



Efeito protetor da atividade física nos sintomas depressivos em idosos: Revisão Sistemática e Meta-Análise

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PALAVRAS-CHAVE: DEPRESSÃO; EXERCÍCIO FÍSICO; ADULTOS MAIS VELHOS; CES-D; GDS.

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Resumo

Introdução: O envelhecimento da população e a crescente esperança média de vida são um problema do mundo atual, havendo cada vez maior importância atribuída a manutenção de uma boa qualidade de vida durante o envelhecimento incluindo não só aspetos físicos, mas também a saúde mental. A depressão é o mais importante problema de saúde mental no idoso, que muitas vezes não é tratada, ou é tratada apenas com medicação. A atividade física tem vindo aos poucos ganhando importância, não só como forma de tratamento, mas também como prevenção deste tipo de sintomas. No entanto, a atividade física não está ainda estabelecida de forma consistente nos protocolos de atuação para a prevenção dos sintomas depressivos. Desta forma, para sintetizar os achados em estudos longitudinais propusemo-nos a fazer uma revisão sistemática e meta-análise, a fim de verificar se a atividade física previne os sintomas depressivos em idosos, e qual a melhor intensidade para alcançar esse efeito.

Metodologia: Potenciais estudos foram pesquisados na Pubmed, Scopus e Ebsco entre 13 e 27 de janeiro de 2021. Dados demográficos, dados sobre a avaliação da atividade física e dos sintomas depressivos, odds ratio e o intervalo de confiança de 95% foram extraídos dos estudos selecionados. Uma meta-análise de efeitos randomizados e uma análise de sensibilidade foram executadas, e as potenciais fontes de heterogeneidade foram exploradas usando o Open Meta-Analyst. A qualidade dos estudos foi avaliada usando a escala Newcastle-Ottawa.

Resultados: De 2821 estudos encontrados, um total de 12 estudos prospetivos eram elegíveis para a extração de dados, com uma amostra total de 38746 participantes. Verificamos que quem praticava atividade física tinha menor probabilidade de desenvolver sintomas depressivos (OR=0.69, 95% CI=0.59, 0.81, $p<0.01$; $I^2=69.95\%$) a longo prazo comparativamente com quem era inativo ou tinha baixos níveis de AF. Por outro lado, verificamos também que níveis de atividade física moderada (OR=0.51, 95% CI=0.33, 0.79, $p<0.01$; $I^2=0\%$) parecem ser mais eficazes na redução das chances de ter sintomas depressivos

comparativamente aos idosos com níveis baixos ou até mesmo com elevados níveis de AF (OR=0.43, 95% CI=0.18, 1.04, p=0.06; I²=75.98%, Heterogeneity p value=0.02). Verificamos que a heterogeneidade era alta, no entanto nos subgrupos do nível de atividade física moderada, dos questionários validados e da cultura do Este asiático a heterogeneidade não era significativa.

Conclusão: Os resultados sugerem que a prática de atividade física reduz a probabilidade de desenvolvimento de sintomas depressivos em idosos pelo que o desenvolvimento e promoção de programas de AF regular nesta população são de vital importância no combate a esta condição cada vez mais comum.

PALAVRAS-CHAVE: DEPRESSÃO; EXERCÍCIO FÍSICO; ADULTOS MAIS VELHOS; CES-D; GDS.

Abstract

Introduction: Population aging and high life expectancy are a problem in current times, with increasing importance being given to maintaining a good quality of life during aging, including not only physical aspects, but also mental health. Depression is an important mental health problem in the elderly, which often goes by untreated, or is treated only with medication. Physical activity has been gradually gaining importance, not only as a form of treatment, but also as prevention for this type of symptoms. However, physical activity has not yet been consistently established in protocols for the prevention of depressive symptoms. Thus, to synthesize the findings in longitudinal studies, we proposed to write a systematic review and meta-analysis, in order to verify if physical activity prevents depressive symptoms in the elderly, and what are the best physical activity levels to achieve this effect.

Methods: Potential studies were searched on Pubmed, Scopus and Ebsco between January the 13th and the 27th of 2021. Demographic data, data on physical activity and depressive symptoms assessment, and odds ratio with 95% confidence intervals were extracted. Random-effects meta-analysis and a sensitivity analysis were conducted, and the potential sources of heterogeneity were explored using Open Meta-Analyst. Study quality was assessed using the Newcastle-Ottawa Scale.

Results: From 2812 studies found, a total of 12 prospective studies were eligible for data extraction, with a total sample of 3987 participants. We found that those engaged in physical activity had lower odds of developing depressive symptoms (OR=0.69, 95% CI=0.59, 0.81, $p<0.01$; $I^2=69.95\%$) in the long term when compared to inactive participants or those with low physical activity. On the other hand, we also found that moderate physical activity levels (OR=0.51, 95% CI=0.33, 0.79, $p<0.01$; $I^2=0\%$) seem to be more effective in reducing the odds having depressive symptoms than high levels (OR=0.43, 95% CI=0.18, 1.04, $p=0.06$; $I^2=75.98\%$, Heterogeneity p value=0.02). Despite this, heterogeneity was high, however the use of valid physical activity questionnaires, moderate level of

physical activity and studies in East asian culture were of non-significant heterogeneity.

Conclusion: The results suggest that being active reduces the odds of developing depressive symptoms in the elderly, so the development and promotion of regular PA programs in this population are of vital importance in preventing this increasingly common disorder.

KEY-WORDS: DEPRESSION; PHYSICAL EXERCISE; OLDER ADULTS; CES-D; GDS.

1. Introdução

1.1. O envelhecimento populacional

A população mundial cresceu bastante no último século. Em 1974 atingiu os 2 bilhões (Housman & Dorman, 2005), em 1999 4 bilhões (Cohen, 2003), e em 2019 7,7 bilhões (United Nations, 2019). É provável que em 2050 a população idosa mundial duplique para cerca de 2 bilhões, correspondendo a 22% da população mundial (World Health Organization, 2021a). Esta população mais envelhecida está mais suscetível a sofrer uma maior taxa de doenças crônicas, exigindo cuidados a longo prazo dispendiosos (Beard et al., 2016).

Portugal segue esta tendência, sendo que 21,7% da população residente no país tem 65 ou mais anos e 13,8% tem menos de 15 anos (PORDATA, 2020). O índice de envelhecimento passou de 27,5% em 1961 para 165,1% em 2020 (PORDATA, 2021), tendo um forte impacto na sociedade como um todo, exigindo adaptações da mesma, como a nível dos sistemas de saúde, segurança social, justiça, educação e transportes (Direção-Geral da Saúde, 2016). Portugal é o 3º país da União Europeia com maior número de pessoas idosas (PORDATA, 2020) e a maior parte dos cenários prevê um avanço desta condição demográfica (Figura 1) (Instituto Nacional de Estatística, 2020).

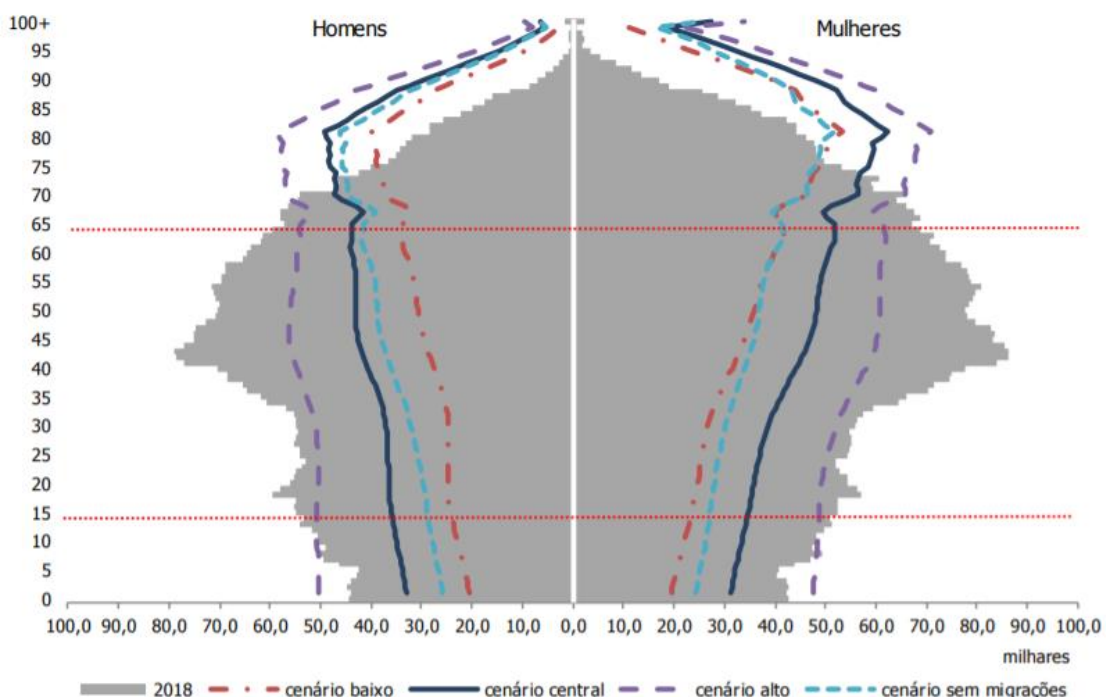


Figura 1: Pirâmide etária em Portugal em 2018 e projeções para 2080 (Instituto Nacional de Estatística, 2020)

1.2. Sintomas depressivos e a depressão

A depressão é uma doença mental que afeta toda a população independentemente da idade. Com mais de 264 milhões de afetados em todo o mundo (Disease et al., 2018) a depressão é uma das principais doenças em todo o mundo (Moussavi et al., 2007) e está associada a uma comorbidade médica aumentada (Vancampfort et al., 2016) e morte prematura (Walker et al., 2015). Esta doença resulta de uma interação complexa de fatores sociais, psicológicos e biológicos (World Health Organization, 2021b). Os sintomas mais comuns de depressão são sentimento de tristeza ou disforia, havendo, no entanto, vários outros sintomas, como a perda de interesse em atividades, alterações do sono e do apetite, sentimentos de culpa e desespero, fadiga, inquietação, problemas de concentração e pensamentos de morte e suicídio (Kanter et al., 2008; World Health Organization, 2021b).

