

International Doctoral Thesis



FITNESS, BODY COMPOSITION, AND DEPRESSIVE SYMPTOMS IN HEALTHY AND DEPRESSED ADULTS AND OLDER ADULTS

The INTERMAE and SONRIE studies



SONIA ORTEGA GÓMEZ

FITNESS, BODY COMPOSITION, AND DEPRESSIVE SYMPTOMS IN HEALTHY AND DEPRESSED ADULTS AND OLDER ADULTS

The INTERMAE and SONRIE studies

CONDICIÓN FÍSICA, COMPOSICIÓN CORPORAL Y SÍNTOMAS
DEPRESIVOS EN ADULTOS Y MAYORES SANOS Y CON
DEPRESIÓN

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RESEARCH PROJECTS

The present Doctoral Thesis was performed as a result of the following research projects:

1. Influence of a physical exercise intervention on markers associated with aging, proteomic profile and fragility. **INTERMAE study** (INfluencia de una inTervención con EjeRcicio Físico sobre Marcadores Asociados al Envejecimiento, Perfil Proteómico y Fragilidad. Estudio INTERMAE)

Project 80% co-financed by the European Union, within the framework of the Andalusia FEDER Operational Programme 2014-2020. Regional Ministry of Health and Families. Regional Government of Andalusia.

Reference: PI-0002-2017

Principal investigator: Jiménez-Pavón, David

Duration: 01/01/2018 to 31/12/2021

Funding: 492,107.54 €

2. ActividadeS físicas en el mediO NatuRal en personas con depresión. Efectos sobre el bienestar psíquico y social. **Estudio SONRIE**.

Project financed by Regional Ministry of Health and Families. Regional Government of Andalusia.

Reference: PI0068-2018.

Principal investigator: España-Romero, Vanesa

Duration: 17/12/2018 to 01/09/2023

Funding: 60,450.00 €

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The PhD candidate of the present Doctoral Thesis was funded by the Program for the financing of biomedical R+D+I and health sciences in the province of Cadiz, published in the Resolution of the Rector of the University of Cadiz UCA/REC07VOAP/2018, of July 3, 2018, by which a public tender of pre-doctoral contracts for research staff in training (del Castellano, Personal Investigador en Formación; PIF).

The aforementioned contract was associated with the INTERMAE project.

During pre-doctoral phase, the candidate enjoyed the following grants:

1. Research Stay in the Xlab Exercise laboratory and the Department of Biomedical Sciences, University of Copenhagen, Denmark.

Reference: EST2021-035 and ERASMUS+ KA103 SMP OUT (6484)

Responsible researcher: Larsen, Steen

Duration: 25/08/2021 to 1/12/2021

Funding: 2,750€ and 1,669€

2. Grant to attend an international congress. European Congress of Sport Science, Sevilla, Spain.

Reference: MV2022-310

Duration: 30/08/2022 to 02/09/2022

Funding: 300€

3. Grant to attend an international congress. European Congress of Sport Science, Online.

Funding from the research group

Duration: 28/10/2020 to 30/10/2020

Funding: 170,00 €

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ABBREVIATIONS

ADL: Activities of Daily Living

b: Unstandardized Regression Coefficient

BDI-II: Beck Depression Inventory II

BMI: Body Mass Index

CI: Confidence Intervals

CPET: Cardiopulmonary exercise testing

CRF: Cardiorespiratory Fitness

DSM-V: Diagnostic and Statistical Manual of Mental Disorders

GDS-15: Geriatric Depression Scale-15

ICD-10: International Classification of Diseases-10

ISAK: International Society for the Advancement of Kinanthropometry

MeSH: Medical Subject Heading

NOS: Newcastle-Ottawa Scale

OR: Odd Ratio

p: P-value

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.

PROSPERO: International Prospective Register of Systematic Reviews

RCT: Randomized controlled trial

SD: Standard Deviation

SFT: Senior Fitness Test

SPPB: Short Physical Performance Battery

VO_{2peak}: Peak oxygen consumption

β: Standardized Regression Coefficient

ABSTRACT

Depression affects around 300 million people worldwide, and it is expected that will be the world's leading disease burden by 2030. Indeed, 13% of the Spanish population aged 15 and over presented depressive symptoms, with a higher impact on women. The frequency of symptoms rises more steeply with aging affecting approximately 24% of older adults. Suffering from depressive symptoms or diagnosed depression is related to other pathologies and health problems. Thus, it is crucial to find strategies to mitigate and protect against this problem in adults and older adults. On the other hand, health-related physical fitness has been demonstrated scientifically to have psychological benefits and, it could be an effective and side-effect-free method of preventing depressive symptoms.

In consequence, determining the relation of each component of fitness and different indicators of body composition with depressive symptoms may have an impact on public health and future interventions focused on improving fitness and body composition since they are modifiable risk factors. Moreover, the research on the population with a diagnosis of depression is even scarcer, so it is a priority to know the relationship in this case as well.

Therefore, the general aim of this International Doctoral Thesis was to investigate the relationship of fitness components and body composition with depressive symptoms in healthy and depressed adults and older adults.

To achieve this objective, three studies have been conducted, a systematic review (**Study I**) and, cross-sectional data from the INTERMAE (**Study II**) and SONRIE (**Study III**) studies. In **Study I**, systematic searches were conducted in PubMed and Web of Science. Longitudinal and cross-sectional studies were included if they measured at least one fitness component and depressive symptoms indicator in healthy and/or depressed adults or older adults (18 years and over). In **Study II**, ninety-two older adults (42 females, 68 ± 3 years) were included. Fitness components were measured by Senior Fitness Test (SFT), Short Physical Performance Scale (SPPB), gait speed, handgrip, and cardiopulmonary exercise tests (CPET). Body composition was assessed by body mass index (BMI), fat mass and muscle mass percentages obtained using a multifrequency

bioimpedance, and waist and hip circumferences. Depressive symptoms were collected by Geriatric Depression Scale-15 (GDS-15). In **Study III**, eighty-two adults with a diagnosis of mild to moderate depression (69 females, 49 ± 10 years) were included. Fitness components were measured by SFT, SPPB, gait speed, unipedal stance, standing long jump and handgrip tests. Body composition was assessed similarly to Study II. Depressive symptoms were collected by Beck Depression Inventory II (BDI-II).

