

Consequences of physical inactivity in older adults: a systematic review of reviews and meta-analyses

Cunningham, C., ⁽¹⁾ O' Sullivan, R., ^(1,3) Caserotti, P., ⁽²⁾ Tully, M. A. ⁽³⁾

1. Institute of Public Health in Ireland, Forestview, Belfast.
2. University of Southern Denmark, Odense, Denmark.
3. Institute of Mental Health Sciences, School of Health Sciences, Ulster University, UK.

Short running title: Consequences of physical inactivity in older adults

Abstract

Background

Globally, populations are ageing. Typically, physical activity levels decline, and health worsens as we age; however, estimates of the impact of physical inactivity for population health often fail to specifically focus on older adults.

Methods

Multiple databases were searched for systematic reviews and/or meta-analyses of longitudinal observational studies, investigating the relationship between physical activity and any physical or mental health outcome in adults aged ≥ 60 years. Quality of included reviews was assessed using AMSTAR.

Results

Twenty-four systematic reviews and meta-analyses were included. The majority of reviews were of moderate or high methodological quality. Physically active older adults (≥ 60 years) are at a reduced risk of all-cause and cardiovascular mortality, breast and prostate cancer, fractures, recurrent falls, ADL disability and functional limitation and cognitive decline, dementia, Alzheimer's disease and depression. They also experience healthier ageing trajectories, better quality of life and improved cognitive functioning.

Conclusion

This review of reviews provides a comprehensive and systematic overview of epidemiological evidence from previously conducted research to assess the associations of physical activity with physical and mental health outcomes in older adults.

Keywords

ageing, exercise, health, physical activity, systematic review

Introduction

A global decline in fertility rates and increased life expectancy has resulted in the growth in the number and proportion of older adults in the world's population ¹. Increase in life expectancy represents one of the greatest public health successes of the 20th century. The global population aged ≥ 60 years numbered 962 million in 2017. This is expected to double by 2050, when it is projected to reach nearly 2.1 billion ¹. Retaining physical and cognitive function and delaying the onset of illnesses and disability is a major challenge for many in older age. Maintaining physical function, independence and quality of life (QoL) among older adults are public health and economic imperatives ^{2,3}.

Evidence suggests that the age-related declines in functional capacity, QoL, and increased risk of morbidity, disability and mortality may be offset or delayed by the adoption of more

physically active lifestyles. International guidelines recommended that older adults should engage in at least 150 minutes of moderate intensity physical activity per week ^{2,3}. However, physical inactivity has become nearly ubiquitous, with an estimated 31% of the world's population not meeting recommended levels of physical activity ⁴. The prevalence of physical inactivity in older Europeans (≥ 55 years) has been reported to range from 5% in Sweden to 29% in Portugal ⁵.

Physical inactivity is recognised as one of the leading risk factors for overweight, obesity, non-communicable diseases (NCDs) and chronic conditions. It has been identified as the fourth leading risk factor for global mortality (6% of deaths globally) ⁶ and is estimated as being the principal cause for approximately 21-25% of breast and colon cancer burden, and approximately 27% of diabetes and 30% of ischaemic heart disease burden ⁶. Globally, physically inactive lifestyles have been estimated to cost (INT) \$53.8 billion in direct health care costs annually. ^{7,8} However, these population health estimates of the impact of physical inactivity on health often fail to specifically elicit the benefits for older adults, despite the fact that this group may have more to gain from physical activity. Older adults are at a particular risk of leading inactive lifestyles. For many, ageing is defined by rapid declines in levels of physical activity, loss of mobility and functional independence and premature morbidity ⁹. This stage of life represents an important period to promote physical activity to improve functions of daily living and slow progression of disease and disability. Therefore, this umbrella review aims to provide a comprehensive and systematic overview of the epidemiological evidence of the specific consequences of physical inactivity on physical and mental health outcomes in older adults.

Methods

Literature search and inclusion criteria

We conducted a systematic search of six bibliographic databases (Medline, PsycINFO, Embase, SPORTDiscus, CINAHL and EBM reviews) from inception to November 1st 2019, for systematic reviews and/or meta-analyses of longitudinal observational studies, investigating the relationship between physical activity and any physical or mental health outcome in adults aged ≥ 60 years. In addition, we hand-searched the reference lists of eligible articles and other narrative overviews of systematic reviews/meta-analyses.

To be included in this umbrella review, articles had to be reviews including: adults aged ≥ 60 years (studies that enrolled participants < 60 years were excluded, even if the sample mean age was ≥ 60 years); case control or cohort longitudinal studies (retrospective and prospective cohorts) investigating the association of physical activity with any health-related outcome (e.g. cardiovascular disease (CVD), cancer, all-cause mortality, obesity/overweight, diabetes and metabolic diseases). Studies had to report these outcomes as relative risk (RR), odds ratio (OR), hazard ratio (HR) or continuous data and be published in English.

Selection of reviews and methodological quality assessment

Initially titles and abstracts of the identified articles were screened independently by two reviewers (MT and CC). Ineligible reviews were removed and the full text of all potentially relevant articles were retrieved and reviewed for eligibility. Disagreements between reviewers were resolved through consensus. We assessed the methodological quality of the included reviews using the Assessment of Multiple Systematic Reviews (AMSTAR) rating scale ¹⁰. Two reviewers (MT and CC) independently evaluated and rated the included reviews.

Scores on the AMSTAR scale range from 0 to 11, with higher scores indicating greater quality¹⁰. The quality of each review was categorised as low (score range: 0-4), medium (score range: 5-7), or high (score range: 8-11).

Data extraction

Two investigators (MT and CC) independently reviewed all selected full-text articles using a structured data extraction form that included: (1) search strategies; (2) inclusion criteria; (3) physical activity measure(s) used; (4) the effect size(s) reported in the review; (5) study design (case-control, retrospective, prospective); (6) number of studies included and total number of participants; (7) year of publication; (8) average age of participants; (9) main conclusions. We also extracted the study-specific estimated relative risk for health outcome (e.g. RR, OR, HR) along with the 95% confidence interval (CI), and the number of cases for each study by active participants and controls if the authors categorized their data, taking the most active population as the group of interest vs the least active group.

