et al., 2016; Rosenbaum et al., 2014) explored PA effects on quality of life outcomes and both reviews reported a moderate, significant effect favouring PA.

### 6.3. Physical health metric

Two reviews (Rosenbaum et al., 2014; Vancampfort, Rosenbaum, et al., 2017) reported physical health outcomes in people with multiple diagnoses. One review (Vancampfort, Rosenbaum, et al., 2017) found PA interventions significantly improved cardio-respiratory fitness in people with a serious mental illness and better results were observed with interventions that involved higher intensities, were completed  $\geq 3$  times per week and were supervised by a qualified instructor (i.e. by a exercise physiologist or physiotherapist). One review (Rosenbaum et al., 2014) reported a small, significant effect favouring exercise to improve anthropometric measures while the other review found no change in BMI (Vancampfort, Rosenbaum, et al., 2017). The difference in these outcomes may be due to the different diagnoses of included study participants. While Rosenbaum et al. (Rosenbaum et al., 2014) demonstrated positive findings including participants with any mental health diagnosis, Vancampfort and colleagues (Vancampfort, Rosenbaum, et al., 2017) review was limited to participants with serious mental illness.

### 6.4. Adverse events and cost

No adverse events were found in one review (Rosenbaum et al., 2014) that reported this outcome. No cost data was reported in the included reviews.

## 7. Anxiety

### 7.1. Symptoms of mental illness

Three reviews reported a positive effect favouring PA to reduce symptoms of anxiety, two of these reviews (Jayakody et al., 2014; Stubbs et al., 2017) stated this effect was significant.

### 7.2. Quality of life

One review (Jayakody et al., 2014) reported a non-significant, positive effect favouring PA to improve quality of life outcomes.

**Table 2**  
Evidence summary.

Current evidence	
<b>Interventions for Depression</b>	
11 studies (n = unknown)	Physical activity is effective in reducing symptoms of depression and increasing quality of life in people with depression. Evidence suggests supervised, moderate to high intensity exercise and aerobic or combined (aerobic/anaerobic) exercise produce the best treatment effect. No adverse event (n = 3) in reviews that reported this. No cost data.
<b>Interventions for Schizophrenia</b>	
10 studies (n = 4140)	Exercise has a positive effect on both mental and physical health outcomes in people with schizophrenia. Changes in anthropometric measures were inconclusive, cardio-respiratory fitness improved in this population. Evidence suggests moderate to high intensity exercise and aerobic or combined (aerobic/anaerobic) exercise produce the best treatment effect. No adverse event (n = 5) in reviews that reported this. No cost data.
<b>Interventions for Mental Illness (multiple diagnosis)</b>	
5 studies (n = unknown)	Physical activity has a positive effect on mental health outcomes. In people with serious mental illness, exercise can improve cardio-respiratory fitness, with better results seen in interventions that were supervised, conducted $\geq 3$ times per week and of higher intensity. No adverse event (n = 1) in reviews that reported this. No cost data.
<b>Interventions for Anxiety</b>	
3 studies (n = 1232)	Exercise reduces anxiety symptoms (variable effect size). Compared to wait-list control or placebo, exercise produced superior results. It is not more effective than current treatment (i.e. anti-depressants). Current systematic reviews suggest no adverse events as a result of the intervention, however adverse events are not routinely reported.
<b>Interventions for Post-traumatic stress disorder (PTSD)</b>	
2 studies (n = 200)	A limited number of studies met the inclusion criteria in this population, thus no definitive conclusions can be drawn. However physical activity appears beneficial in reducing PTSD symptoms and symptoms of depression in this population. No adverse event (n = 1) in reviews that reported this. No cost data.
<b>Interventions for Substance Use Disorder (SUD)/Alcohol Use Disorder (AUD)</b>	
2 studies (n = unknown)	A limited number of studies were included, thus no definitive conclusions can be drawn. However physical activity appears effective in reducing symptoms of depression in people with AUD and illicit drug use. Results are inconclusive with respect to reducing consumption/withdrawal. No adverse event (n = 1) in reviews that reported this. No cost data.

### 7.3. Physical health metric

None of the included reviews reported on physical health outcomes for people diagnosed with an anxiety disorder.