The main findings of this International Doctoral Thesis are i) Cardiorespiratory fitness (CRF), strength, and gait speed were inversely related to depressive symptoms longitudinally. ii) All fitness components except flexibility and other gait parameters were inversely related to depressive symptoms cross-sectionally in healthy adults and older adults. iii) There is no evidence regarding the specific population with diagnosed depression. (**Study I**); iv) Higher levels of fitness, notably gait speed, and muscle strength and lower fatness seem to contribute to having fewer depressive symptoms in older adults. In addition, higher performances in gait speed, agility, upper-limb muscular strength and CRF, as well as, more appropriate fat and muscle levels, appear to have a beneficial impact, individually, on these symptoms. (**Study II**); v) Better perceived fitness and higher balance performance may have a protective effect against depressive symptoms in adults with depression. Additionally, a larger hip circumference may be related to more depressive symptoms. (**Study III**); Older adults and adults with depression identified as low-fit and high-fat might have increased odds of higher depressive symptoms compared to their high-fit and low-fat peers. (**Study II and Study III**).

The findings of the present International Doctoral Thesis show that all components of fitness and body composition, except flexibility, appear to have a beneficial impact on depressive symptoms in healthy adults and older adults. However, for the specific population with depression, only balance, hip circumference and self-reported fitness are related. In both populations, those with low fit and high fat profile could further increase depressive symptoms.

RESUMEN

La depresión afecta a unos 300 millones de personas en todo el mundo, y se prevé que será la principal enfermedad mundial en 2030. De hecho, el 13% de la población española mayor de 15 años presenta síntomas depresivos, con mayor incidencia en las mujeres. La frecuencia de los síntomas aumenta de forma más acusada con el envejecimiento, afectando aproximadamente al 24% de los adultos mayores. Padecer síntomas depresivos o depresión diagnosticada está relacionado con otras patologías y problemas de salud. Por lo tanto, es crucial encontrar estrategias para mitigar y proteger contra este problema en adultos y ancianos. Por otro lado, se ha demostrado científicamente que la condición física relacionada con la salud tiene beneficios psicológicos y, podría ser un método eficaz y sin efectos secundarios para prevenir los síntomas depresivos.

En consecuencia, determinar la relación de cada componente de la forma física y los diferentes indicadores de la composición corporal con los síntomas depresivos puede tener un impacto en la salud pública y en futuras intervenciones centradas en mejorar la forma física y la composición corporal, ya que son factores de riesgo modificables. Además, la investigación en población con diagnóstico de depresión es aún más escasa, por lo que es prioritario conocer la relación también en este caso.

Por ello, el objetivo general de esta Tesis Doctoral Internacional ha sido investigar la relación de los componentes de la condición física y la composición corporal con los síntomas depresivos en adultos sanos y deprimidos y en adultos mayores.

Para alcanzar este objetivo, se han realizado tres estudios, una revisión sistemática (**Estudio I**) y, datos transversales de los estudios INTERMAE (**Estudio II**) y SONRIE (**Estudio III**). En el **Estudio I**, se realizaron búsquedas sistemáticas en PubMed, Web of Science, y se incluyeron estudios transversales y longitudinales si medían al menos un componente de la forma física y un indicador de síntomas depresivos en adultos sanos y/o deprimidos o adultos mayores (18 años o más). En el **Estudio II**, se incluyeron noventa y dos adultos mayores (42 mujeres, 68 ± 3 años). Los componentes de la forma física se midieron mediante el Senior Fitness Test (SFT), la Short Physical Performance Scale (SPPB), la velocidad de la marcha, la prensión de la mano y las pruebas de ejercicio cardiopulmonar (CPET). La composición corporal se evaluó mediante el índice de masa

corporal (IMC), los porcentajes de masa grasa y masa muscular obtenidos con una bioimpedancia multifrecuencia, y las circunferencias de cintura y cadera. Los síntomas depresivos se recogieron mediante la Escala de Depresión Geriátrica-15 (GDS-15). En el **Estudio III**, se incluyeron ochenta y dos adultos con diagnóstico de depresión de leve a moderada (69 mujeres, 49 ± 10 años). Los componentes de la forma física se midieron mediante SFT, SPPB, velocidad de la marcha, postura unipodal, salto de longitud de pie y pruebas de agarre de manos. La composición corporal se evaluó de forma similar al Estudio II. Los síntomas depresivos se recogieron mediante el Inventario de Depresión de Beck II (BDI-II).

Los principales hallazgos de esta Tesis Doctoral Internacional son i) La capacidad cardiorrespiratoria (CRF), la fuerza y la velocidad de la marcha estaban inversamente relacionadas con los síntomas depresivos longitudinalmente. ii) Todos los componentes de la condición física, excepto la flexibilidad y otros parámetros de la marcha, estaban inversamente relacionados con los síntomas depresivos transversalmente en adultos sanos y adultos mayores. iii) No hay evidencia con respecto a la población específica con depresión diagnosticada. (**Estudio I**); iv) Además, un mayor rendimiento en velocidad de la marcha, agilidad, fuerza muscular de las extremidades superiores y CRF, así como unos niveles más adecuados de grasa y músculo, parecen tener un impacto beneficioso, individualmente, sobre estos síntomas. (**Estudio II**); v) Una mejor forma física percibida y un mayor rendimiento en equilibrio pueden tener un efecto protector contra los síntomas depresivos en adultos con depresión. Además, un mayor perímetro de cadera puede estar relacionado con más síntomas depresivos. (**Estudio III**); Los adultos mayores y los adultos con depresión identificados como de baja forma física y alto nivel de grasa podrían tener mayores probabilidades de presentar síntomas depresivos más elevados en comparación con sus compañeros de alta forma física y bajo nivel de grasa. (**Estudio II y Estudio III**).

Los hallazgos de la presente Tesis Doctoral Internacional muestran que todos los componentes de la condición física y la composición corporal, excepto la flexibilidad, parecen tener un impacto beneficioso sobre los síntomas depresivos en adultos sanos y adultos mayores. Sin embargo, para la población específica con depresión, sólo el equilibrio, la circunferencia de la cadera y la forma física autodeclarada están

relacionados. En ambas poblaciones, las personas con baja forma física y alto nivel de grasa podrían aumentar aún más los síntomas depresivos.