Results

After duplicates were removed, a total of 5,596 citations were identified from searches of electronic databases and review article references. Based on the title and the abstract, 5,311 were excluded, with 285 full text articles retrieved and assessed for eligibility. A PRISMA flowchart of the systematic literature search (Figure 1) is provided. 24 systematic reviews were considered eligible.

Characteristics of included reviews

Table S1 summarises characteristics of the 24 systematic reviews and meta-analyses that included prospective cohort studies, case-control studies and longitudinal study designs. The majority of studies included mixed gender samples conducted in Europe and North America (64%). There was considerable variation in total sample sizes (ranging from n=855 to 2,463,599 participants) and follow-up time (ranging from one year to 40 years). Reviews reported a variety of physical activity measurement techniques, including; accelerometry and doubly-labelled water¹¹; pedometers¹² and self-report and interviewer administered questionnaires¹³

Methodological quality of included reviews

Table S2 summarises the quality assessment of the 24 included systematic reviews and meta-analyses. Nineteen out of 24 reviews (79%) scored ≥ 6 points in the 11 items AMSTAR criteria, indicating that the majority of included systematic reviews and meta-analyses were of a moderate to high methodological quality.

Summary of main findings

Table 1 summarises the main findings for the included reviews and associations between physical activity and physical and mental health outcomes in older adults. The narrative synthesis of findings below describes in detail the association between physical activity and outcomes for chronic disease prevention and risk reduction (all-cause mortality, cardiovascular disease (CVD) risk and CVD mortality, arterial stiffness, cancer prevention and mortality), functional status outcomes (musculoskeletal health, activities of daily living disability, functional limitations, healthy ageing, quality of life and risk of falling) and mental health outcomes (cognitive decline, dementia, Alzheimer's disease and incident depression) in older adults. We have reported all instances where the included reviews reported pooled effect sizes for analyses in older adult populations (Table 1). Table S3 summaries the main findings of included reviews without meta-analysis.

Chronic disease prevention and risk reduction

All-cause mortality: Three systematic reviews with meta-analysis were included^{14,16}. Two reviews were rated as low quality^{14,16} and one was rated as high quality¹⁵ (Table S2). Overall, the reduction in all-cause mortality ranged from 22% in older adults (≥60 years) who performed a low dose of MVPA (1-499 Metabolic Equivalent of Task (MET)-min)¹⁶ to 34% in participants (≥70 years) with high levels of total physical activity¹⁵. A dose-response relationship between physical activity and all-cause mortality was evident^{14,16}. The greatest reduction in risk for older adults was seen in the difference in those doing the least- or no MVPA to some MVPA (1-499 MET-min per week)¹⁶. For those meeting guidelines of 150mins of MVPA per week (500-999 MET-min) mortality was reduced by 28%¹⁶ (Table 1). The reduction in all-cause mortality was also considerably greater in older women compared to older men (32% compared to 14%)¹⁶.

Cardiovascular disease (CVD) risk and CVD mortality: Two reviews assessed the association of physical activity and coronary heart disease (CHD) in older adults,^{16,17} both of which were rated as low quality (Table S2). Batty (2002) concluded that older men benefit from a reduced CHD risk from physical activity but did not conduct a meta-analysis of the n=8 prospective cohort studies (n=19,085 participants) and n=1 case-control study (543 participants). In a separate included study, a significant reduction in the risk of CVD mortality of 25% for low doses of MVPA to 40% for high doses of MVPA compared to those who were inactive was identified in a meta-analysis of n=3 prospective cohort studies (n=66,316 participants)¹⁶ (Table 1).

Arterial stiffness: One low quality systematic review and meta-analysis concluded that physically active individuals had significantly lower arterial stiffness than their sedentary peers (standardized mean difference: -1.017 ± 0.340 , 95% CI: -1.684 to -0.350 , $p = 0.003$)¹⁸.

Cancer prevention and mortality: Three low quality systematic reviews^{16,19,20} (Table S2) assessed the relationship between physical activity and cancer. Physical activity was significantly associated with a 12% reduction in risk of breast cancer when comparing the highest vs the lowest level of activity²⁰. A dose-response analysis revealed that breast cancer risk decreased by 2% for every 25 MET-h/week increment in non-occupational activity, 3% for every 10 MET-h/week increment in recreational activity, and 5% for every 2 h/week increment in moderate plus vigorous recreational activity, respectively²⁰.

Functional status outcomes

Musculoskeletal (MSK) health: One high quality review²¹ assessed the relationship between physical activity and MSK health. The meta-analysis of 22 prospective cohort studies (n=1,235,768 participants; 14,843 fracture cases) reports a 29% reduction in risk of total fractures (hip, wrist- and vertebral fractures) for the highest vs lowest category of physical activity (RR=0.71, 95% CI: 0.63 to 0.80). An analysis of fracture subtypes showed a significant reduction in risk of wrist fracture (28%) (RR=0.72, 95% CI: 0.49 to 0.96) among individuals with the highest category of physical activity compared to those with the lowest category. A sensitivity analysis of 10 studies with participants aged ≥62 years old reported a 31% reduction in relative risk of fracture according to the highest vs lowest category of physical activity (RR=0.69, 95% CI: 0.61 to 0.76)²¹.

Activities of daily living disability: An included meta-analysis of (prospective) longitudinal studies for the prevention of onset and progression of basic activities of daily living (BADL) disability by physical activity²² concluded that there was a 49% reduction in the incidence of BADL disability in older adults (aged ≥50 years) with a medium/high level of physical activity

compared with those with a low physical activity level (OR=0.51, 95% CI: 0.38- to 0.68; n=9 studies; n=17,176 participants; medium quality review). In this review 'disability' was defined as having any difficulty in performing BADL (measured using self-report questionnaires and instruments including the ADL disability scale and the Physical Activities of Daily Living-Help (PADL-H) scale) to distinguish it from 'functional limitations' (defined as restrictions in basic and mental actions). A medium/high physical activity level vs low levels of physical activity also reduced the progression of BADL disability by 45% (OR=0.55, 95% CI: 0.42 to 0.71, p<0.001; n=4 studies, n=8625 participants). The preventative effect was found in both older (≥ 75 years) and younger (<74 years) individuals with and without diseases, and in older adults who already had functional limitations or disability ²².