Um episódio depressivo pode afetar uma pessoa a nível pessoal, familiar, social, educacional, ocupacional, e possivelmente noutras áreas importantes de funcionamento (World Health Organization, 2021b).

A depressão crónica é mais comum na terceira idade do que em idades mais jovens (Cole et al., 1999; Comijs et al., 2015), levando os idosos a um risco superior de suicídio quando comparando com idosos não depressivos (Conwell & Brent, 1995; Conwell et al., 2011). A depressão em idosos pode-se apresentar de forma diferente, tendo estes menor probabilidade de sofrerem de sintomas cognitivo-afetivos, incluindo a disforia e sentimentos de culpa (Gallo et al., 1994). No entanto, têm maior probabilidade de sofrerem distúrbios do sono, retardo psicomotor, perda de interesse em viver e desespero relativamente ao futuro (Christensen et al., 1999). Queixas de má memória e fraca capacidade de concentração são também frequentes entre os idosos depressivos. Testes objetivos encontram geralmente uma velocidade de processamento cognitivo mais lenta e disfunção executiva (Butters et al., 2004).

O tratamento tradicional para os sintomas depressivos é considerado inadequado para a maior parte da população idosa, agravado por um aumento

da prevalência de efeitos secundários devido à medicação, polifarmácia e baixa aderência ao tratamento (Birrer & Vemuri, 2004; Fernandez et al., 2007; Zivin & Kales, 2008).

O Inquérito Nacional de Saúde (2014) recolheu informação relativa a sintomas depressivos, estimando-se uma frequência de cerca de 10% para a população portuguesa. Nas faixas etárias mais avançadas, havia uma maior frequência de pessoas com sintomas depressivos, sendo que 38,7% das pessoas com sintomas depressivos estavam reformadas (Instituto Nacional de Estatística, 2016).

A participação regular em atividade física, juntamente com uma dieta equilibrada e a abstenção de utilização do tabaco, contribuem para a redução do risco de doenças não transmissíveis, e melhoram as capacidades físicas e mentais, adiando a necessidade de ficar dependente de terceiros (World Health Organization, 2021a). Pessoas com transtornos depressivos têm uma probabilidade muito menor de atingirem os níveis mínimos recomendados de atividade física em relação a pessoas saudáveis (Schuch et al., 2017), sendo que a baixa atividade física é um fator de risco potencialmente modificável para a depressão (Hallgren et al., 2017). Sabe-se que a atividade física estruturada reduz os sintomas depressivos (Schuch et al., 2018), sendo livre de efeitos adversos quando praticada corretamente (Wright & Cattan, 2009). A atividade física tem também a vantagem adicional de ser gratuita ou de baixo custo.

Um estudo sugere que o aumento da atividade física em mulheres idosas pode reduzir o risco de episódios depressivos futuros (Gudmundsson et al., 2015), e outro mostrou que níveis mais altos de atividade física em adultos predizem uma melhor resposta à terapia cognitiva-comportamental (Hallgren et al., 2016). Uma meta-análise demonstrou que o exercício físico é eficaz na redução dos sintomas depressivos em idosos, com um tamanho de efeito grande de -0,90 (Schuch, Vancampfort, Richards, et al., 2016). Estes mesmos autores verificaram que o exercício feito em grupo com um formato misto de sessões supervisionadas e não supervisionadas, têm maior efeito. No entanto, idosos com outras comorbidades clínicas, obtiveram menores benefícios do exercício físico

(Schuch, Vancampfort, Richards, et al., 2016). No entanto, os autores de uma meta-análise de 2013 sugerem que o exercício físico é apenas moderadamente mais eficaz em adultos que uma intervenção de controlo, com um tamanho de efeito de -0,68 para todos os estudos, e de -0,18 nos estudos de alta qualidade (Cooney et al., 2013).

Alguns estudos demonstram que uma combinação de exercício aeróbio e treino de resistência são o tratamento mais eficaz para idosos (Bridle et al., 2012; Schuch, Vancampfort, Rosenbaum, et al., 2016), enquanto outros concluem que exercícios mente-corpo são mais eficazes (Heinzel et al., 2015).

As diretrizes atuais propõem a utilização do exercício físico para o tratamento da depressão com base em resultados meta-analíticos (Cleare et al., 2015b; Malhi et al., 2015). No entanto, não existe consenso de qual a intensidade adequada para o tratamento e/ou prevenção dos sintomas depressivos, apesar de ser geralmente aceite que a atividade física tem efeitos benéficos na prevenção e/ou tratamento. Um estudo sugere um frequência semanal de 3-5 sessões de 45-60 minutos, com uma intensidade de 50-85% da frequência cardíaca máxima ou por volta de 80% de 1-RM, durante 10 semanas (Rethorst & Trivedi, 2013). Outro estudo sugere 3-4 sessões por semana, com uma duração de 30-40 minutos, a uma intensidade aeróbica baixa ou moderada (Stanton & Reaburn, 2014). Os resultados de uma meta-análise sugerem que exercício moderado a vigoroso têm um efeito superior (Schuch, Vancampfort, Rosenbaum, et al., 2016). Parecendo não existir, portanto, um modelo de atuação único. Vários estudos e revisões sistemáticas demonstraram os efeitos positivos da atividade física como prevenção e/ou terapia para os sintomas depressivos, tanto para pessoas saudáveis (Mortazavi et al., 2012; Tsutsumi et al., 1998) como para os deprimidos (Anderson, 2001; Barbour & Blumenthal, 2005; Cooney et al., 2014; Krogh et al., 2011; Sjösten & Kivelä, 2006). No entanto alguma desta literatura tem sido criticada devido a um baixo rigor metodológico, pequenas amostras e fraca qualidade da análise de dados (Sjösten & Kivelä, 2006). Não existe ainda muita literatura recente focada nos idosos, principalmente estudos longitudinais de longo prazo, sendo os estudos randomizados com um pequeno número de participantes o tipo de literatura mais comum. Alguns destes estudos focam-se

em idosos sofrendo de um tipo de comorbidade ou em idosos saudáveis, deixando de fora algumas variáveis importantes da população idosa em geral, incluindo aqueles que já sofrem de depressão.

2.Objetivos

De modo a contribuir para o esclarecimento da relação a longo prazo entre a atividade física e os sintomas depressivos em idosos, o nosso objetivo é explorar se a prática de AF atribui alguma proteção ou se tem um efeito atenuante contra os sintomas depressivos. Para isso será realizada uma revisão sistemática e meta-análise sobre o efeito da AF no surgimento de sintomas depressivos no idoso.

Foram colocadas as seguintes hipóteses:

H1: Os idosos ativos têm menor probabilidade de apresentar sintomas depressivos comparativamente aos inativos;

H2: Idosos com maiores níveis elevados de AF tem maior a proteção para os sintomas depressivos do que idosos com níveis baixos ou moderados de atividade física.

3.Revisão Sistemática e Meta-Análise

Protective effect of physical activity on depressive symptoms in the elderly. A Systematic Review and Meta-Analysis of observational longitudinal studies

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ABSTRACT

Background: With the increase of life expectancy, there's a bigger focus on improving the quality of life of older people, including mental health. Depression is the most important mental health problem in the elderly, sometimes going by untreated. Physical activity is a non-pharmacologic way of prevention and treatment, together with the effectiveness of medication and therapy. However physical activity isn't currently applied in a consistent way in protocols for the prevention of depressive symptoms.

Aim: This study aims to examine the association between physical activity and depressive symptoms, and if different levels of physical activity have differential effects on depressive symptoms development.

Methods: Potential studies were searched on Pubmed, Scopus and Ebsco between January the 13th and the 27th of 2021. Demographic data, data on physical and depressive symptoms assessment, and odds ratio with 95% confidence intervals were extracted. Random-effects meta-analysis and a sensitivity analysis were conducted, and the potential sources of heterogeneity were explored. Study quality was assessed using the Newcastle-Ottawa Scale.

Results: From 2812 studies found, a total of 12 prospective studies were eligible for data extraction, with a total sample of 3987 participants. Compared to inactive or participants with low levels of physical activity, active elders had lower odds of developing depressive symptoms (OR=0.69, 95% CI=0.59, 0.81, $p<0.01$; $I^2=69.95\%$). Those that practiced moderate levels of physical activity had lower odds of developing depressive symptoms (OR=0.51, 95% CI=0.33, 0.79, $p<0.01$; $I^2=0\%$) than those that practiced high levels (OR=0.43, 95% CI=0.18, 1.04, $p=0.06$; $I^2=75.98\%$). Average study quality was fair (Newcastle-Ottawa Scale score of 5.8).