INTRODUCTION

INTRODUCTION

Depressive disorders and depression

Depressive symptoms, diagnosis, and comorbidities

Depression is a common illness that has as a distinctive feature a *"sustained negative affect and diminished positive affect"* (1). Precisely, it is characterised by *"the presence of sad, empty, or irritable mood, accompanied by somatic and cognitive changes that significantly affect the individual's capacity to function"* (2) and *"diminishes quality of life"* (3).

Depression is manifested by core depressive symptoms which can be classified into three main categories (2,3): emotional, neurovegetative, and neurocognitive symptoms. Emotional symptoms include a persistent feeling of sadness or emptiness, loss of interest or pleasure in activities (anhedonia), feelings of worthlessness or guilt, and recurrent thoughts of death or suicide and anxiety (2,3). Neurovegetative symptoms comprise changes in appetite, weight loss or gain, sleep disturbances and fatigue or low energy (2,3). Neurocognitive symptoms involve difficulty concentrating or making decisions, and negative thoughts or pessimism, low confidence and self-esteem, and psychomotor agitation or retardation (2,3).

Specifically, the central core of the symptoms of depression is associated with problems of cognitive control and the regulation of emotion, negatively affecting the mood of individuals (1). Consequently, depressive mood and loss of interest are considered fundamental depressive symptoms (3).

This classification of depressive symptoms is shown in **Figure 1**.

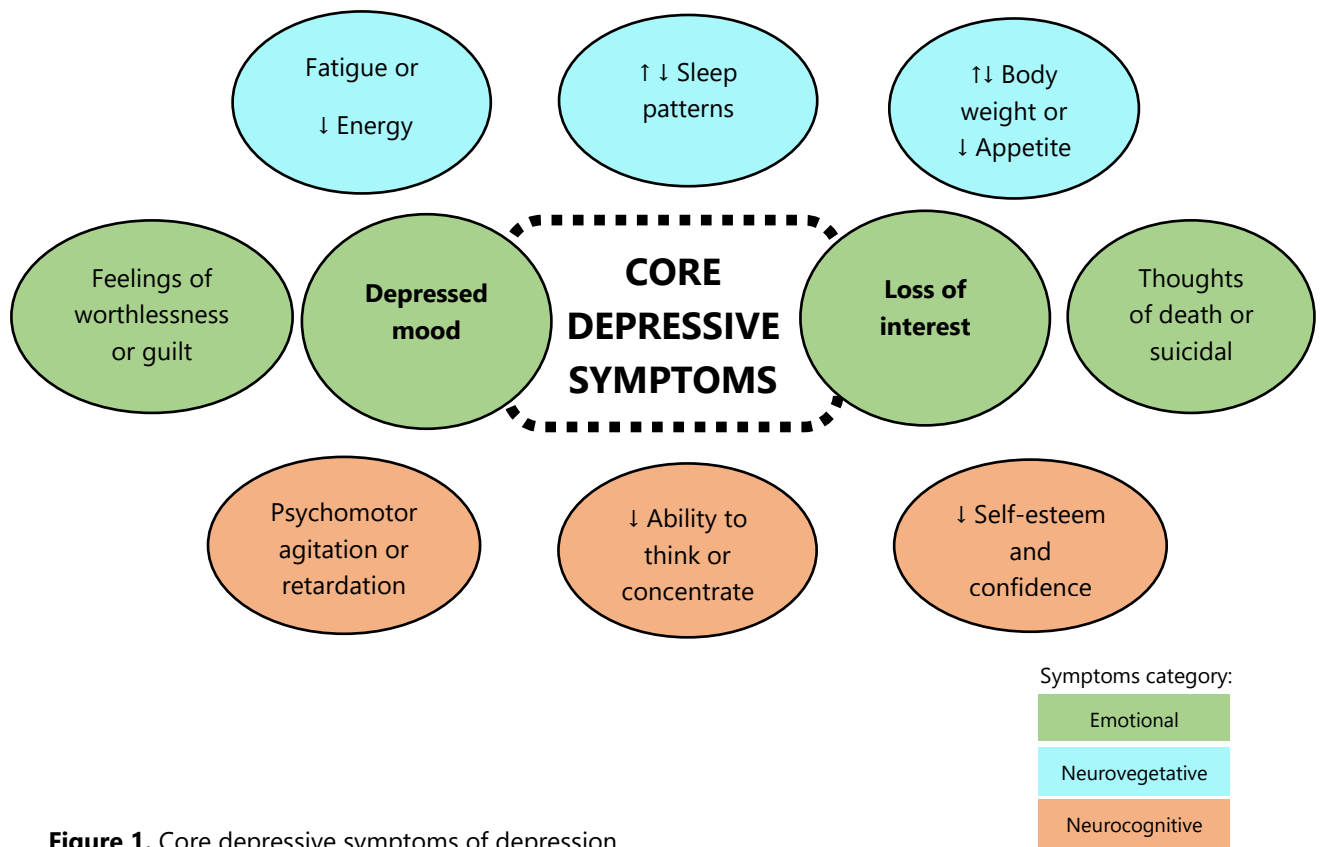


Figure 1. Core depressive symptoms of depression.

Depression is highly variable, as the same individual may show symptoms of different kinds, but will nevertheless present core symptoms (3). Understanding the different types of symptoms associated with depression is important in the diagnosis and treatment of the disorder. Research has shown that the type and severity of symptoms can affect an individual's response to treatment (3). Therefore, it is essential for mental health professionals to assess all types of symptoms when diagnosing depression and to tailor treatment plans accordingly.

The Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) (2) and the International Classification of Diseases-10 (ICD-10) (4) are the main diagnostic manuals for depression. According to DSM-V criteria (2), a diagnosis of depression is made when an individual experiences at least one depressive episode characterized by at least five of the following symptoms: depressed mood, loss of interest or pleasure, significant weight loss or gain, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive guilt, diminished ability to think or concentrate, and recurrent thoughts of death or suicidal ideation. At least one of the

symptoms must be fundamental: depressed mood or loss of interest or pleasure. Similarly, according to the ICD-10 criteria (4), a diagnosis of depressive episode is made when an individual experiences at least two of the following symptoms: depressed mood, loss of interest or pleasure, loss of energy or increased fatigue, feelings of worthlessness or guilt, impaired concentration or indecisiveness, or recurrent thoughts of death or suicide. In addition, symptoms, to be considered, must be experienced nearly every day for 2 weeks and involve functional decline (2,4). Depending on the type, severity, number of symptoms, and degree of functional disability, a mild, moderate, or severe episode will be identified. The heterogeneity and multiple factors that influence depression make it difficult to diagnose, so it is often overlooked or misdiagnosed (3).