Functional limitations: A medium quality systematic review for the relationship between physical activity and outcomes of impairment or functional limitation in older adults (>65 years old) was included ²³. Functional outcomes included assessment of functional status decline, impairment or functional status limitations, or disability, measured using self-report questionnaire assessments such as the Health Assessment Questionnaire (HAQ) and the HAQ disability index, or via physical performance tests (e.g. hand-grip strength, mobility activities, walking distance, stair climbing) ²³. Higher levels of physical activity predicted increased functional status in older age. Moderate and high levels of physical activity appeared effective in conferring a ~50% reduction in risk of functional limitations or disability (average odds ratio ~0.5). In higher-level functions (such as walking a distance or climbing stairs) the relative risk or odds of functional decline or limitation was significantly reduced in those more physically active (~50% reduction in the high activity group). Longitudinal data from 6 studies (n=3918) also reports that those exercising at high levels in middle age (e.g. jogging regularly) postponed a disability or functional limitation and prolonged disability-free life (13.2 years mean follow-up time) ²³.

Healthy ageing: One high quality systematic review with meta-analysis was included ²⁴. Healthy ageing is defined as the process of developing and maintaining the functional ability that enables wellbeing in older age ²⁵. In the included review, healthy ageing was used as a collective term whereby a number of outcomes were grouped, for example; living to a specific age or during follow up; health status (measures included the patient health questionnaire (PHQ) and the self-rated life satisfaction questionnaire); physical performance; diseases (assessed via medical history questionnaire) ²⁴. A sensitivity analysis with participants aged ≥ 65 years of age at baseline showed a significant positive association between physical activity and healthy ageing (ES=1.14, 95% CI: 1.07 to 1.22, p<0.001).

Quality of Life (QoL): A medium quality systematic review for the association between physical activity and QoL in older adults was included ¹². Measures of QoL in this review included the World Health Organisation QoL-100 (WHO QoL-100), Health Related QoL (HR-QoL), Short Form-36 (SF-36), and the Satisfaction with Life Scale (SWLS) ¹². Physical activity had a consistent positive association with a number of QoL domains; functional capacity; general QoL; autonomy; past, present and future activities; death and dying; intimacy; mental health; vitality; and psychological ¹². However, only four of the 31 included studies were prospective cohort studies.

Risk of falling: A high quality systematic review and meta-analysis of population-based and longitudinal studies for the association of physical activity and risk of falling in community dwelling older adults concluded that the risk of being a recurrent faller (two or more self-reported falls over the follow-up period of 12-36 months) was 39% higher in those older

adults with the lowest levels of physical activity. However, the association between any fall and physical activity level was inconclusive (Table 1)²⁶.

Mental health outcomes

Cognitive decline: Three medium quality^{23,27,28} and three high quality systematic reviews with meta-analysis for the relationship between physical activity and cognitive decline were included^{11,29,30}. Common diagnostic criteria included use of the Modified Mental State Examination (MMSE) and clinical evaluation, Cognitive Abilities Screening Instrument (CASI) and the Mental State Questionnaire (MSQ). The reduction in risk of cognitive decline ranged from a 26% reduction from moderate levels of physical activity compared with no/lowest levels of physical activity²⁹ to a 38% reduction in those who performed a high level of physical activity³⁰. Low-to-moderate level of activity showed a significant protection (35% reduction in RR) against cognitive impairment³⁰. Furthermore, an analysis of participants aged ≥ 65 years reported a reduction in the risk of cognitive decline of 36% by staying highly physically active²⁹. The collective evidence from a number of the included reviews suggests that physical activity may help to improve cognitive function and, consequently, delay the progression of cognitive impairment in older adults^{23,27,28}

Dementia: Two high quality reviews with meta-analysis^{11,29}, two medium quality systematic literature reviews^{23,31} and one medium quality systematic review with meta-analysis were included³². Common diagnostic criteria included the Mini Mental State Examination (3MS), MMSE, the Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification of Diseases (ICD). The evidence suggests that habitual physical activity reduces the subsequent risk of dementia in healthy older adults²³. Higher levels of physical activity are associated with a 14%¹¹ to 21%²⁹ reduction in the risk of dementia. Higher intensity of physical activity reduced all-cause dementia risk by 28%³². An analysis of moderate intensity physical activity reported a risk reduction of 24%²⁹. Observations of the protective effect of physical activity were consistent in comparative analysis of studies with a follow up period greater- and less than 5 years, and with sample sizes greater- and less than 1000 participants. There is a significant risk reduction effect (26%) of physical activity for people beyond the age of 65 developing all-cause dementia while insignificant for people below the age of 65 years²⁹ (Table 1). Both moderate and high levels of physical activity reduced risk of vascular dementia in older adults (Table 1)³².

Alzheimer's disease (AD): Three medium^{33,34,32} and two high-quality^{29,35} reviews with meta-analysis were included. Studies included in the reviews represented a global distribution of older adult populations. Diagnostic criteria included the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA), MMSE and the DSM. The relative risk reduction of AD with physical activity ranged from 32%³² to 42%³⁴ in participants with higher levels of physical activity compared to those with lower levels. The findings indicate that physical activity may be an important protective factor against AD in older adults. For those older adults (~70-80 years on average) meeting international physical activity recommendations of ≥ 150 min/week of MVPA, risk of development of AD (approximately 5 or more years later) was reduced by 40%³⁵. Furthermore, the estimated Population Attributable Risk percentage (PAR%) was particularly high for lower vs higher physical activity level (31.9%)³⁴.

Incident depression: One high quality meta-analysis was included³⁶. The study evaluated participants who were free of depression or depressive symptoms at baseline, and evaluated incident depression as the outcome, including (among other measures) increased depressive

symptoms through established cut-offs of depression screening instruments, or based on self-report or physician diagnosis of depression³⁶. Participants with higher physical activity levels were at reduced odds (17% reduction in risk) of incident depression when compared with people with lower physical activity levels. Completing 150 minutes per week of MVPA was protective for incident depression in adjusted OR and adjusted RR analyses. A sensitivity analysis of data from cohorts of older participants with higher physical activity levels reported a 21% reduction in incident depression when compared with people with lower physical activity levels in adjusted OR and adjusted RR analyses (30% reduction in RR).