Conclusions: Evidence supports that physical activity has a protective effect against depressive symptoms in the elderly as the physically active groups report lower odds of depressive symptoms compared to the non-active groups. Moderate levels of physical activity seem to particularly reduce these odds,

however only 3 studies reported PA levels. Our results accentuate the need of policies targeting a physically active style of life for the elderly.

Key-words: Physical exercise, Depression, Older Adults, CES-D, GDS.

INTRODUCTION

Depressive disorders are a mental disease that affects both young and old, with more than 264 million people affected worldwide (Disease et al., 2018), being one of the top causes of disease burden around the globe (Moussavi et al., 2007), associated with increased medical comorbidity (Vancampfort et al., 2016) and premature mortality (Walker et al., 2015).

Clinically significant depressive symptoms affect around 15% of the community-dwelling older adults (Blazer, 2003). Late-life depression is more frequently chronic than in younger age groups (Cole et al., 1999; Comijs et al., 2015), leading to a higher risk of suicide, when comparing with non-depressed elderly (Conwell & Brent, 1995; Conwell et al., 2011). With an increasing elderly population in the whole world, especially in western countries, there is also a higher long-term care costs, due to this specific age group suffering the highest rate of chronic diseases and conditions (Beard et al., 2016). In order to keep aging in a healthy way during a longer lifespan, it's important to know how to prevent and treat conditions that will decrease the quality of life of the elderly, who have an elevated risk of acute and chronic depression compared to younger people (Luppa et al., 2012; Seitz et al., 2010; Volkert et al., 2013).

The treatment for depression is considered inadequate for most of the elderly population, aggravated by an increased prevalence of medication side-effects, polypharmacy and poor adherence to treatment (Birrer & Vemuri, 2004; Fernandez et al., 2007; Zivin & Kales, 2008).

Evidence supports that there's a mutual relation between depression and physical activity. People with major depressive disorder are less likely to meet the recommended weekly physical activity levels compared to healthy people

(Schuch et al., 2017), with the less active elderly being at 83% increased risk of developing depressive symptoms (Paulo et al., 2016). It is known that structured physical activity reduces depressive symptoms of people suffering from depression (Schuch et al., 2018), while being free from adverse effects when done correctly (Wright & Cattani, 2009). Some studies suggest that physical exercise should be included in guidelines as a treatment for depression, based on meta-analytical findings (Cleare et al., 2015a; Malhi et al., 2015). Physical activity also has the added bonus of being free or inexpensive.

Several studies and meta-analysis have shown the positive effects of physical activity as prevention and/or therapy for depressive symptoms for both the healthy (Mortazavi et al., 2012; Tsutsumi et al., 1998) and the already depressed (Anderson, 2001; Barbour & Blumenthal, 2005; Cooney et al., 2014; Krogh et al., 2011; Sjösten & Kivelä, 2006). However, some of this literature has been criticized for poor methodological rigor, small samples and poor quality of data analysis (Sjösten & Kivelä, 2006).

Although there are studies focusing on how the different types of physical exercises affect depressive symptoms, with some defending that a combination of aerobic and resistance training are the most effective treatment for older adults (Bridle et al., 2012; Schuch, Vancampfort, Rosenbaum, et al., 2016), while others concluded that mind-body exercises are more effective (Heinzel et al., 2015), there is a lack of information on how long term physical activity and different levels of physical activity affect depressive symptoms, with some recent reviews focusing on either gender or specific conditions of the elderly, on PA as treatment instead of a form of prevention, or not being completely up to date. There aren't many recent studies focusing solely on the elderly, mainly long-term longitudinal studies, with randomized controlled trials with a low number of participants being the most common studies. Some of these studies focus on older adults that suffer from a single type of comorbidity or that suffer from none at all, leaving some important variables from an elderly population out, including those that already suffer from depressive symptoms.

The aim of this systematic review and meta-analysis is to explore the association between physical activity at baseline and the development of depressive symptoms in the elderly in prospective studies. We also aimed to explore if different levels of physical activity changed the odds of depressive symptoms.

METHODS

This review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) (Page et al., 2021).

Literature search strategy

PubMed, EBSCO (Psychinfo and Psycarticles) and Scopus were searched from the date of their inception up to January 27th, 2021. The search strategy combined the following groups of keywords or similar words and MeSh terms: physical activity; depressive symptoms; elderly; cohort studies. Searches were adapted for each database, and full search terms and strategy can be found in the attachments. A sample search strategy used in PubMed to was: aged, 80 and over[Mesh] OR "late-life"[Title/Abstract] OR older[Title/Abstract] OR elderl*[Title/Abstract] OR senior*[Title/Abstract] OR geriatric*[Title/Abstract] OR retired[Title/Abstract] OR gerontol*[Title/Abstract] AND exercise[MeSH Terms] OR "physical activity"[Title/Abstract] OR "weight training"[Title/Abstract] OR "weight lifting"[Title/Abstract] OR "resistance training"[Title/Abstract] OR "strength training"[Title/Abstract] OR "balance training"[Title/Abstract] OR "aerobic training"[Title/Abstract] OR "anaerobic training"[Title/Abstract] OR yoga[Title/Abstract] OR "tai chi"[Title/Abstract] OR taiji[Title/Abstract] OR qigong[Title/Abstract] OR danc*[Title/Abstract] OR cycl*[Title/Abstract] AND Depression[MeSH Terms] OR "Depressive symptom*" [Title/Abstract] OR "depress*" [Title/Abstract] AND "cohort studies"[MeSH] OR "case-control"[Title/Abstract]. A manual search was also conducted on the references of other systematic reviews.

Eligibility criteria

Articles were eligible if they met the following criteria according to PICOS guideline (participants, intervention, comparison, outcome, study design):

1. Included participants with 60 years old or older, or with an average age of at least 55 years old, with or without established diseases. Both sexes and any ethnicity;
2. Physical activity was measured with either objective (accelerometer and pedometers) or subjective (e.g. self-reported) assessments. Physical activity was defined as any body movement generated by skeletal muscles that results in energy expenditure (Caspersen et al., 1985). Included active and inactive, and/or different levels of PA as comparator;
3. The outcome was depression, including depressive symptoms, , major depressive disorder, or incident depression assessed through common screening instruments or diagnostic interviews;
4. Both observational and intervention studies were considered specifically: Longitudinal observational, retrospective and prospective studies with at least 1 year of follow-up and 100 or more participants at baseline. Randomized controlled trials (RCT) with at least 12 weeks of intervention, a Physical Activity only intervention, and 15 or more participants in each group;
5. Studies written in English, Spanish or Portuguese in any date;
6. The studies reported adjusted or unadjusted OR and 95%CI.

Grey literature, case-studies, editorials, abstracts of conference proceedings, methods papers, reviews, meta-analyses, validation studies, commentaries, cost-effectiveness studies and qualitative studies, protocols and feasibility studies were excluded.

Studies that did not meet the age requirements, the follow-up time or intervention time, that were in other languages, that the outcome was not depression or depressive symptoms, that used genetic and biomolecular markers as the independent variable, that did not have a clear measurement of PA, or

interventions where PA was not the only independent variable (example: Physical activity and nutrition group) were also excluded.

Study selection and data extraction

In the first stage of study selection, four authors (A.J., A.P., C.M., C.L.) screened the titles and abstracts of the articles, to identify those that were compliant with the eligibility criteria. In this phase, disagreements were resolved through discussion. Mediation was done by one of the authors (A.P.). In a second stage, the full text of the potentially eligible articles was reviewed in detail by the author (A.J.), with one reviewer available for consultation (A.P.).

One person (A.J.) extracted the data, including first author, year of publication, study design, country of research, study name, sample size, age and gender of participants, comorbidities, PA assessment, PA categories, PA type, PA intensity, time of exposure, depression assessment, outcome categories, follow-up period, date of baseline data collection, main findings (Odds Ratio (OR) and 95% Confidence Interval (CI)). This data was reviewed and confirmed by a second person (J.T.).

Study quality assessment

For observational studies, the Newcastle-Ottawa Scale was used to assess the quality of the studies. This instrument uses three elements to evaluate the risk of bias: 1) selection of participants (representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure, and demonstration that the outcome of interest was not present at the beginning of the study); 2) comparability (comparability of cohorts on the basis of the design analysis); 3) outcome (adequate assessment of outcome, adequate follow-up time, and adequacy of follow-up). Each study can be awarded a maximum of 1 point for each question of the selection and outcome categories, and a maximum of two points can be given for comparability, for a maximum of 9 points. We

considered scores of 0-3 for low quality, 4-6 for fair quality, and 7-9 for high quality.

Data analysis

Data was analyzed and figures were generated using Open Meta-Analyst (Wallace et al., 2012). A binary random-effects meta-analysis was executed using odds ratio (OR), when both crude and adjusted OR were available, we've used the adjusted ratios. A random-effects model assumes variance both within and between studies, explaining heterogeneity of treatment effects (Borenstein et al., 2010). Because not all studies use the same definitions and measures, the inactive group was considered either the inactive participants of the study, or the ones in the lowest level of PA. The active group, in the studies that used more than one level of PA as comparison, was calculated as the summary of all active groups (eg: moderate and high levels of PA) using the Open Meta-Analyst option to create a binary random-effects meta-analysis, and using the resulting OR as the active group value. A multivariate random-effects sub-analysis was performed for the different levels of PA (frequency x intensity).

Statistical heterogeneity was evaluated using the I^2 statistic (Higgins et al., 2003). I^2 values from 30% to 60% represented a moderate level of heterogeneity, and values above 60% a substantial heterogeneity. A p value of $< 0,1$ defined the presence of heterogeneity.