This illness has different patterns of incidence and can be a single-episode depressive disorder when it is the individual's first and only episode, or a recurrent depressive disorder when the person has a history of at least two depressive episodes at least 2 months apart. These episodes may show features of other clinical disorders, such as anxious distress and psychotic state (2,3). Otherwise, when depressive episodes do not disappear and last for long periods, it is considered chronic depression (3). Concerning remission status, it can be partial remission when symptoms of the episode are still present but not all criteria are met, or there is a period lasting less than 2 months without significant symptoms; and complete remission when no significant symptoms have been present for the last 2 months (2).

Knowledge of the pathophysiology of depression has advanced considerably, but no single mechanism successfully explains all aspects of the disorder (3). Although, risk and prognostic factors have been established (2). The predominance of negative affective personality traits (neuroticism) will predispose to depressive episodes in response to stressful life events. Also, environmental factors mainly related to adverse childhood experiences and stressful life events. Genetic heritability is another well-studied factor, whereby having first-degree relatives with the disorder increases the likelihood of depression by 2-4 times. Finally, course modifiers, essentially all major non-emotional disorders (i.e., diabetes, morbid obesity, and heart disease) increase an individual's risk of developing depression (2).

Nevertheless, it is important to understand the distinction between depression and depressive symptoms. All people with depressive symptoms do not inherently suffer from depression but may be due to negative feelings of demoralisation and grief, other disorders or a normal response to a significant loss (2). People who are depressed but without clinical depression report depressive symptoms that differ in duration and intensity from those diagnosed, and suicidal thoughts are much less likely, as is prolonged loss of functioning (4,5). Indeed, people with diagnosed depression will have more recurrent depressive symptoms (3). However, the research on depressive symptoms should also be studied in undiagnosed people because of their negative impact on quality of life (6).

Scientific evidence has shown that suffering from depressive symptoms or diagnosed depression is related to other pathologies and health problems. Depressed people, in the broadest meaning of the term, are at increased risk of diabetes, coronary heart disease (7), dementia (8), musculoskeletal disorders (9), among others. In addition, these diseases work in a cyclical fashion with each one exacerbating the other (10). Depression is also associated with increased mortality (11,12), and in the most severe cases, it may lead to suicide (13), which is currently the forth cause of death among young people aged 15 to 29 years (14). It is also related to work incapacity (15) and a reduced ability to function independently and frailty (16).

Overview and prevalence

Depressive disorder has been a leading cause of morbidity and disability for the past 30 years and it was the second leading cause in 2019 (17,18), affecting around 300 million people worldwide (18,19). Namely, the prevalence of this disorder in adults in European countries is 5.16% (in Spain is 6.75%) (19). In the subsequent years, the COVID-19 pandemic has caused a notable increase in depression cases (20). Moreover, it is expected that will be the world's leading disease burden by 2030 (3).

Globally, depression events are usually diagnosed in adulthood (21,22). Indeed, it is estimated that 5% of adults and 5.7% of the elderly suffer from depression; being women more severely hit than men (19,23). Furthermore, adults were mainly affected during the COVID pandemic period, and currently, there are no updated post-pandemic data (20).

Depression, in addition to the emotional cost of illness, is a public health problem that increases healthcare costs (23). It is noteworthy that the prevalence of depressive disorders does not differ considerably between high-income and low- and middle-income countries, reflecting this prevalence that it is not merely a consequence of current lifestyles in developed countries, nor of poverty. While it is true that socio-economic status, as an environmental factor, may play a role in depressive disorders, it is ultimately biological factors that determine the onset of the illness (3).

Hence, European Health Interview Survey 2020 in the Spanish population reported that 12.74% of the population aged 15 and over presented depressive symptoms, with important differences between men (8.9%) and women (16.3%). The frequency of symptoms rises more steeply with aging affecting approximately 24% of older adults (24).

Thus, it is crucial to find strategies to mitigate and protect against this problem in adults, since it is mainly in the 20s that depressive episodes emerge (3), and in the elderly (25).

Physical fitness

Fitness: multidimensional construct and components

Physical fitness (hereinafter fitness) is defined as "*a set of attributes related to a person's ability to perform physical activities*" (26). Physical fitness is characterized by various components, including cardiovascular endurance, muscular strength, muscular endurance, flexibility, and body composition(27). It is a state of well-being that allows individuals to perform daily activities, sports, and other physical pursuits without experiencing excessive exhaustion or injuries (28).

Fitness is determined by genetic heredity and environmental factors, including regular exercise and PA; and has been shown to be an important marker of health at all ages (26). Health-related fitness components comprise cardiorespiratory fitness (CRF), muscle strength, flexibility, and motor fitness (26,29), and, certain scientific classifications included body composition (27,28). Specifically, motor fitness encompasses components such as balance, agility, coordination and gait speed, which are commonly considered skill-related fitness components (27).

These fitness components have commonly been separated into two categories (health and skill- related fitness). However, current evidence has suggested that they are not mutually exclusive and, are all important for achieving health goals in different populations (27). For instance, agility, coordination, balance, and gait speed showed a strong relationship with frailty in older people (30).

The components are defined as follows:

Health-related fitness components

- Cardiorespiratory fitness: the ability of the circulatory and respiratory system to supply oxygen during sustained PA or prolonged strenuous exercise (28,31).
- Muscle strength: the ability of a specific muscle or muscle group to generate force or torque. to perform repeated contractions over time or to maintain a contraction for a prolonged period (muscular endurance), or to carry out a maximal, dynamic contraction in a short period of time (explosive strength, or muscular power) (28,32).
- Flexibility: the range of motion available at a joint (27,29).
- Motor fitness (*skill-related fitness components*) is the performance aspect of fitness in activities of daily living (ADL) which involves (27,29):
 - Agility: the ability to change the position of the body in space quickly and with control. Therefore, this component is a combination of speed, balance, and coordination (27,29).
 - Coordination: the ability to use the senses (usually sight and hearing) combined with the parts of the body to perform tasks fluently and accurately (27,29).
 - Balance: the maintenance of equilibrium while stationary or moving (27,29).
 - Speed: the ability to perform a movement within a short period of time. Precisely, usual gait speed is the ability to walk at a comfortable speed, and maximal gait speed is walking as fast as possible without running (27,33).