### 7.4. Adverse events and cost

One review (Jayakody et al., 2014) reported on adverse events, stating no adverse events were associated with the PA intervention. No cost data was included in the reviews.

## 8. Post-traumatic stress disorder

Two reviews (S. Lawrence et al., 2010; Rosenbaum et al., 2015) met our inclusion criteria, however one of these reviews (S. Lawrence et al., 2010) did not find any individual studies that met their inclusion criteria. The two reviews were conducted five years apart, with the earlier review (S. Lawrence et al., 2010) failing to find any individual studies that met their inclusion criteria. As such, the evidence reported below demonstrates the most recent data for patients with PTSD and is derived from one review (Rosenbaum et al., 2015).

### 8.1. Symptoms of mental illness

One review (Rosenbaum et al., 2015) reported a small/moderate effect favouring PA to reduce symptoms of PTSD and reduce symptoms of depression.

### 8.2. Quality of life

No review has reported on quality of life outcomes in this population.

### 8.3. Physical health metric

One review (Rosenbaum et al., 2015) reported a significant reduction in waist circumference favouring the PA group.

### 8.4. Adverse events and cost

No adverse events were found in the one review (Rosenbaum et al., 2015) that reported on this outcome. No cost data was reported in the included review.

## 9. Alcohol use disorder/substance use disorder

### 9.1. Symptoms of mental illness

Two reviews (Hallgren et al., 2017; Wang et al., 2014) reported positive effects favouring PA to reduce symptoms of depression in people diagnosed with AUD/SUD. One review (Wang et al., 2014) suggested a positive effect favouring PA to improve abstinence in SUD. A second review (Hallgren et al., 2017) showed no impact on consumption of alcohol in AUD. These findings suggest that the different diagnosis (SUD versus AUD) and the different outcomes measured may influence the effectiveness of exercise interventions in this population.

### 9.2. Quality of life

The included reviews did not report any quality of life outcomes.

### 9.3. Physical health metric

One review reported a moderate, significant effect favouring PA to improve maximal exercise capacity (i.e.  $VO_2$ ) in AUD (Hallgren et al., 2017).

### 9.4. Adverse events and cost

No adverse events were found in the one review (Hallgren et al., 2017) that reported this outcome. No cost data was reported in the included reviews.

## 10. Evidence summary

Table 2 provides a summary of the evidence from the review. Notwithstanding the inconsistent reporting of adverse events and lack of cost data, the clinical outcomes suggest that positive gains could be

achieved in people diagnosed with depression, schizophrenia, multiple mental health diagnoses and anxiety through participation in PA interventions. Preliminary evidence is promising in PTSD and AUD/SUD, however, due to the limited number of systematic reviews and included studies, more research is required in these areas.

## 11. Discussion

From the 33 systematic reviews/meta-analyses included in this review, 32 reported outcomes that support the effectiveness of PA interventions (including yoga, tai chi, general PA and structured exercise) on at least one of the main *clinical* outcomes of interest (symptoms of mental illness, quality of life and/or physical health metric). There was large variation in the effect size and significance of the results (including non-significant findings); however, the overall trend was positive and favoured PA interventions. Reporting on adverse events was inconsistent across reviews and no cost data was found. This represents a major gap in the evidence base that is a possible barrier to translation and implementation efforts of PA interventions within mental healthcare.