The following subgroup analyses were performed: levels of PA, depressive symptoms at baseline (for studies that included depressed individuals in main analysis), tools used to measure depressive symptoms, culture (Western, East Asian), PA questionnaire validity, follow-up time (<5 years, ≥ 5 years), sample size (<3000 , ≥ 3000), and population representativeness.

A sensitivity analysis was performed by executing a "leave one-out meta analysis" function one Open Meta-Analyst, and executing a "meta-analysis" while omitting one of each study, to acquire the p-value.

Results

Selected studies

A PRISMA flow diagram is presented in Figure 1. A total of 3987 articles were retrieved from initial search. 1105 were duplicates and were removed. Another 70 were removed for being grey literature. After reading the titles and abstracts, 2562 studies were excluded, and 251 relevant studies were assessed for eligibility. After reading the full texts, a total of 12 articles were selected.

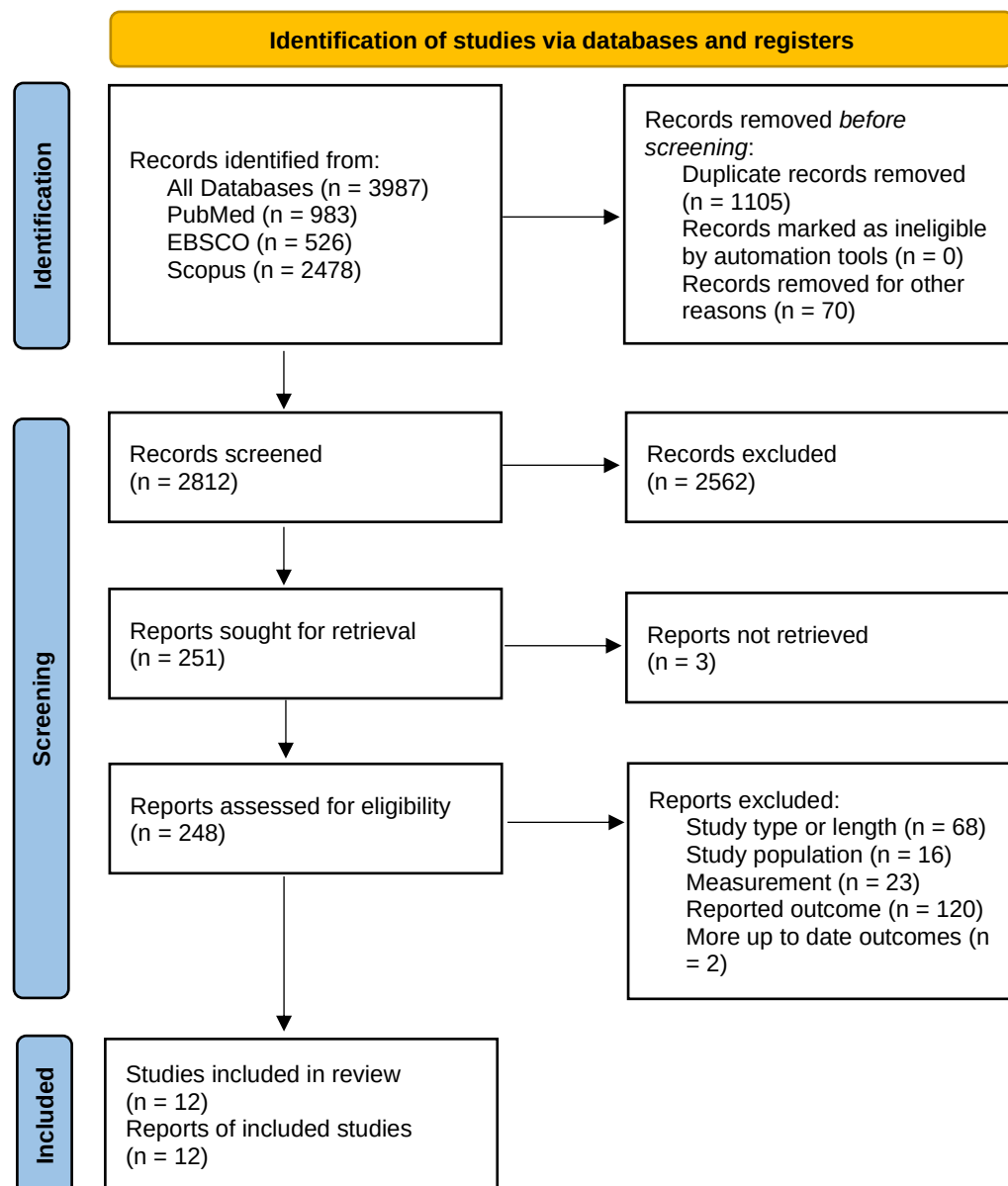


Figure 1: PRISMA Flow diagram of articles included in the present study

Study characteristics

The detailed characteristics from the 12 studies are presented in Table 1. Data from a total population of 38746 participants was included, with the mean age ranging at baseline from 52 (Chang et al., 2016) to 74 years old (Chang et al., 2017).

Table 1: Study Characteristics

Author	Study	Country	Sample Size	Age (years)	Follow-up (years)	PA measure	Depression measure
Chang et al, 2016	Age Gene/Environment Susceptibility (AGES)—Reykjavik Study	Iceland	4140	52	25 ($\pm$ 4)	Interview, hours per week	15-item GDS
Chang et al, 2017	Taiwan Longitudinal Study on Aging, TLSA	Taiwan	2673	74.2	8	Questionnaire, frequency, duration and intensity	CES-D modified 10 item scale
Garcia-Peña et al, 2013	Integrated Study of Depression Among the Elderly	Mexico	7449	70.96	2	Interview, regular exercise	30- item GDS
Giltay et al, 2006	Zutphen Elderly Study	Netherlands	464	70.8	15	Questionnaire, total minutes per week	Zung self-rating depression scale (SDS)

Table 1 (continued)

Author	Study	Country	Sample Size	Age (years)	Follow-up (years)	PA measure	Depression measure
Hamer et al, 2014	English Longitudinal Study of Ageing ELSA	UK	3454	63.7	8	Interview, frequency of participation in vigorous, moderate and light PA	8-item CES-D
Joshi et al, 2016	The New York City Neighborhood and Mental Health in the Elderly Study II	USA	3497	65 - 75	3	Physical Activity Scale for the Elderly (PASE)	Patient Health Questionnaire (PHQ-9)
Kanamori et al, 2018	Japan Gerontological Evaluation Study (JAGES)	Japan	1422	72.5	2	Questionnaire, frequency/pattern of exercise	GDS-15
Mc Dowel et al, 2018	TILDA	Ireland	4556	≥50	3	Short-form International Physical Activity Questionnaire (IPAQ-SF)	CES-D
Park et al, 2015	Yeoncheon Elderly Depression and Dementia (YEDD) Study	South Korea	701	72.24	5	Korean version of the International Physical Activity Questionnaire (IPAQ-SF)	Korean Short Form GDS-K

Table 1 (continued)

Author	Study	Country	Sample Size	Age (years)	Follow-up (years)	PA measure	Depression measure
Pasco et al, 2011	Geelong Osteoporosis Study (GOS)	Australia	547	≥60	4.1	Questionnaire: participation in habitual physical activity throughout the prior year	Structured Clinical Interview for DSM-IVTR Research Version, Non-patient edition (SCIDI/NP)
Roh et al, 2015	Living Profiles of Older People Survey in Korea ((LPOPS))	South Korea	6647	69.8	3	Interview: frequency and duration	Korean 15-item SGDS-K
Smith et al, 2010	Honolulu-Asia Aging Study (HAAS)	USA	3196	71-93	8	Questionnaire, walking distance (city blocks)	11-question version of CES-D

Four studies were conducted in Asia (Chang et al., 2017; Kanamori et al., 2018; Park et al., 2015; Roh et al., 2015), four in Europe (Chang et al., 2016; Giltay et al., 2006; Hamer et al., 2014; McDowell et al., 2018), three in North America (Joshi et al., 2016; Smith et al., 2010), and one in Oceania (Australia) (Pasco et al., 2011).

Depression was the reported outcome in 6 studies (Joshi et al., 2016; Kanamori et al., 2018; McDowell et al., 2018; Park et al., 2015; Pasco et al., 2011; Roh et al., 2015), with depressive symptoms being reported in the other 6 (Chang et al., 2016; Chang et al., 2017; Garcia-Pena et al., 2013; Giltay et al., 2006; Hamer et al., 2014; Smith et al., 2010). A total of 5 different tools were used to evaluate depression and depressive symptoms, with 5 using the Geriatric Depressive Scale (GDS) or an adapted version

of it (Chang et al., 2016; Garcia-Pena et al., 2013; Kanamori et al., 2018; Park et al., 2015; Roh et al., 2015), 4 used the Centers for Epidemiological Studies Depression Scale (CES-D) or a modified version of it (Chang et al., 2017; Hamer et al., 2014; McDowell et al., 2018; Smith et al., 2010), 1 applied a Clinical Interview based on the Diagnostic and Statistical Manual of Mental Disorders ,4th Edition, Text Revision (DSM-IVTR) (Pasco et al., 2011), 1 used the Zung self-rating depression scale (SDS) (Giltay et al., 2006), and another one the Patient Health Questionnaire (PHQ-9) (Joshi et al., 2016).