On the other hand, functional capacity (34) is an aspect of physical fitness as refers the individual ability to perform ADL independently (i.e. walking, climbing upstairs, carrying groceries or housekeeping). It is a widespread term used and measured in older population since aging implies a functional decline at the physical and cognitive levels. That functional decline is associated with multiple factors (such as cognitive impairment, depression, change in body composition, lower extremity functional limitation, low frequency of social contacts, low level of physical activity, etc) (35) and an increased risk of institutionalisation and falls (36), which can lead to a deterioration of well-being (37). Accordingly, physical performance scales specifically assess lower limb fitness, mainly, balance, gait speed and strength, to determine the functional capacity of older people (38,39).

Health-related fitness has been demonstrated scientifically to have physiological and psychological benefits and to protect against the development of disorders and chronic diseases (40). What is more, fitness could be an effective and side-effect-free method of preventing depressive symptoms (41).

Subjectively measured fitness

Subjectively measured fitness is measured as self-reported fitness (42,43). Assessing fitness is often time-consuming and not feasible in large epidemiological studies, as well as being a practical and cost-effective alternative (44). Therefore, questionnaires to assess self-reported fitness have been found useful in epidemiological studies aimed at estimating the fitness level of a given population (44). Self-reported fitness can be assessed by means of single-item measures asking individuals to rate their own fitness in comparison with their age peers, respectively.

Associations of fitness with depressive symptoms

Scientific literature has shown that there is an association between physical fitness and depressive symptoms (45,46). Individuals who are physically fit tend to experience fewer symptoms of depression, have a lower risk of developing depression, and show better responses to depression treatment (47,48). However, some studies have reported no significant association between the two factors (49–53).

Cardiorespiratory fitness

While there is significant evidence supporting the inverse association between CRF and depressive symptoms in adult to older population (45), a scarce number of studies (41,52,54,55) have found no relationship between CRF and depressive symptoms. Related to adults, Gerber et al. (56) showed that the lowest CRF level group showed higher depressive symptoms compared to the highest group. Also, Jin et al. (57) found that those adults, both men and women, with minimal depressive symptoms showed higher levels of CRF. Contrastingly, Mollaoglu et al. (52) reported that CRF was not associated with depressive symptoms for men or women adults. Regarding older adults, Vanoh et al. (58) and Lee et al. (59) concluded that nondepressed group showed higher performance in CRF. In contrast, other articles found no association in the whole sample (54), or only in women (55).

It is important to note that the specific measures used to assess CRF associated with depressive symptoms could vary across studies, from walking minutes tests to cardiopulmonary exercise testing (CPET), which may contribute to inconsistent findings. In this line, few articles focused on the association of this fitness component with depressive symptoms in the elderly (55,60) employed direct measures to assess CRF, instead of estimating it from speed, time, distance etc.

To our knowledge, scarce research is found (45) about the association between CRF and depressive symptoms in the population with diagnosed depression. A current systematic review and meta-analysis (45) reported that a reduced number of randomized controlled trial studies (61,62) had a full sample of diagnosed depression, and another part (63,64) included both healthy and depressed people.

Muscle strength

There is evidence that suggests a potential inverse association between muscular strength and depression symptoms. On one hand, several review studies (46,65,66) have reported that higher muscular strength resulted in fewer depression symptoms. On the other hand, there are studies (50,67) that have reported no relationship between the two factors. It is important to highlight that evidence may vary between studies that assessed muscular strength from the upper (66) or lower limbs (46).

Most of the scientific evidence shows that both adults (41,68,69) and older adults (58,64,70–72) with higher upper limbs muscle strength have lower severity of depressive symptoms. On the other hand, some articles found no such relationship in both adult (50) and older populations (73–75). Precisely, the study of Smith et al. (75) found that older adults of normal weight group with higher levels of strength no showed lower severity of symptoms in women and men.

There also seems to be robust evidence that increased lower-limbs muscle strength leads to a lower incidence of depressive symptoms in older adults (58,59,84–87,76–83). For example, the study of Chen et al. (78) with a sample population over 60 years of age, showed that those with better lower limbs muscle strength performance experienced fewer depressive symptoms.. Conversely, the few studies analysing the association between lower-limbs muscle strength and depressive symptoms in adults reported no relationship (50,67). For example, a study of middle-aged and older adults (67) found no significant association between lower limbs muscle strength and depressive symptoms.

The relevant evidence on muscle strength is mainly obtained by handgrip, finding that those with a higher level of upper limbs muscle strength have a lower risk of depressive symptoms in both adults and older adults (66,88). For instance, a cross-sectional study of older adults (89) found that lower handgrip strength was associated with a higher risk of depression. In this line, some studies have shown an inverse relationship between upper-limbs muscle strength measured by other tests such as the arm curl with depressive symptoms (54,59,82), mainly in older adults. In the case of lower limbs muscle strength, chair stand tests in all their variants are commonly used in all population.

In the case of research in people diagnosed with depression, the association between upper-limbs muscle strength and depressive symptoms was reported as inverse in all the articles that studied it, although most of them with a very low percentage of the sample with a diagnosis (64,90–92), as opposed to one with its full sample with depressive disorders (93). These articles had a sample age of over 50 years, only the article by Lee et al. (92) covered the age range of 19 to 80 years. The inverse association between lower-limbs muscle strength and depressive symptoms in people with a diagnosis of depression was only reported in 2 articles (64,86) on older adults, again with a very low percentage of the sample with a diagnosis.

Other fitness components

The influence of other fitness components on depressive symptoms has been less studied. Flexibility has hardly been explored, and the previous studies reported that increased upper-limbs (54,58,82) and lower-limbs (58,59,82) flexibility was associated with lower depressive symptoms in older adults. In healthy adults, most of the evidence reported no association between upper-limbs (49) and lower-limbs (49,57) flexibility with depressive symptoms. Whereas only one study (67) reported a negative relationship between depressive symptoms and lower-limbs flexibility. Otherwise, this association was not studied in the depressed population.