Discussion

This umbrella review has identified that physically active older adults (≥ 60 years) are at a reduced risk of all-cause and cardiovascular mortality (low quality evidence); breast and prostate cancer (low quality evidence); fractures (high quality evidence); ADL disability, functional limitation (medium quality evidence) and risk of falling (high quality evidence); and cognitive decline, dementia, Alzheimer's disease and depression (high quality evidence). They also experience healthier ageing trajectories (high quality evidence); better quality of life (medium quality evidence) and improved cognitive functioning (medium quality evidence). Emerging evidence demonstrates that there are health benefits of physical activity for older adults below levels that are currently recommended.

The findings provide compelling evidence of positive associations between physical activity and lower rates of morbidity and mortality in older adults. This evidence is consistent with the evidence for the health benefits of physical activity in younger age groups². Typically, the analyses in the included reviews compared the highest and lowest categories of physical activity. However, evidence in the included reviews demonstrates emerging evidence that there are protective effects for older adults who participate in a level of activity well below current recommendations. A weekly dose of MVPA corresponding to 75 min per week has been shown to be associated with a reduction in all-cause mortality by 22%¹⁶. This level of physical activity represents a reasonable primary target for older inactive adults. Starting with small increases in physical activity may encourage some older adults, who were previously physically inactive or chronically ill, to progressively incorporate more activity into their daily routine.

Fractures, which are often a consequence of falls, are one of the most serious musculoskeletal problems seen in the older adult population³⁷. Physical activity has been identified as a lifestyle factor that may influence the risk of falls and fractures in adults through maintaining mobility, physical functioning, bone mineral density, muscle strength, and balance³⁸. The risk of recurrent falls was reduced in older adults with higher levels of physical activity, and although the association of falling (any fall) with physical activity was inconclusive²⁶, other reviews evaluating the association of usual physical activity with the risk of falling in the general population have suggested a general decrease in risk³⁸, and a strong positive relationship between fall-related efficacy (perceived self-confidence at avoiding falls during essential, relatively non-hazardous activities) and activity¹³. Increasing levels of physical activity within an appropriate range has been shown to reduce the risk of hip fractures in general population studies of men and women^{38,39}. Engaging in higher levels of physical activity also reduced the risk of total fractures by 29% and significantly reduced the risk of wrist fracture by 28%²¹.

Maintaining functional status is an important part of active ageing and reducing age-related morbidity. The evidence in this review suggests that greater physical activity predicts higher functional status in older age. Physical activity reduces the age-related decline in functional capacity and maintains muscle strength and mass among adults aged 65-85 years²³. The risk of developing functional limitations or BADL disability^{22,23} and the progression of BADL disability was reduced by participation in physical activity²². Emerging evidence also highlights the positive impact of physical activity on the healthy ageing process, by improving QoL¹² and increasing the odds of maintaining well-being in older age²⁴.

Finally, as the global population ages, the number of people living with cognitive impairment or dementia is expected to increase dramatically, with some estimates suggesting that the number of people living with dementia will triple from 50 million to 152 million by 2050⁴⁰. Changes in physical function often occur with cognitive losses, which can then accelerate the risk of disability and need for care. Evidence contained within this review suggests that all levels of physical activity confer significant and consistent protection against the occurrence of cognitive decline in people without dementia^{11,29,30}. Growing evidence also reports that physical activity can improve cognitive function and, consequently, delay the progression of cognitive impairment in older adults^{23,27,28,41}

Strengths and limitations

We employed strict criteria in the final selection of searched literature and implemented procedures to ensure high-quality implementation of the methodology. Two independent investigators followed an a priori protocol to perform the data extraction, data analysis and quality assessment of the methods of included systematic reviews and meta-analyses.

The inclusion of only longitudinal study designs (most often in the form of cohort studies) is a strength of this review, enabling an evaluation the relationship between physical activity, risk factors and the development of disease over time. This allows some inference regarding causation from the evidence, however reverse causality cannot be completely ruled out.

This review has several limitations: 'gray' literature was not included and the search was limited to journal articles published in English. We also did not meta-analyse data from individual studies, therefore there may be some overlap in the evidence presented in different reviews. We did however report effect sizes that reflected the greatest control for potential confounders from each meta-analysis. It is also worth noting that the main methodological limitation of the majority of studies in the included reviews was the use of subjective methods for physical activity assessment. This heterogeneity may have led to some underestimation or exaggeration of the observed relationships, although the majority of studies reported the use of appropriate methods to assess publication bias and adjust for heterogeneity in analysis.

Implications for research and policy

For those older adults meeting international physical activity recommendations there is a significant reduction in risk of all-cause mortality, Alzheimer's disease and incident depression. The included reviews also consistently report that the greatest risk reduction across health outcomes comes with higher levels and intensities of physical activity.

This review also contains emerging meta-analytic evidence that moderate intensity physical activity may be sufficient for reducing the risk of all-cause dementia in older adults²⁹ and that some of the protective benefits of physical activity for older adults are accrued well below current guidelines for health¹⁶, both areas which require further investigation to potentially support a greater number of older adults to become more physically active. A number of included reviews also advocate the need for further research to demonstrate the

relationships between health outcomes and habitual physical activity with objective measurement of physical activity. An emerging area requiring further research is the influence sedentary behaviour exerts on health in older adults, independent of physical activity. Physical activity plays a key role in the 'compression of morbidity' decreasing the time spent in ill-health as people age and ensuring that an increase in life expectancy is also an increase in life-time spent in good health. To make active and healthy ageing a reality by keeping older adults healthy, independent and fulfilled, it is imperative that policies and actions in addressing physical inactivity in older adults reflect this emerging evidence.

Perspectives

This review highlights that regular physical activity concurrently reduces the risk of developing multiple physical and mental health outcomes in older adults. The reported emerging meta-analytic evidence highlights the protective effect of regular physical activity against cognitive decline and the development of dementia and Alzheimer's disease.

Promising initiatives, including Exercise is Medicine ⁴² and Moving Medicine ⁴³ are working towards the integration of this emerging evidence base into routine clinical practice for the prevention and treatment of many medical conditions that are common in older adults.