Overwhelmingly, the available research investigates the effect that PA has on the symptoms of mental illness (27/28 = 96.4%). Taken together, the results suggest PA has a positive effect on symptoms of mental illness in people diagnosed with depression, schizophrenia, multiple diagnose, anxiety, PTSD and AUD/SUD. Given more reviews have been completed in people diagnosed with depression (8 reviews), schizophrenia (8 reviews) and multiple diagnoses (4 reviews) compared to people diagnosed with anxiety (3 reviews), PTSD (1 review) and AUD/SUD (2 reviews), the smaller number of reviews and unequal distribution of sample sizes across reviews must be acknowledged in the context of drawing general conclusions. We note our results for positive findings in PA and depression differ from a recent review by Krogh and colleagues (Krogh J, Hjorthøj C, Speyer H, Gluud C, & Nordentoft M, 2017). The authors of that study concluded, that when limited to ‘high-quality trials’ (n = 4) (studies with a low-risk of bias), exercise had no anti-depressant effect or impact on quality of life outcomes. The difference in results should be considered in light of a number of methodological discrepancies including that within the assessment of risk of bias, two of the four studies identified as being of low risk of bias in the Krogh review were published by the authors of the review themselves (Krogh J, Saltin B, Gluud C, & M, 2009; Krogh J, Videbech P, Thomsen C, Gluud C, & Nordentoft M, 2012) and both of which were excluded from the 2016 review of Schuch et al. (Schuch, Vancampfort, Richards, et al., 2016c) (which met criteria for being a “high-quality” systematic review) for using active control conditions. Contention about the strength of evidence for PA effects on depression have been previously documented (Ekkekakis, 2015), with reports suggesting the conflicting advice can prevent healthcare professionals from recommending this treatment to patients. This concern is conferred within the implementation literature that suggests the perceived strength of the evidence-base can influence the uptake and use of new interventions in clinical practice (Damschroder et al., 2009). Through pooling the results of 11 systematic reviews in depression and PA, our findings suggest PA improves symptoms of depression and, whilst acknowledging inconsistent reporting on adverse events, the current literature suggests it is also a safe intervention.

Reviews that investigated physical health outcomes suggest an overall, small to moderate effect favouring PA to improve cardio-respiratory fitness. Changes in anthropometric measures (i.e. BMI and weight) were inconclusive. A possible explanation for this is the differences in the severity of mental health diagnosis (i.e. serious mental illness versus any mental health diagnosis) and the corresponding standard treatment. For example, anti-psychotic medication is the cornerstone treatment in schizophrenia with weight gain being a common side-effect of this medication, making it challenging for this population to lose weight (Bak, Franssen, Janssen, van Os, & Drukker,

2014). The clinical implications of these findings in relation to addressing the high levels of cardio-metabolic disease and mortality in people with serious mental illness, have been detailed previously (Firth et al., 2015; Vancampfort, Rosenbaum, et al., 2017) and our review confers with previous recommendations. That is, despite PA interventions showing an inconclusive impact on anthropometric measures, positive health gains can still be achieved in this population by focusing on improving fitness to reduce cardio-metabolic risk. Independent of changes in weight, improved fitness is associated with reduced cardio-metabolic risk (Barry et al., 2014). As such, improving fitness in this population should be viewed as an important treatment goal to reduce overall cardio-metabolic risk and associated mortality (Vancampfort et al., 2015a).

Routine reporting on adverse events was limited, consistent with advice that adverse events are under-reported (Greenhalgh, Howick, & Maskrey, 2014), and cost data was not reported in any of the included reviews. This may suggest an overreliance of studies focusing on efficacy outcomes at the possible expense of building evidence in other areas important in healthcare. For example, whilst confirming the efficacy of an intervention is imperative in establishing treatment effects, the evidence base (which includes considerations of both expected benefits and possible adverse outcomes from the intervention) and cost of the intervention can also influence the uptake and use of new interventions (Damschroder et al., 2009). Further, at a fundamental level, “good” (World Health Organization, 2007) health services are designed to deliver safe and effective quality interventions with consideration to the most efficient use of resources. In the USA, policy reform in medical technologies have been proposed to reduce healthcare spending whilst minimising losses to health outcomes (Garber et al., 2014). Given much of the higher healthcare spending in the USA is attributed to workforce and product costs (including high pharmaceutical costs) (Papanicolaou et al., 2018), it would be useful to understand whether PA participation can reduce pharmaceutical use in this population and thus reduce overall health spending with no net loss to health outcomes. We suggest the development of this type of evidence in PA and mental healthcare may be more useful than the continued reporting on efficacy alone. Editorials within this journal concur with this statement and have called for more translation research that includes, amongst other priorities, consideration of PA interventions within the context of health services and economic feasibility (Taylor & Faulkner, 2014).