Motor fitness or skill-related fitness components (i.e. agility, coordination, balance and gait speed) have been mostly studied in older adults, and often grouped in batteries or scales (78,94,95). As for agility, older adults with better agility had fewer depressive symptoms (58,76,83,96). However, no association between the two variables has been observed in adults in the few studies that have analysed it (50,67). Concerning coordination, only one article (77) studied this component and its relationship with depressive symptoms in older adults. It reported that more coordinated older adults had fewer depressive symptoms (77). In terms of balance, some articles of adults (49) and elderly sample (76,83,96) reported a negative association versus others that did not, in adults (49,50) and elderly (77,79). Finally, usual gait speed appears to have a consistent inverse association with depressive symptoms in the elderly (76,83,96). In contrast, in healthy adults, studies were very few (49,50) as was the case when maximum gait speed was specifically studied in both populations, adults and elderly (77).

The previous scientific evidence analysing the role of flexibility and motor fitness on depressive symptoms in people diagnosed with depression is very scarce, with only older population samples studied. In this sense, articles with a sample of older adults and a diagnosis of depression, in part (53,64) or all (93) the population, studied functional capacity scales (i.e. balance, gait speed and lower-limbs muscle strength). Among all the fitness components studied in association with depressive symptoms in these studies, no concordant results are obtained. They only agree in that none found a relationship of usual gait speed.

Subjectively measured fitness

Previous studies on self-reported fitness have shown it to be a strong predictor for mortality (97), cardiovascular disease risk (98), and resilience to stress in adults (99). No studies specifically investigated the association between self-perceived physical fitness and depressive symptoms in healthy adults and older adults or those with diagnosed depression.

However, studies in other populations, such as pregnant women (42), perimenopausal women (43) and healthy adolescents (100), have found an inverse association between self-reported fitness and depressive symptoms.

In conclusion, determining the relation of each fitness component and subjectively measured fitness with depressive symptoms in healthy population or diagnosed with depression, may have an impact on public health and interventions focused on improving fitness since it is a modifiable risk factor. A conclusive finding in both, healthy and depressed, adults and older adults, is a challenge due to the diversity of physical measurement tests and the underdiagnosis of depression in some cases (3).

Body composition

Definition, compartments, methods, and obesity comorbidities

Body composition is defined as *"the relative amounts of muscle, fat, bone, and other vital parts of the body"* (27). To be more precise, it is the scientific field that studies the in vivo quantification of body components (101). Body composition can be assessed by the division of body mass into compartments according to different levels, including chemical and anatomical-tissular levels. The division at the chemical level divides the body into fat mass and fat-free mass. Fat mass includes adipose tissue, or body fat, while fat-free mass includes all other tissues in the body, such as muscle, bone, organs, and water (102). Besides, the anatomical-tissular level division allows identifying fat-free mass into lean body mass and bone mineral content, as well as dividing lean body mass into muscle mass and non-muscle mass (101). This level of detail can provide valuable information about the distribution of different tissues in the body and their relative contributions to overall health and fitness (103–105).

Some of the direct methods commonly used that provided accurate information for assessing body composition and dividing it into these different compartments include dual-energy X-ray absorptiometry (106), bioelectrical impedance analysis (105), and magnetic resonance imaging (107). However, these techniques can be inaccessible, expensive and require specialisation. Therefore, simple anthropometry assessments are often the most commonly used (101,108). These methods provide the most common health-related measures such as fat mass percentage and body mass index (BMI) (108).

Obesity and being overweight are physical states of illness due to an increased or abnormal body fat volume, amount of adipose tissue, or excessive fat deposits in specific areas (109). BMI (110), body circumferences (111,112) and fat mass percentage (113) can be used to determine these physical states. Scientific evidence has established cut-off points for BMI, and age- and sex-specific cut-off points for the latter two measures.

Nowadays, obesity has become a pandemic illness affecting all ages (114). It is well established that being overweight or obese is associated with an increased risk of numerous cardiovascular, metabolic, respiratory, mental and other diseases and disorders, as well as a reduced life span (114). In addition, ageing is associated with a slowdown in weight loss that becomes more intense after the age of 75 and, a decline in muscle mass that is commonly referred to as sarcopenia (108).

Associations between body composition and depressive symptoms

It has been widely shown that overweight and obesity (by means BMI and abdominal fat) in the general population are directly related to suffering from depression (115,116), even suggesting a reciprocal relationship in adults (117,118). However, this evidence in older adults is inconsistent, with publications claiming that being overweight or obesity may be protective against depression (119). In this line, several studies (120,121) reported an inverse relationship between obesity and depressive symptoms in middle-aged and older adults. On contrary, other articles (122,123), in a similar aged population, reflected a direct relationship of + BMI and abdominal fat with depressive symptoms. Otherwise, another recent work in older adults (124) found a U-shaped association between BMI and depressive symptoms, finding the highest levels of depressive symptoms in underweight and the next highest in obese people. Consequently, further research is

needed on the relationship of obesity and fat mass to depressive symptoms in older adults.

Scientific literature on adiposity in terms of body fat mass percentage and depressive symptoms is less well studied. A study of adults in the age of 60 (125) showed that depressive symptoms were closely related to high levels of fat mass. Another recent article (126) reported that middle-aged women who reported depressive symptoms had higher visceral fat than those who did not, but there were no differences in BMI or total body fat mass.

On the other side, the inverse relationship between muscle mass and increased depressive symptoms in all populations seems to be robust. In other words, there is clear evidence that the increased muscle mass reduces depressive symptoms in adults and older adults (127,128). In fact, the role of muscle mass on depressive symptoms is mainly studied in connection with sarcopenia and frailty in the elderly population (127,129).

Meanwhile, current research has used the term “depression” both for the diagnosis of the pathology and for the presence of a minimum number of depressive symptoms, so the relationship that may exist between obesity or muscle mass and depressive symptoms in people with diagnosed depression does not seem to have been studied. Thus, it is important to know the relationship between body composition and depressive symptoms in people with clinical depression. This allows us to promote strategies that are appropriate for this population and that achieve an improvement in their body composition, such as through diet and physical exercise.