Physical activity was measured with subjective tools, through questionnaires or questions in an interview. Six of the studies used valid questionnaires (Giltay et al., 2006; Joshi et al., 2016; McDowell et al., 2018; Park et al., 2015; Pasco et al., 2011; Smith et al., 2010), while the other six used unclear or not validated questionnaires (Chang et al., 2016; Chang et al., 2017; Garcia-Pena et al., 2013; Hamer et al., 2014; Kanamori et al., 2018; Roh et al., 2015).

Risk of Bias and applicability

The total score regarding quality assessment of the 12 included articles is shown in Table 2. The scores ranged from 4 to 7, with a mean value of 5,8. The overall classification was of “fair quality”. We considered that all studies had an adequate follow-up period for the outcome to occur, and all the non-exposed cohort was recruited from the same sample than the same one. No study scored in the ascertainment of exposure because all used subjective tools to measure physical activity. The 7 studies that did not score in the assessment of outcome, was due to using “depression” as the outcome, while using scales or questionnaires that are used to measure depressive symptoms.

Meta-Analysis: Main outcome

Physical activity and depressive symptoms

People that committed to doing some physical activity weekly, at least in a moderate amount, were at reduced odds of having depressive symptoms compared to those that were inactive or had a low amount of physical activity (Odds Ratio=0.69, 95% CI=0.59; 0.81, $p<0.01$; $I^2=69.95\%$, Heterogeneity p value <0.01 , $Q=36.60$) (Figure 2).

Given that heterogeneity was found to be of moderate level we have performed several sub-analyses trying to clarify the sources of heterogeneity, namely measures of PA and depressive symptoms, levels of PA, cultural groups, duration of follow-up, sample size, and population representativeness.

Table 2: Newcastle Ottawa Scale

Study	Selection				Comparability	Outcome			Quality Score (Maximum = 9)
	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Demonstration that the current outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Chang et al, 2016	/	*	/	*	**	*	*	/	6
Chang et al, 2017	*	*	/	/	**	*	*	/	6
Garcia-Peña et al, 2013	/	*	/	/	**	*	*	*	6
Giltay et al, 2006	/	*	/	/	**	*	*	*	6
Hamer et al, 2014	*	*	/	*	*	/	*	/	5
Joshi et al, 2016	*	*	/	*	**	/	*	/	6
Kanamori et al, 2018	/	*	/	*	**	/	*	/	5
Mc Dowel et al, 2018	*	*	/	*	*	/	*	*	7
Park et al, 2015	*	*	/	/	*	/	*	/	4
Pasco et al, 2011	/	*	/	*	*	/	*	*	5
Roh et al, 2015	*	*	/	*	*	/	*	*	6
Smith et al, 2010	/	*	/	*	**	*	*	*	7

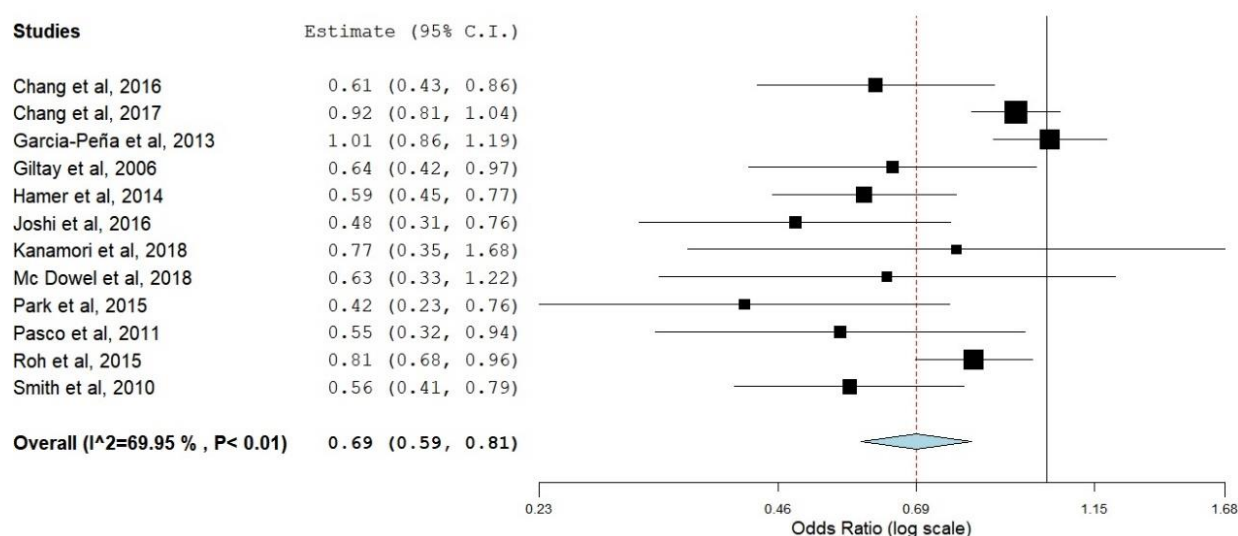


Figure 2: Forest plot for the association between PA and depressive symptoms

Subgroup and sensitivity analysis

The association for levels of PA (time x intensity) as prevention for depressive symptoms was determined in 3 studies (Joshi et al., 2016; McDowell et al., 2018; Park et al., 2015). Moderate levels of PA (time x intensity) were significantly effective at preventing depressive symptoms (OR=0.51, 95% CI=0.33, 0.79, $p<0.01$; $I^2=0\%$, Heterogeneity p value=0.64), while high levels were did not reduced significantly the odds of this outcome (OR=0.43, 95% CI=0.18, 1.04, $p=0.06$; $I^2=75.98\%$, Heterogeneity p value=0.02). The cumulative analysis of the data showed a significant association of moderate and high levels of PA as preventive of depressive symptoms (OR=0.50, 95% CI=0.33, 0.76, $p<0.01$; $I^2=50.99\%$, Heterogeneity p value=0.07) (Figure 3).

Studies that included depressed elders in the analysis showed no effect of PA as prevention/treatment of depressive symptoms (OR=0.67, 95% CI=0.44, 1.04, $p=0.07$; $I^2=68.94\%$, Heterogeneity p value=0.00), while those that did not include depressed people showed a significant effect (OR=0.68, 95% CI=0.56, 0.82, $p<0.01$; $I^2=76.58\%$, Heterogeneity p value=0.01) (Figure 4), nevertheless heterogeneity was high.

Statistically significant protective effects of PA ($p<0.001$) for depressive symptoms were found for cumulative effects and each of depressive symptoms measuring tools, namely CESD-D and GDS (Figure 5), validity of PA questionnaires (Figure 6), both western and east asian groups (Figure 7), duration of follow-up (Figure 8), sample size (Figure 9), and population representativeness (Figure 10). Studies that used valid questionnaires to evaluate PA (OR=0.55, 95% CI=0.46, 0.66, $p<0.01$; $I^2=0\%$, Heterogeneity p value=0.87) did not show significant heterogeneity whether using non-valid questionnaires resulted in a significantly high heterogeneity. Moreover, East Asian studies (OR=0.80, 95% CI=0.65, 0.98, $p=0.03$; $I^2=58.03\%$, Heterogeneity p value=0.07), showed a non-significant heterogeneity, but smaller PA protective effect, compared to the high heterogeneity and larger effect of PA in Western studies (OR=0.64, 95% CI=0.50, $p<0.01$; $I^2=72.72\%$, Heterogeneity p value=0.00).

We performed sensitivity analysis (Figure 11), with every result for each omitted study having a p value <0.001 , showing that preventive effect of PA on depressive symptoms remained.

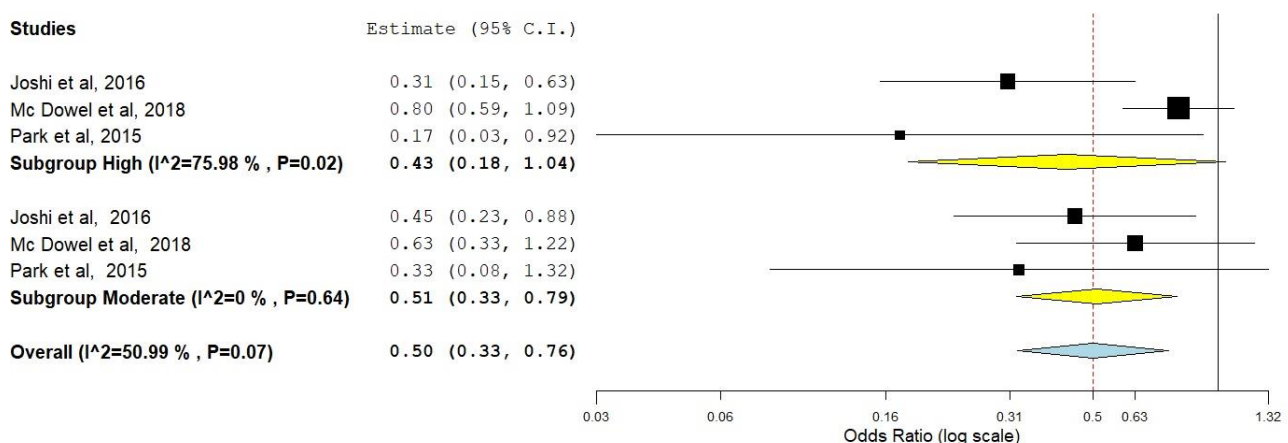


Figure 3: Forest plot for sub-analysis of preventive effect of Levels of PA on depressive symptoms