This review highlights that those older adults who are physically active experience healthier ageing trajectories. However, evidence shows that many older adults are not engaging in sufficient levels of physical activity to attain these health benefits ⁵. This stage of life represents an important period to promote physical activity to improve functions of daily living and slow progression of disease and disability. To unlock the benefits of physical activity it is imperative that policy and practice supports older adults to achieve the recommended levels of physical activity ⁴⁴.

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Table 1: Relationship between physical activity on health outcomes: results from umbrella reviews with meta-analyses

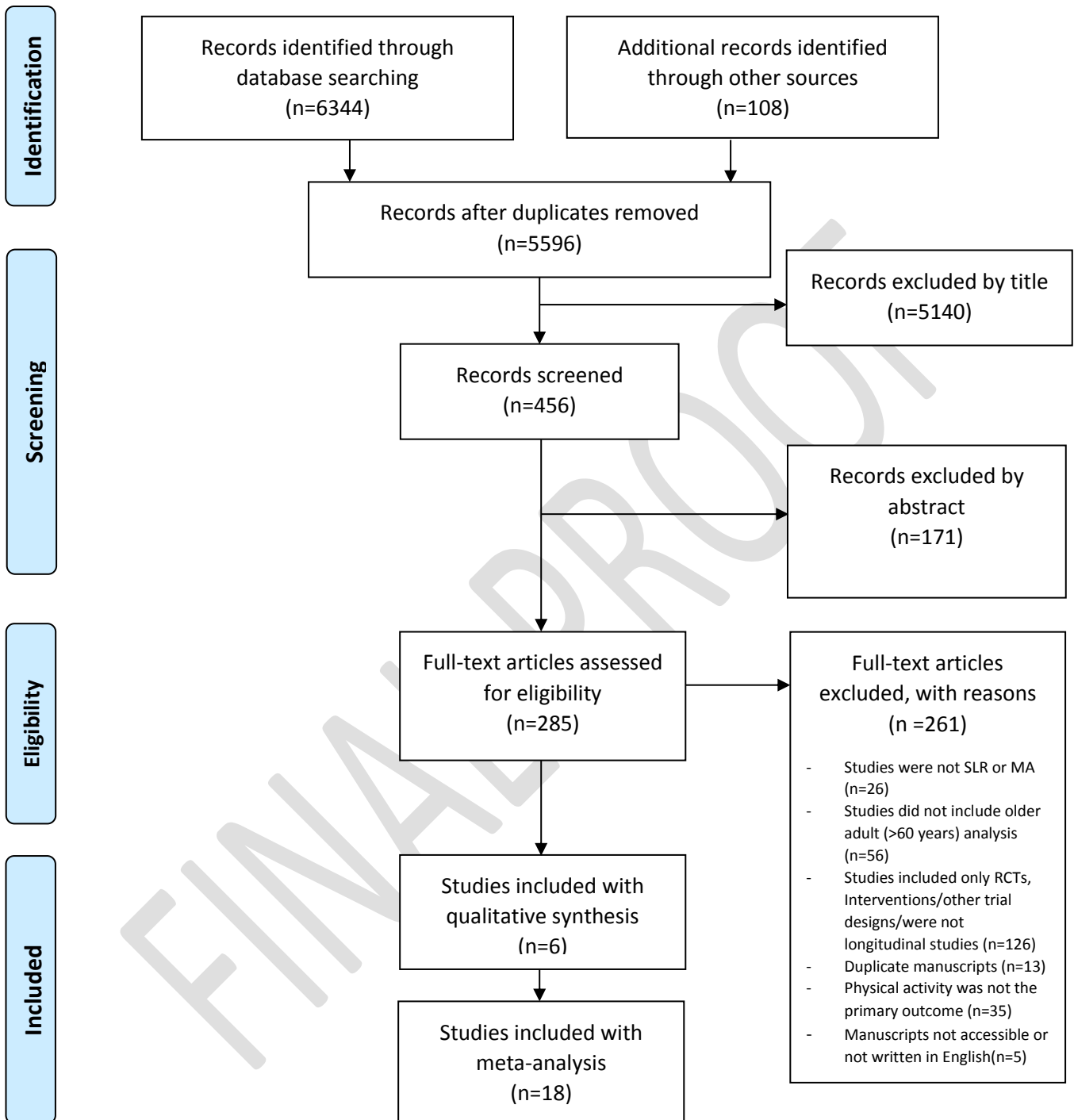
Author, Date: sub-divided by health outcome	Number of studies included in analysis of older adults	Total population of studies included in analysis of older adults	Comparison	Effect Size (RR unless stated)	95% CIs	Heterogeneity (I ²)
Chronic disease prevention and risk reduction						
All-cause Mortality						
Hupin et al., 2015	9	122,417	low dose of MVPA (1–499 MET-min per week) vs non-active (0 MET-min per week)	0.78	0.71 to 0.87	33%
			Meeting current recommendations of 150 min of MVPA (500–999 MET-min) per week vs non-active (0 MET-min per week)	0.72	0.65 to 0.80	44%
			MVPA well above current recommendations (≥1000 MET-min per week) vs non-active (0 MET-min per week)	0.65	0.61 to 0.70	20%
Hupin et al., 2015 <i>Cardiovascular disease mortality</i>	3	66,316	low dose of MVPA (1–499 MET-min per week) vs non-active (0 MET-min per week)	0.75	0.68 to 0.84	NS
			Meeting current recommendations of 150 min of MVPA (500–999 MET-min) per week vs non-active (0 MET-min per week)	0.74	0.67 to 0.82	NS
			MVPA well above current recommendations (≥1000 MET-min per week) vs non-active (0 MET-min per week)	0.60	0.53 to 0.69	NS
Hupin et al., 2015 <i>All-cancer mortality</i>	2	60,813	low dose of MVPA (1–499 MET-min per week) vs non-active (0 MET-min per week)	0.89	0.80 to 0.99	NS
			Meeting current recommendations of 150 min of MVPA (500–999 MET-min) per week vs non-active (0 MET-min per week)	0.84	0.75 to 0.93	NS
			MVPA well above current recommendations (≥1000 MET-min per week) vs non-active (0 MET-min per week)	0.69	0.59 to 0.80	NS
Löllgen et al., 2009	3	4,619	Moderate level of PA vs Lowest level of PA	0.78	0.59 to 0.96	NS
			Highest PA vs Lowest PA	0.68	0.56 to 0.82	NS
Samitz et al., 2011	80	1,338,143	(Overall) Highest PA vs lowest PA (total activity)	0.65	0.60 to 0.71	79.40%
	4	NS	(≥70yrs) Highest PA vs lowest PA (total activity)	0.66	0.50 to 0.88	33.5%