Fatness and fitness

Fat but Fit paradox and its association with depressive symptoms

The Fat but Fit paradox began in one study published in the Journal of the American Medical Association in 1996, where Blair and colleagues analysed data from over 25,000 men and women and found that regardless of BMI, individuals who were physically fit had a lower risk of mortality compared to those who were unfit (130). Additionally, it was noted that while there is a higher risk of cardiovascular disease associated with obesity, physical activity and fitness can still provide important health benefits for overweight and obese individuals (131). For example, a study published in the Progress in Cardiovascular

Diseases Journal in 2014 found that overweight and obese individuals who were physically fit had similar risks of mortality compared to normal-weight individuals who were physically fit (132). Similarly, a study published in the PloS one Journal in 2018 found that overweight and obese individuals who were metabolically healthy and physically fit had lower risks of cardiovascular disease compared to those who were metabolically unhealthy and physically unfit, regardless of their BMI (133). Even more, several studies have shown that people who are normal weight but not fit may be at higher risk all-cause mortality than people who are obese but fit (134,135). Therefore, these research conclusions suggest that a moderate to high CRF could protect against the negative consequences of obesity on many other aspects of health in many population groups. Otherwise, current evidence has limitations, such as uncontrolled aspects like the diet of the participants (135). In contrast, some research reflected controversy on this paradox (136,137). The study of Diaz et al. (136) showed that high weight was associated with the combination of cardiovascular disease risk factors such as insulin resistance, C-reactive protein, and dyslipidaemia, and not CRF. Also, researcher Mukamal (137) highlighted the role of the reciprocal relationship between obesity and CRF, and the need for repeated and more precise measurements and studies with larger sample sizes to confirm this concept.

This paradox has been studied mainly by considering fitness as a CRF (130,132,138) and just a few with muscle strength (139,140). Subsequently, upper-limb muscle strength has been studied in this combined association. The study by Kim et al. (139) reported that obese but stronger adults had a lower risk of all-cause mortality than non-obese but muscularly weak adults. On the other hand, the study by Stenholm et al. (140) reported that for participants aged 50-69 years, those obese with low strength had the highest mortality. For adults older than 70 years, it was for those with normal weight and low strength. Furthermore, in older participants, being overweight or obese and high strength was associated with lower mortality than being normal weight and high strength.

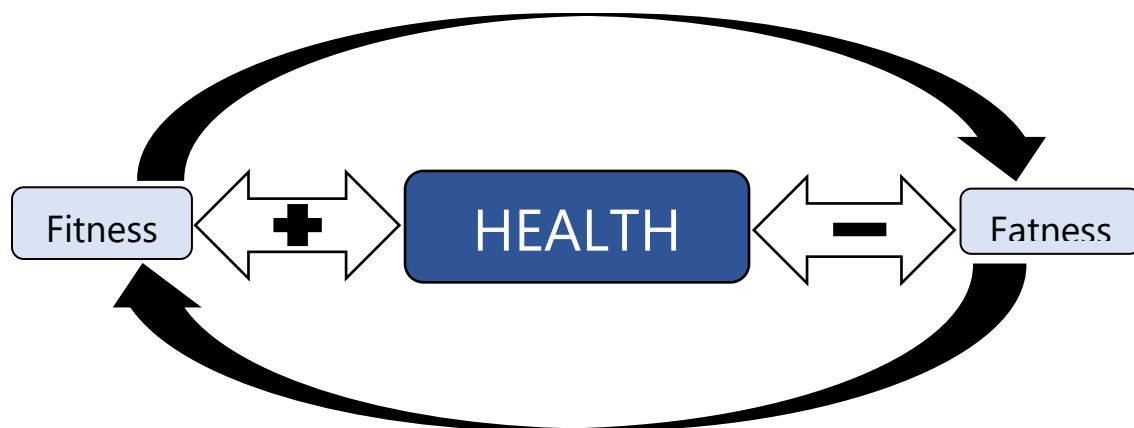


Figure 2. Relationship of fitness and fatness to health. Adapted from Ortega et al. (26).

The combined role of fitness and obesity on depressive symptoms is poorly studied in the whole population. Only the landmark study of Becofsky et al. (138) established in the general population, between 20-100 years, that the role of CRF on depressive symptoms was stronger than the level of obesity. Precisely, fat but fit people have a 50% reduction in the risk of developing depressive symptoms compared with their fat and unfit peers. Similar results were reported in several articles on youth populations (141–143), but to the best of our knowledge, it has not been studied in older people and population with diagnosed depression.

While there is some evidence to suggest that fitness may be associated with lower rates of depression among overweight and obese individuals, more research is needed to fully understand the potential relationship between the "fat but fit" paradox and depressive symptoms.

AIMS

AIMS

General aim

The general aim of the present International Doctoral Thesis was to investigate the relationship of fitness components and body composition with depressive symptoms in healthy and depressed adults and older adults.

Specific aims

- 1) To systematically synthesize the evidence available on the associations between fitness components and depressive symptoms in healthy and depressed adults and older adults **(Study I)**.
- 2) To analyse the independent and combined associations of fitness components and body composition with depressive symptoms in older adults **(Study II)**.
- 3) To establish the independent and combined associations of fitness components and body composition with depressive symptoms in adults diagnosed with mild to moderate depression **(Study III)**.

OBJETIVOS

Objetivo general

El objetivo general de la presente Tesis Doctoral Internacional fue investigar la relación de los componentes de la condición física y la composición corporal con los síntomas depresivos en adultos y mayores sanos y con depresión.

Objetivos específicos

- 1) Revisar sistemáticamente la evidencia disponible sobre las asociaciones de los componentes de la condición física con los síntomas depresivos en adultos y mayores sanos y con depresión **(Estudio I)**.
- 2) Analizar las asociaciones independientes y combinadas de los componentes de la condición física y composición corporal con los síntomas depresivos en mayores **(Estudio II)**.
- 3) Establecer las asociaciones independientes y combinadas de los componentes de la condición física y composición corporal con los síntomas depresivos en adultos diagnosticados con depresión leve o moderada **(Estudio III)**.

MATERIAL AND METHODS

MATERIAL AND METHODS

The material and methods of each individual study comprising the present International Doctoral Thesis are presented below.

STUDY I. Is physical fitness a key element to prevent depressive symptoms in healthy and depressed adults and elderly? A systematic review of cross-sectional and longitudinal studies.