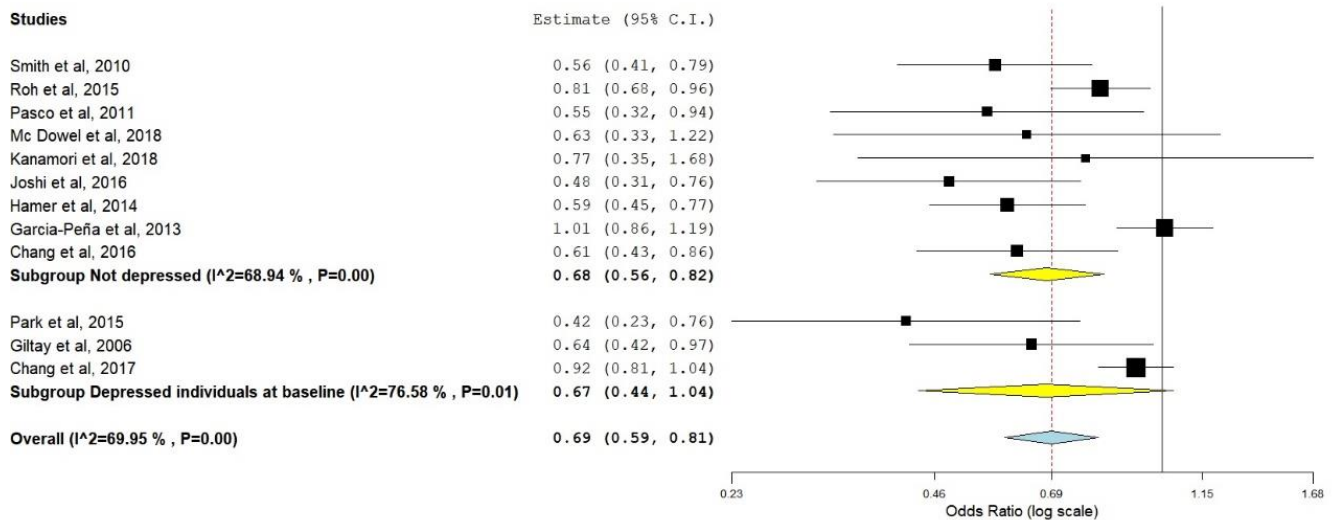


Figure 4: Forest plot for sub-analysis for PA effect on depressive symptoms of non-depressed and mixed depressed/non depressed sample

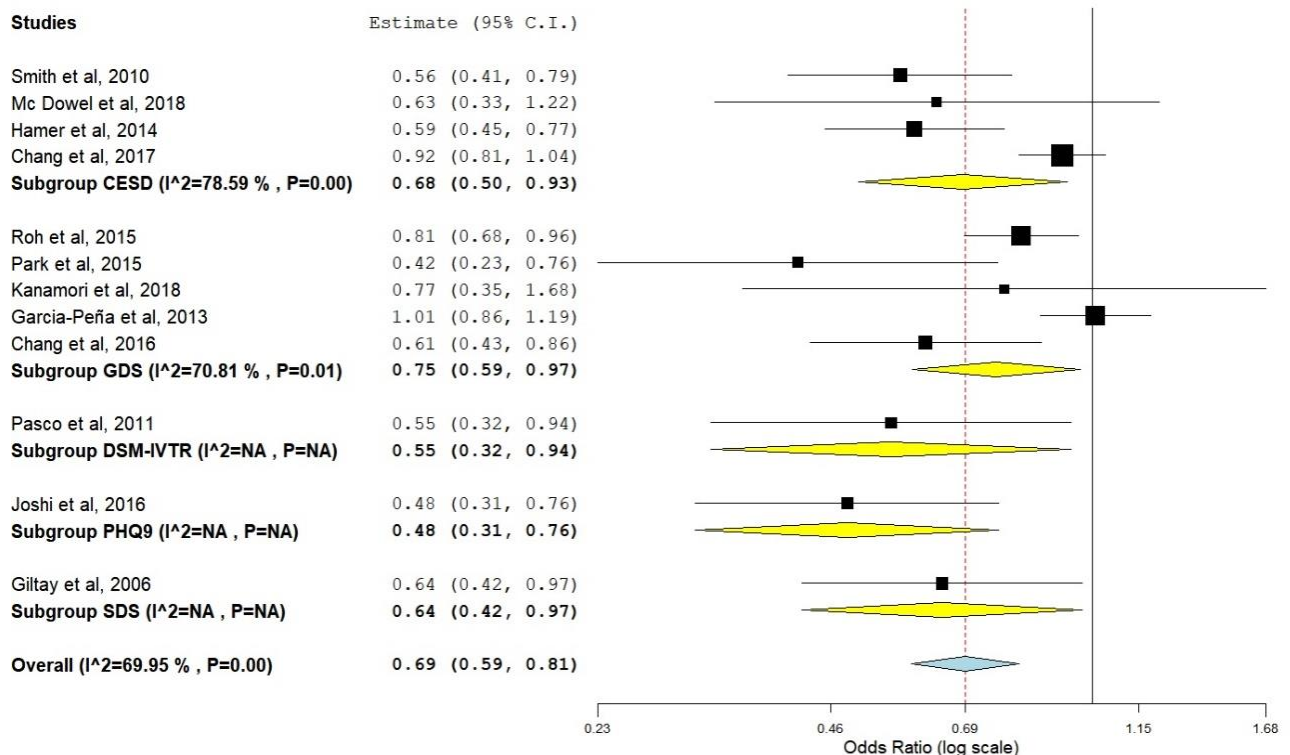


Figure 5: Forest plot for sub-analysis for PA effect on depressive symptoms by depressive symptom measurement tools

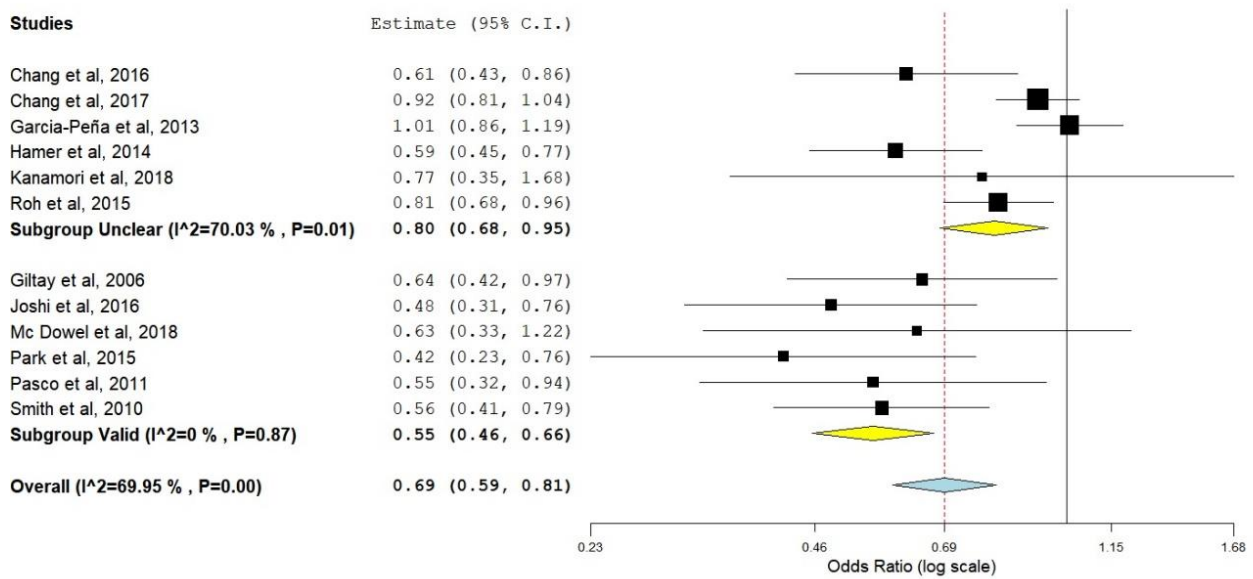


Figure 6: Forest plot for sub-analysis for PA effect on depressive symptoms by questionnaire validity

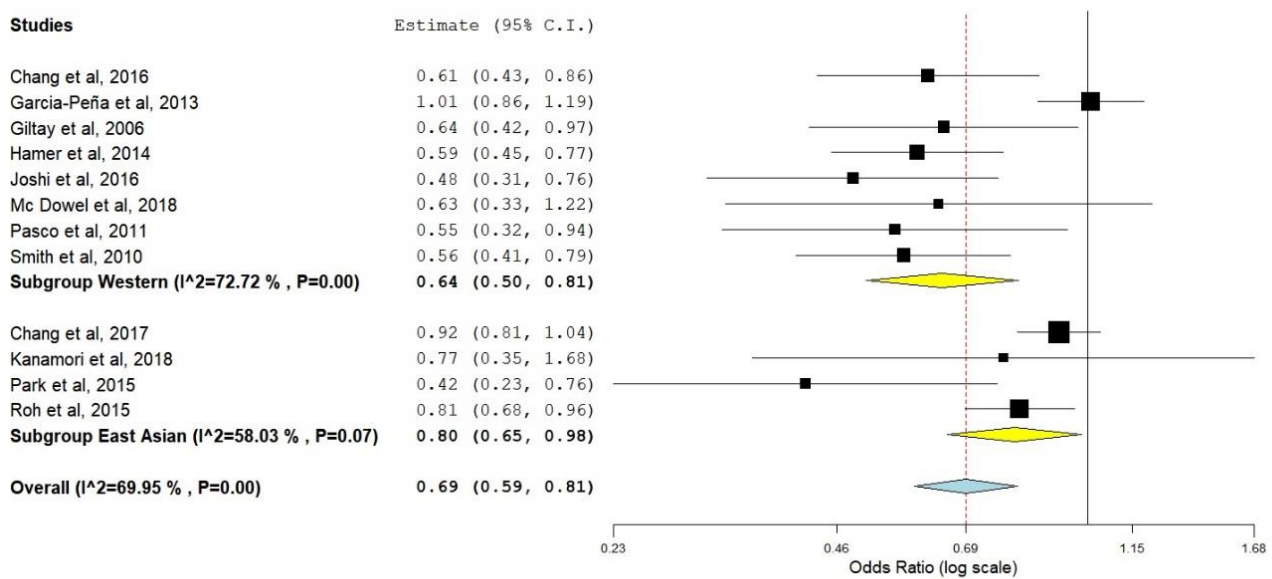


Figure 7: Forest plot for sub-analysis for PA effect on depressive symptoms by culture