Cardiovascular disease: Arterial stiffness						
Park et al., 2017	6	2,932	Active vs non-active	Hedge's g=-1.02	1.68 to 0.35	96%
Cancer: Breast cancer						
Wu et al., 2013	31	2,463,599/63,786 cases	Active vs non-active	0.88	0.85 to 0.91	29.50%
	11	620,882	Active vs non-active (Random effect model) (participants aged >50 years)	0.83	0.76 to 0.91	42.2%
			Active vs non-active (Fixed effect model) (participants aged >50 years)	0.88	0.83 to 0.92	42.2%
Cancer: Prostate cancer						
Liu et al., 2011	58	2,120,204	Overall: High PA vs low PA	0.90	0.84 to 0.95	61.65%
	39	NS	High PA vs low PA (45 - 65years)	0.91	0.86 to 0.97	64.33%
	17	NS	High PA vs low PA (≥65years)	1	0.84 to 1.19	56.82%
Functional status						
Physical function: Healthy ageing						
Daskalopoulou et al., 2017	17	NS	Active vs non-active (Main analysis)	E.S=1.27 (ADJ)	1.11 to 1.45	81%
	8	NS	Active vs non-active (≥65 years)	1.14	1.07 to 1.22	NS
Physical function: Activities of Daily Living Disability						
Tak et al., 2013	9	17,000	Medium/ high vs low PA (Incidence of BADL-disability)	OR: 0.51	0.38 to 0.68	NS
	4	8,625	Medium/ high vs low PA (progression of BADL-disability)	OR: 0.55	0.42 to 0.71	NS
Physical function: Risk of falling						
Soares et al., 2018	4	7,927	Highest vs lowest levels of PA (risk of falling)	1.05	0.93 to -1.18	70%
	2	2,240	Highest vs lowest levels of PA (risk of recurrent falling)	1.39	1.17 to 1.65	0%
Mental health outcomes						
Cognitive decline						
Sofi et al., 2011	15	33,816	High level of physical activity	HR: 0.62	0.54 to 0.70	
			Low to moderate level of physical activity	HR: 0.65	0.57 to 0.75	
Cognitive decline & Dementia						
Blondell et al., 2014 <i>Cognitive decline</i>	17	48,821	High vs lower levels of PA	0.65	0.55 to 0.76	52%
Blondell et al., 2014 <i>Dementia</i>	21	40,348	High vs lower levels of PA	0.86	0.76 to 0.97	66%
Cognitive decline, all-cause dementia, Alzheimer's disease, vascular dementia						
Guure et al., 2017	32	46,909	High PA vs low PA	OR: 0.79	0.69, 0.88	τ=0.05

<i>All-cause dementia</i>	15	20,771	Moderate PA vs Low PA	OR: 0.76	0.61, 0.94	$\tau=0.06$
	24	30,980	High PA vs low PA (participants ≥ 65 years)	OR: 0.74	0.63 to 0.83	$\tau=0.06$
Guure et al., 2017 <i>Alzheimer's disease</i>	21	32,057	High PA vs low PA	OR: 0.62	0.49 to 0.75	$\tau=0.12$
	12	15,326	Moderate PA vs Low PA	OR: 0.71	0.56 to 0.89	$\tau=0.04$
Guure et al., 2017 <i>Vascular Dementia</i>	8	NS	High PA vs low PA	OR: 0.92	0.62 to 1.30	NS
Guure et al., 2017 <i>Cognitive Decline</i>	22	38,343	High PA vs low PA	OR: 0.67	0.55, 0.78	$\tau=0.06$
	11	27,596	Moderate Pa vs Low PA	OR: 0.74	0.60, 0.90	$\tau=0.04$
	16	21,342	High PA vs low PA (participants ≥ 65 years)	OR: 0.64	0.50 to 0.77	$\tau=0.40$
Lee, J. 2019 <i>All-cause dementia</i>	3	3,117	Vigorous PA vs Low intensity PA	OR: 0.72	0.59 to 0.86	43.51%
Lee, J. 2019 <i>Vascular dementia</i>	8	31,372	Highest PA vs lowest levels of PA	OR: 0.54	0.42 to 0.69	32.47%
	5	22,111	Moderate PA vs lowest levels of PA	OR: 0.72	0.54 to 0.97	44.68%
Cognitive impairment/decline, Dementia and Alzheimer's disease						
Beydoun et al., 2014 <i>Alzheimer's disease</i>	8	17,595	High Pa vs Low PA	0.58	0.49 to 0.70	NS
Alzheimer's disease						
Beckett et al., 2015	9	20,326	Active vs inactive	0.61	0.52 to 0.73	NS
Santos-Lozano, A. et al., 2016	10	23,345	More active vs less active	0.65	0.56 to 0.74	NS
	5	10,615	≥ 150 min/wk of MVPA	0.60	0.51 to 0.71	NS
Lee, J. 2019	12	40,994	Highest PA vs lowest levels of PA	OR: 0.72	0.66 to 0.80	69.80%
	12	37,165	Moderate PA vs lowest levels of PA	OR: 0.68	0.60 to 0.77	67.60%
Incident depression						
Schuch, 2018	36	266,939	High PA vs low PA (overall)	OR: 0.83 (ADJ)	0.79 to 0.88	NS
	4	NS	≥ 150 min/wk of MVPA	OR: 0.78 (ADJ)	0.62 to 0.99	NS
				RR/HR: 0.69 (ADJ)	0.49 to 0.95	NS
	16	NS	High PA vs low PA (participants ≥ 65 years)	OR: 0.79 (ADJ)	0.73 to 0.87	NS
	7	NS	High PA vs low PA (participants ≥ 65 years)	RR/HR: 0.70 (ADJ)	0.57 to 0.88	NS
Musculoskeletal health: Osteoporotic fractures						
Qu, et al., 2014	22	1,235,768	High PA Vs low PA (Total fractures)	0.71	0.63 to 0.80	74.20%
	13	NS	High PA Vs low PA (Hip fracture)	0.61	0.54 to 0.69	50.30%
	2	NS	High PA Vs low PA (Wrist fracture)	0.72	0.49 to 0.96	45.50%
	10	NS	High PA Vs low PA (Fracture risk)	0.69	0.61 to 0.76	28.7%