An ‘a priori’ decision was made to include all forms of PA because previous research identified poor reporting of PA interventions that rendered protocols unable to be replicated (Slade & Keating, 2012). Recent reviews appear to address this complaint by referencing a standard definition of PA, and its subset exercise, and also referring to the ACSM guidelines to define exercise protocols. These efforts are crucial in supporting implementation and dissemination efforts and identifying the optimal ‘dosage’ of PA that is required to maximise the treatment effect (Taylor & Faulkner, 2014; Vina, Sanchis-Gomar, Martinez-Bello, & Gomez-Cabrera, 2012). During implementation a balancing act exists to maintain the fidelity of an effective intervention whilst accommodating the adaptations that occur to help “fit” with the implementation site (Durlak & DuPre, 2008). As such, reporting on the moderators (i.e. type, frequency, intensity of PA intervention) that produce optimal treatment effects is important to ensure these elements are retained during the implementation process, or enhanced over time (Shelton, Cooper, & Stirman, 2018). Whilst not a direct aim of this study, six reviews reported data on moderating factors that can produce optimal treatment effects for people with depression, schizophrenia and serious mental illness (reported in Table 2). Our results are broadly consistent with recommendations provided to patients with other non-communicable diseases, where PA is an established treatment (i.e. diabetes management) (American Diabetes Association, 2015). However, previous literature (Vancampfort et al., 2015c), suggests that achieving PA recommendations should be viewed as an “aspirational goal” for this population due to barriers that impede activity efforts (i.e.

a-motivation, side-effects of medications).

A concurrent aim of this review of reviews was to improve practical application of the evidence in real-world health services. New methods have evolved to address the complexity that exists with using evidence to inform healthcare practices. This review has been able to draw together a broader evidence-base than would have been possible with a traditional systematic review and identify evidence gaps, however it is questionable as to whether this method can improve the use of this evidence in real-world health services. For example, the method is limited by the inclusion/exclusion criteria of the original systematic reviews and meta-analyses (i.e. systematic reviews of randomised control trials). This can result in the exclusion of studies that offer nuanced details of PA interventions which may be more valuable to translation and implementation efforts. Realist reviews are a possible solution to this issue, with realist reviews seeking to describe interventions within the broader context of what works for whom under what circumstances (Pawson, Greenhalgh, Harvey, & Walshe, 2005; Rycroft-Malone et al., 2012). Whilst outside the scope of this review, understanding the application of realist reviews within PA and mental health and the potential to improve evidence-informed practice is warranted.

### 11.1. Limitations

While the lack of cost data is considered a key finding, others have suggested that a review of reviews may not be the right study design for collecting this type of data because of the difficulty in pooling results that use different currencies and changing values (Caird, Sutcliffe, Kwan, Dickson, & Thomas, 2015). However, the authors from that study also noted that data from cost-consequence analysis would be suitable for gathering through a review of review design, because of its application in decision-making process that can justify where resources and budgets are allocated. This potential limitation was accounted for when developing our search terms by including multiple cost-terms that would capture such studies.

The inconsistent reporting on adverse events may be indicative of publication bias. The “file drawer effect” suggests researchers fail to report on negative outcomes, which may skew results towards a positive effect (Rosenthal, 1979). Finally, we relied on the review authors reporting of the included study quality. The quality of the systematic reviews (AMSTAR score) and the quality of the included studies in those reviews was inconsistent, suggesting caution is required when interpreting the results of this review.

## 12. Conclusion

A large body of evidence reports the positive impact PA interventions have on clinical outcomes in people with a mental illness. However, adverse events are not routinely reported and to date no cost data exists in systematic reviews and/or meta-analyses. To build an evidence base that is applicable in real-world health services it is essential to collect and report this, and other relevant data in research studies. While reviewing the full range of evidence needed to influence translation and real-world use was outside the scope of this review, there is a critical need to understand whether studies in PA and mental health are exploring factors that are important to translation efforts. For example, is the intervention feasible in this population?, what resources are needed by the organisation to implement the intervention?, what are the core components of the intervention that produce the desired outcomes and therefore should not be removed when implementing? Despite this, and the study quality (of reviews and included studies) being highly variable, the results from 32 separate systematic reviews suggests that PA has a positive effect on at least one of the main clinical outcomes of interest, including symptoms of mental illness, quality of life or physical health metrics. We recommend future research build on this evidence base by conducting more effectiveness and

implementation and dissemination studies (Pinnock et al., 2017). This includes reporting outcomes that matter to decision makers and are relatable to real-world, complex, health services delivery.

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## All authors declare they have no conflict of interest in relation to this study

This article does not contain any studies with human participants performed by any of the authors.

This study does not involve human participants and informed consent was therefore not required.

This article does not contain any studies with animals performed by any of the authors.

## Appendix A. Supplementary data

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