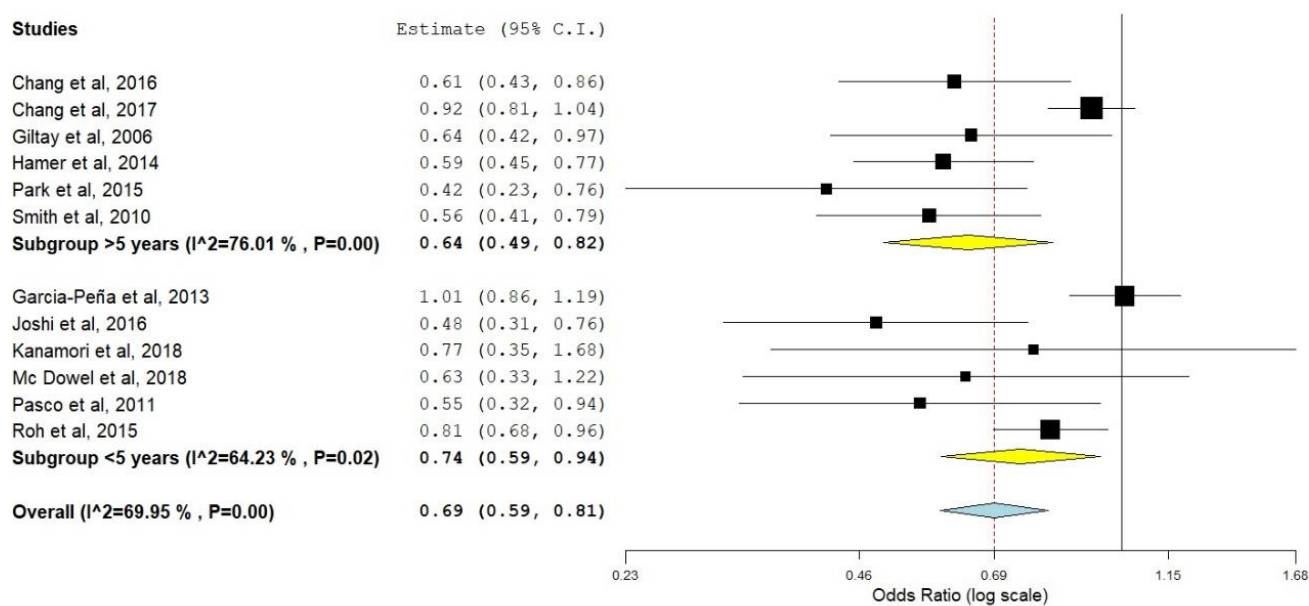


Figure 8: Forest plot for sub-analysis for PA effect on depressive symptoms by follow-up period

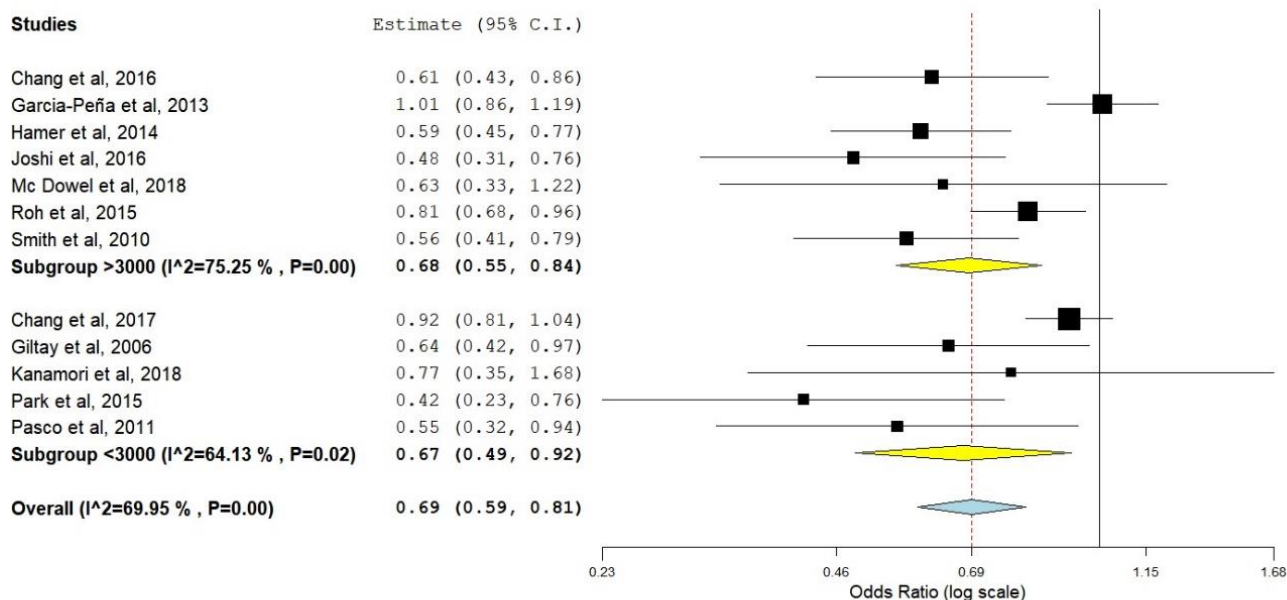


Figure 9: Forest plot for sub-analysis for PA effect on depressive symptoms by sample size

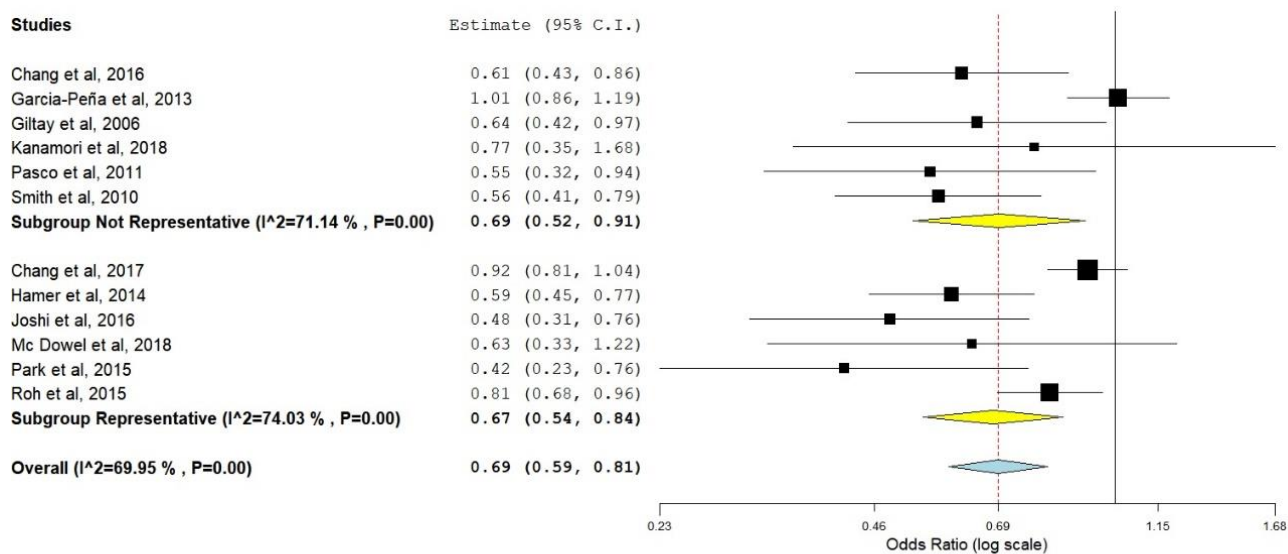


Figure 10: Forest plot for sub-analysis for PA effect on depressive symptoms by population representativeness