ES: Effect Size; NS: Not stated; PA: Physical Activity; MVPA: Moderate to Vigorous Physical Activity; ADJ: Adjusted

Figure 1. PRISMA flow diagram of systematic search of systematic reviews and meta-analyses for the association of physical activity and physical and mental health outcomes in older adults



Supplementary files

Table S1: Characteristics of included reviews

Author, Date: sub-divided by health outcome	Number of studies in analysis of older adults (Total number of studies included in the review)	Total population included in longitudinal, prospective cohort and case control studies	Age of participants in eligible studies	Gender of participants in eligible studies	Length of follow-up (Years)	Physical activity measurement
Chronic disease prevention and risk reduction						
All-cause Mortality						
Hupin et al, 2015	9 (9)	122 417	Range= 60 years and over. Mean age= 72.9 years (± 4.5). Ranging from 60 to 101.	60.2% female	Mean= 9.8 (± 2.7)	NS
Löllgen et al, 2009	3 (38)	271 000	65 years and over	Mixed	Range= 4 to 40 (Median= 12)	NS
Samitz et al, 2011	4 (80)	1 338 143	70 years and over Median cohort age at baseline= 56.4 years	Mixed	Range= 4 to 40	SR
Cardiovascular disease						
Batty, 2002	11 (12)	20 169	≥ 55 years at baseline	Mixed	Range= 18 months to 12	NS
Cardiovascular disease: Arterial stiffness						
Park et al, 2017	6 (6)	2 932	59 years and over (mean age ≥ 65 years)	NS	NS	NS
Cancer: Breast cancer						
Wu et al, 2013	11 (31)	2 463 599	>50 years	Female	Range= 4.7 to 32	NS
Cancer: Prostate cancer						
Liu et al, 2011	17 (43)	2 126 844	65 years and over	NS	NS	NS
Functional status outcomes						
Healthy ageing						
Daskalopoulou et al, 2017	8 (23)	174 114	65 years and over	70% female	Range= 2 to death	NS

Quality of Life						
Vagetti et al, 2014	4 (42)	855	Range= 59-85 years	Mixed	Range= 1 to 2 years	SR and objective
Activities of Daily Living Disability						
Tak et al, 2013	9 (13)	17 000	Majority= ≥70 years at baseline. Only 1 study reported on participants aged 50 years and over	NS	Range= 3 to 10	SR
Risk of falling						
Soares et al, 2018	4 (4)	11 282	60 years and over	Mixed	Range= 1 to 4.5	SR and objective
Mental health outcomes						
Cognitive function (mild cognitive impairment or cognitive impairment)						
Lü & Liu, 2016	33 (11)	24 192	60 years and over	NS	NS	NS
Cognitive function						
Carvalho et al, 2014	17 (27)	29 543	65 years and over	Mixed	Range= 1.5 to 15	NS
Cognitive decline						
Sofi et al, 2011	15 (15)	30 331	65 years and over. Only 1 study reported on participants aged <65 years	Mixed	Range= 1 to 12	NS
Cognitive decline & Dementia						
Blondell et al, 2014 <i>Cognitive decline</i>	17 (37)	48 821	60 years and over. 3 studies report on participants aged <60 years	Mixed	Range= 1 to 21	SR and objective
Blondell et al, 2014 <i>Dementia</i>	21 (37)	40 348	60 years and over. 2 studies reported on participants aged <60 years	Mixed	Range= 1 to 26	SR and objective
Cognitive decline, all-cause dementia, Alzheimer's disease, and vascular dementia						
Guure et al, 2017	40 (45)	117 410	65 years and over	Mixed	Range= 1 to 28	SR and objective

Lee, J. 2019 <i>All cause dementia</i>	3 (44)	258 138	65 years and over	NS	Range= 3.9 to 24.4	SR
Lee, J. 2019 <i>Vascular dementia</i>	8 (44)	258 138	65 years and over	NS	Range= 3.9 to 11.9	SR
Cognitive impairment/decline, Dementia and Alzheimer's disease						
Beydoun et al, 2014	24 (28)	73 334	60 years and over. 3 studies reported on participants aged <60 years	Mixed	NS	NS
Dementia & Alzheimer's disease						
Stern & Konno, 2009	12 (17)	NS	60 years and over. Only 1 study reported on participants aged <60 years	Mixed	Range= 1 to 16	SR and objective
Alzheimer's disease						
Beckett et al, 2015	9 (9)	20 326	65 years and over	Mixed	Range= 3.9 to 7	SR
Santos-Lozano et al, 2016	15 (24)	46 345	65 years and over	Mixed	Range= 3 to 31	SR and objective
Lee, J. 2019	12 (44)	258 138	65 years and over	NS	Range= 3 to 21	SR
Incident depression						
Schuch et al, 2018	16 (49)	266 939	65 years and over (subgroup analysis)	47% male	Range= 2 to 26	SR and objective
Functional status (limitations)						
Paterson & Warburton, 2010	35 (66)	83 740 (88 599)	65 years and over	Mixed	Range= 2 to 35	SR and objective
Musculoskeletal health: Osteoporotic fractures						
Qu et al, 2014	10 (22)	1 235 768	20 years and over (sensitivity analysis in participants aged ≥62 years)	Mixed	Range= 3.7 to 35	SR