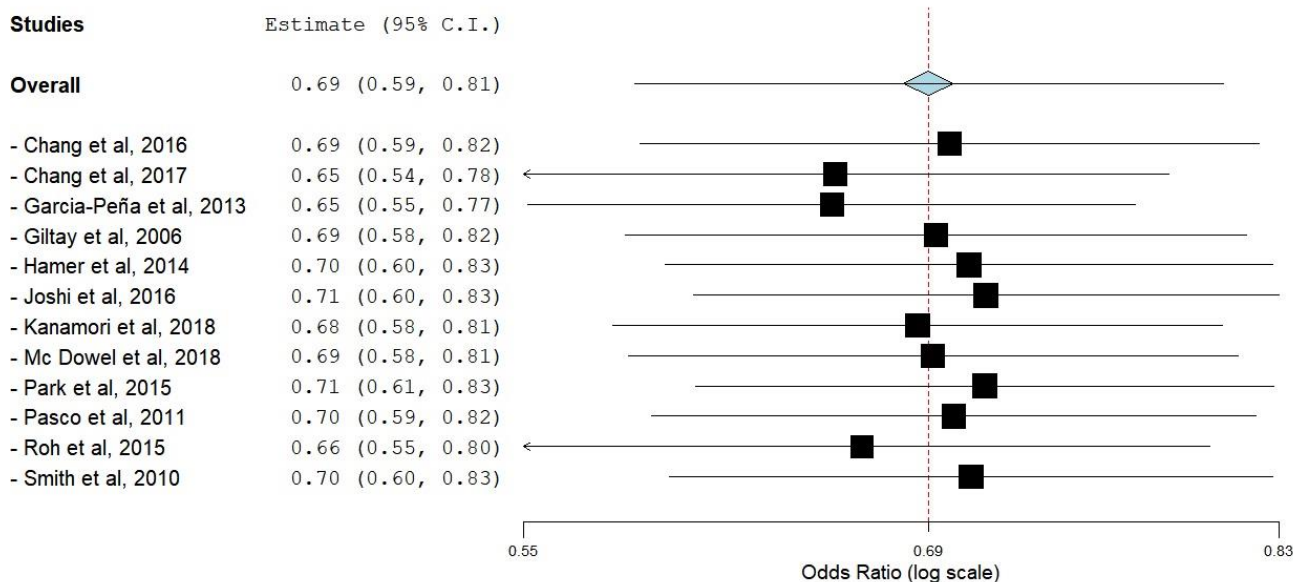


Figure 11: Forest plot for sensitivity analysis

Discussion

The purpose of this systematic review and meta-analysis was to evaluate if participation in regular physical activity protected the elderly against depressive symptoms, and if higher levels of PA, through the combination of weekly frequency and intensity, were more protective. By including 12 studies and a total sample of 38746 elders, we found that being active (ie engaging in regular physical activity) was protective against depressive symptoms, and that moderate levels of physical activity were more effective than higher levels.

Our results are in line with previous systematic reviews that have suggested that physical activity is effective at preventing depression on adults (Dishman et al., 2021; Hu et al., 2020; Mammen & Faulkner, 2013; Schuch et al., 2018; Teychenne et al., 2008), and at reducing depressive symptoms of the elderly (Schuch et al., 2018; Schuch, Vancampfort, Rosenbaum, et al., 2016). However, this review is based on randomized controlled trials, with a more limited follow-up time, with some comparing physical activity to standard depression treatment.

Our study distinguishes itself by comparing a time x intensity combination of PA, which we called as “levels of PA”. A recent meta-analysis has suggested that higher levels of PA offer a protective effect against depression (Schuch et al., 2018), but only comparing to low levels of PA. Our results indicate that moderate levels of PA are more effective as protection against depressive symptoms when compared to high levels of PA, which was unexpected, since previous reviews have suggested that there is an inverse relationship between levels of physical activity and depressive symptoms or risk of depression (Mammen & Faulkner, 2013; Vancampfort et al., 2015). Since the we only had 3 available longitudinal studies for this analysis, and our results suggest a different effect of high levels of PA, we think that more studies are needed to better investigate the long term effects of higher levels of PA on depressive symptoms.

The positive effects of PA on depressive symptoms were high, however heterogeneity was also high. East Asian studies showed non-significant heterogeneity, having more reliable results. Studies with valid PA questionnaires showed inexistent and non-significant heterogeneity, and as such, we suggest

that future studies always use valid questionnaires to measure PA. The use of unclear or invalid methods, that showed very high heterogeneity, can influence the results of the real association between PA and depressive symptoms, therefore close attention should be undertaken when interpreting results from studies with unclear methods of assessing PA.

Results from the depressed elderly at baseline and the moderate level of PA subgroups did not show a significant effect of PA as protective against depressive symptoms. None of the remaining subgroup analysis seem to influence the protective effect of PA on depressive symptoms, therefore reinforcing the importance of PA.

While the results of our study suggest that PA is associated with a decrease in the odds of developing depression in the elderly, and that moderate levels of PA are the most effective, some questions remain unanswered: What is the optimal combination of types of exercise, volumes, frequency, duration and intensity to prevent depressive symptoms in this age group? And future studies need to be developed in order to answer this main question.

Strengths and Limitations

Our systematic review and meta-analysis has some limitations. High heterogeneity was present across the studies, and despite some studies have controlled for common variables uncontrolled variables may have influenced the results.

Most studies analyzed used self-reported questionnaires to measure both PA and depressive symptoms, increasing the risk of recall bias, therefore studies with objective measures of PA are needed. Most studies do not have depressed individuals at baseline or have a separate analysis for depressed or non-depressed, but 3 studies have included both on the same analysis, increasing publication bias.

Also, most studies used different measures of PA, or vague definitions for “active” individuals, with PA being measured at least one year before the outcome in most studies.

The number of participants and the fact that most studies assessed regular PA instead of last week PA can be seen as strengths of this review.

Conclusions

Being active reduces the odds of older adults developing depressive symptoms. Moderate levels of physical activity seem to be more protective than higher levels of PA. Our results accentuate the need of policies targeting the promotion of a physically active lifestyle for the elderly in order to improve mental health, besides the known physical benefits.

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Ethics approval

Not applicable.

4. Conclusão

Após a realização deste estudo, verificamos que os resultados suportam apenas a primeira hipótese colocada, de que os idosos ativos têm menor probabilidade de desenvolver sintomas depressivos, apesar de apresentar heterogeneidade alta. No entanto estudos em populações asiáticas e usando instrumentos validados para avaliação da AF parecem reduzir significativamente esta heterogeneidade pelo que devem ser preferencialmente usados para retirar conclusões nesta área. Sugerimos, assim, que futuros estudos utilizem questionários válidos, de forma a não comprometer a verdadeira associação entre atividade física e sintomas depressivos.

Não verificamos a segunda hipótese de que níveis de atividade física mais altos reduzem mais as probabilidades de os idosos desenvolverem sintomas depressivos, sendo que níveis de atividade física moderada são mais eficazes do que a elevada. Devido aos poucos estudos desta subanálise, é importante conduzir mais investigações com níveis elevados de atividade física, de forma a fortalecer o conhecimento da sua eficácia para proteger contra sintomas depressivos em idosos.

Além do mais, contribuímos para a literatura, comparando os níveis de atividade física semanal, em METs ou através de questionário que combinam intensidade e frequência semanal. Os resultados demonstram que um nível moderado de atividade física consegue ser mais eficaz a combater os sintomas depressivos, relativamente a níveis elevados.

Salientamos, assim, a importância da atividade física na proteção dos idosos contra sintomas depressivos, como também no combate à tendência crescente de doenças mentais, e para que os idosos beneficiem de todos os outros efeitos positivos da atividade física. Deste modo, sugerimos que se dê um maior relevo à atividade física nas políticas de promoção da saúde em geral e da saúde mental, em particular.

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6. Anexos

Search Strategies

PUBMED search strategy:

aged, 80 and over[Mesh] OR "late-life"[Title/Abstract] OR older[Title/Abstract] OR elderl*[Title/Abstract] OR senior*[Title/Abstract] OR geriatric*[Title/Abstract] OR retired[Title/Abstract] OR gerontol*[Title/Abstract]

AND

exercise[MeSH Terms] OR "physical activity"[Title/Abstract] OR "weight training"[Title/Abstract] OR "weight lifting"[Title/Abstract] OR "resistance training"[Title/Abstract] OR "strength training"[Title/Abstract] OR "balance training"[Title/Abstract] OR "aerobic training"[Title/Abstract] OR "anaerobic training"[Title/Abstract] OR yoga[Title/Abstract] OR "tai chi"[Title/Abstract] OR taiji[Title/Abstract] OR qigong[Title/Abstract] OR danc*[Title/Abstract] OR cycl*[Title/Abstract]

AND

Depression[MeSH Terms] OR "Depressive symptom*"[Title/Abstract] OR "depress*"[Title/Abstract]

AND

"cohort studies"[MeSH] OR "case-control"[Title/Abstract]

Ebsco

Nonagenarian* or Octogenarian* or Centenarian* or "late-life" or older or elderl* or senior* or geriatric* or retired or gerontol*

AND "physical exercise" or "physical activity" or "weight training" or "weight lifting" or "resistance training" or "strength training" or "balance training" or "aerobic training" or "anaerobic training" or yoga or "tai chi" or taiji or qigong or danc* or cycl* or "isometric exercise" or "acute exercise" or walk* or run*

AND Depression or "emotional depression" or "Depressive symptom*" or "depress*"

AND "cohort study" or "case control study" or "case-control study" or "longitudinal study" or "follow-up study" or "follow up study" or "prospective study" or "retrospective study"

Scopus results: 2629 (27 janeiro)

Ebsco results: 532

Scopus

(TITLE-ABS-KEY (nonagenarian* OR octogenarian* OR centenarian* OR "late-life" OR older OR elderl* OR senior* OR geriatric* OR retired OR gerontol*) AND TITLE-ABS-KEY ("physical exercise" OR "physical activity" OR "weight training" OR "weight lifting" OR "resistance training" OR "strength

training" OR "balance training" OR "aerobic training" OR "anaerobic training" OR yoga OR "tai chi" OR taiji OR qigong OR danc* OR cycl* OR "isometric exercise" OR run* OR "acute exercise" OR walk*) AND TITLE-ABS-KEY (depression OR "emotional depression" OR "Depressive symptom*" OR "depress*") AND TITLE-ABS-KEY ("cohort study" OR "case control" OR "longitudinal study" OR "follow up study" OR "prospective study" OR "retrospective study"))