NS: Not Stated; SR: Self-report

Table S2: Quality assessment of the included reviews using the AMSTAR checklist

Author, Date	Was an 'a priori' design provided	Was there duplicate study selection and data extraction	Was a comprehensive literature search performed?	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of studies (included and excluded) provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies assessed and documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	Was the likelihood of publication bias assessed?	Was the conflict of interest included?	Sum quality score	Quality of the review
Hupin et al, 2015	No	No	Yes	No	No	Yes	Yes	No	Yes	No	No	4	Low
Löllgen et al, 2009	No	CA	Yes	No	No	Yes	No	CA	Yes	CA	No	3	Low
Samitz et al, 2011	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	9	High
Batty, 2002	No	No	Yes	No	No	Yes	No	CA	CA	No	No	2	Low
Park et al, 2017	No	Yes	Yes	No	No	Yes	No	CA	Yes	No	No	4	Low
Wu et al, 2013	Yes	Yes	Yes	CA	No	Yes	No	CA	Yes	Yes	No	6	Low
Liu et al, 2011	No	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	6	Medium
Daskalopo. et al, 2017	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	8	High
Vagetti et al, 2014	No	CA	Yes	No	No	Yes	Yes	Yes	Yes	No	No	5	Medium
Tak et al, 2013	No	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	No	6	Medium
Lü & Liu, 2016	No	Yes	Yes	No	No	Yes	Yes	No	Yes	No	No	5	Medium
Carvalho et al, 2014	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	No	No	7	Medium
Sofi et al, 2011	Yes	Yes	Yes	CA	Yes	Yes	CA	Yes	Yes	Yes	No	8	High
Blondell et al, 2014	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	8	High
Guure et al, 2017	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	9	High
Beydoun et al, 2014	No	Yes	No	No	No	Yes	No	CA	Yes	Yes	No	4	Medium
Paterson & Warburton, 2010	No	Yes	Yes	No	No	Yes	Yes	No	Yes	No	No	5	Medium

Stern & Konno, 2009	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	CA	CA	No	7	Medium
Beckett et al, 2015	Yes	Yes	No	No	Yes	No	No	Yes	Yes	Yes	No	6	Medium
Santos-Lozano et al, 2016	Yes	Yes	Yes	CA	No	Yes	Yes	Yes	Yes	Yes	No	8	High
Schuch, 2018	Yes	Yes	Yes	CA	No	Yes	Yes	Yes	Yes	Yes	No	8	High
Qu et al, 2014	Yes	Yes	Yes	Yes	CA	Yes	Yes	Yes	Yes	Yes	No	9	High
Soares et al, 2018	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	8	High
Lee, J. 2019	No	Yes	Yes	No	No	Yes	No	No	Yes	Yes	Yes	6	Medium

CA: Cannot Answer; NA: Not Applicable

FINAL PROJECT

Table S3: Relationship between physical activity and health outcomes in older adults: results of included reviews without meta-analyses

Author, Date	Number of included studies	Total population / included in analysis	Review aim	Overall qualitative results of the review	Overall limitations of the review	Overall Recommendations
Batty, 2002	12 (including 9 prospective cohort studies, one case-control and one nested case-control study)	20 365 (20 169)	A systematic review of epidemiological studies for the association of physical activity with coronary heart disease in older adults.	Eight studies reported an inverse relation between physical activity and CHD, and statistical significance was seen in four of these.	Most studies featured men only. There were too few data on older women to draw clear conclusions regarding the association in this group. The review was rated as <i>low</i> quality on the AMSTAR scale.	Except where such advice is contraindicated, older adult men may benefit from physical activity in terms of reduced CHD risk.
Vagetti et al, 2014	44 (including 4 cohort studies)	409 192 (855)	A systematic review for the association between physical activity and quality of life (QoL) in older adults.	Most included studies demonstrated a positive association between physical activity and QoL in older adults. Physical activity had a consistent association with several QoL domains; functional capacity; general QoL; autonomy; past, present and future activities; death and dying; intimacy; mental health; vitality; and psychological.	Only a small number of studies evaluated the different domains of QoL.	PA was positively and consistently associated with some QoL domains among older individuals, supporting the notion that promoting PA in the elderly may have an impact beyond physical health. However, the associations between PA and other QoL domains were moderate to inconsistent and require further investigation.
Lü & Liu, 2016	33 (including 7 case control studies/4 cohort studies)	84 583 (24 192)	A systematic review of physical activity and cognitive function among older adults in China.	Observational studies (22 cross-sectional, 7 case-control and 4 cohort) showed an association of reduced risk of cognitive-related diseases (i.e., mild cognitive impairment, Alzheimer's disease, and dementia) through physical activity.	Further studies of individuals with cognitive impairments and prospective and RCT studies having high scientific rigor are needed to corroborate the findings reported in this review.	This systematic review provides initial evidence that physical activity may benefit cognition in older Chinese adults.
Carvalho et al, 2014	27 (including 15 prospective cohort studies and 1 case control study)	29 675 (27 383)	A systematic review of physical activity and cognitive function in	Twenty-six studies reported a positive correlation between physical activity and maintenance or enhancement of cognitive function. Five studies reported a dose-response relationship between	Most of the evidence was of medium quality with a moderate risk of bias.	The preponderance of evidence suggests that physical activity may help to improve cognitive function and, consequently, delay the progression of cognitive impairment in older adults.

			individuals over 60 years of age.	physical activity and cognition. One study showed a nonsignificant correlation.		
Paterson & Warburton, 2010	66 (including 44 prospective cohort studies and one case-control/one longitudinal study)	101 384	A systematic review of physical activity in older adults (>65 years) and outcomes of functional limitations, disability or loss of independence.	Greater physical activity of an aerobic nature was associated with higher functional status in older age. Moderate and high physical activity appeared effective in conferring reduced risk of functional limitations or disability. Limitation in higher level performance outcomes was reduced with vigorous (or high) physical activity with an apparent dose-response of moderate through to high activity.		It appears moderate to higher levels of activity are effective at maintaining functional independence and there may be a threshold of at least moderate activity for significant outcomes.
Stern & Konno, 2009	17 (including 15 cohort and 2 case-control studies)	NS	A systematic review of physical leisure activities and their role in preventing dementia.	The evidence was equivocal regarding the relationship between participation in physical activities during midlife and later life and the prevention of dementia.	One of the biggest issues was the lack of clarity regarding the classification of what a physical leisure activity was, the grouping systems utilised, and the method in which participation was measured.	Participating in physical activities during middle and later adult life can be neither refuted nor recommended to prevent the onset of dementia. Engaging in some physical activities (i.e. gardening, walking) appears to be more beneficial than engaging in other activities.