Study 1. Is physical fitness a key element to prevent depressive symptoms in healthy and depressed adults and elderly? A systematic review of cross-sectional and longitudinal studies.

Protocol and registration

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) guidelines (144) shown in **Supplementary Table S1**. Inclusion and exclusion criteria, as well as analytical methods, were specified in advance and registered in the International Prospective Register of Systematic Reviews database (PROSPERO reference number: CRD42021236067).

Literature search strategy

The search was conducted in the PubMed and Web of Science electronic databases, from their inception until February 8th, 2021. The search terms included a combination of keywords related to the following topics: fitness and functional capacity (cardiorespiratory fitness, aerobic capacity or fitness, muscular fitness or strength, muscle strength, range of motion, flexibility, physical fitness, functional capacity, physical characteristic, maximal oxygen consumption, peak oxygen consumption [VO_{2peak}], oxygen capacity, speed-agility, motor fitness and balance), depressive symptoms (depressive symptom, depression, emotional depression and depressive disorder), and age population (adult, middle-aged, aged, aging, ageing, elderly and older people or adult). The connectors 'OR', 'AND' and 'NOT' were used to combine the search terms. Specifically, for PubMed search, we used Medical Subject Heading (MeSH) terms combined with the same term but using the tag for searching in title, abstract, and keywords. As an example for CRF, we introduced ("cardiorespiratory fitness" [Title/Abstract] OR cardiorespiratory fitness [MeSH]). Search terms and search strategies were adapted to each database and can be found in **Supplementary Table S2**. The electronic search was supplemented with a manual review of reference lists from relevant publications to locate additional publications.

Study selection and data extraction

After executing the search strategies for both databases, we imported all the references found into Rayyan QCRI software (145). All processes, including removing duplicates, screening, data extraction, and risk of bias analysis, were conducted using this web-based systematic review tool by two independent researchers (JSM and SOG). Disagreements were resolved by discussion with a third reviewer (VER).

Gray literature (e.g., abstracts, conference proceedings, and editorials), case and intervention studies, and reviews were excluded from the analysis. We also excluded studies including individuals with physical or psychological disorders (except obesity, frailty disorder-related, depression, and major depression), pregnant and postpartum women, or alcoholics and abstinent people. Only cross-sectional or longitudinal studies examining fitness by field and laboratory testing and depressive symptoms using validated scales were included. Studies meeting each of the following criteria were selected for the systematic review: *i*) adults ≥ 18 years, *ii*) healthy or diagnosed depressed people. Studies initially selected by the systematic search were preliminarily screened by title and abstract. The full text of those studies meeting the inclusion criteria was checked to elucidate their eligibility.

We collected the following data from each study, when available: *i*) author's name and year of study publication, *ii*) years of follow-up for longitudinal studies, *iii*) sample characteristics (including the number of participants, sex, and age), *iv*) fitness measurements (such as CRF, upper-limbs muscle strength, lower-limbs muscle strength, upper-limbs flexibility, lower-limbs flexibility, gait (speed and other performance variables), agility-coordination, balance, and functional capacity), *v*) depressive symptoms scale (such as the Beck Depression Inventory, the Geriatric Depression Scale, or the Center for Epidemiologic Studies Depression Scale), and *vi*) main study results (including associations between fitness components and depressive symptoms, and significant or not significant relationships). This data was then synthesized and analysed by fitness component and functional capacity to draw conclusions regarding the associations between fitness and depressive symptoms in healthy and depressed adults and older adults. A detailed description of the tests included in each component is provided in **Supplementary Table S3**.

Quality assessment of the included studies

Study quality in both study designs was evaluated with the Newcastle-Ottawa Scale (NOS) (146). The scale has been designed to assess the quality of non-randomised studies in scientific reviews, and has been applied to longitudinal studies and, subsequently adapted for cross-sectional studies (88,147,148). The NOS scale evaluates three quality parameters: Selection, Comparability and Outcome, each divided into specific items. For longitudinal studies, the Selection item consists of 4 sub-items, the Comparability item consists of 2 sub-items, and the Outcome item consists of 3 sub-items, with a maximum score of 1 point per sub-item. For cross-sectional studies, the Selection item consists of 4 sub-items, and the Comparability item consists of 2 sub-items. However, the sub-items "Ascertainment of the exposure" and "Assessment of the outcome" under Comparability and Outcome, respectively, can receive a maximum of 2 points. The maximum total score for longitudinal studies is 9 and for cross-sectional studies is 10.

Cross-sectional studies with scores of 8-10 were considered high quality (i.e., low risk of bias), scores of 5-7 were considered moderate quality (i.e., moderate risk of bias), and scores less than 5 were considered low quality (i.e., high risk of bias) (147). For longitudinal studies, scores of 8-9 were considered high quality, scores of 6-7 were considered moderate quality, and scores of 5 or less were considered low quality (149,150). Two authors (JSM and SOG) independently scored the studies, and disagreements were resolved by discussion with a third author (ACB).

Qualitative Evidence Synthesis

The data were analysed qualitatively, and the studies included in this systematic review were classified according to the presence of a negative association ($p < 0.05$) or no significant association found, as positive associations were not reported. The level of evidence was classified based on the amount of results of included studies (articles are duplicated when showing significant and non-significant results from multiple analyses), their methodological quality (categorized as low, moderate, or high), and the consistency of the results, as described in previous literature (150,151). The evidence was labeled as "insufficient" if up to 33% of paper's results informed a significant association;

"inconsistent/uncertain" if 34–59% of paper's results reported a significant association or if fewer than four papers reported on the relevant association; and "negative" if 60% or more of paper's results reported a significant negative association. Additionally, following the method developed by Lubans et al. (151), a "consistent negative" association was considered present if $\geq 60\%$ of the "high quality" studies found a significant negative association.



STUDY II. Independent and combined associations of physical fitness components and body composition with depressive symptoms in older adults. INTERMAE STUDY.

Study II. Independent and combined associations of physical fitness components and body composition with depressive symptoms in older adults. INTERMAE STUDY.

Participants and selection criteria

The current study used cross-sectional baseline data of a randomized controlled trial (RCT registered in "ClinicalTrials.gov", Identifier: NCT03923712). Two hundred eighty older adults were recruited from 13 public health care centres from Cádiz (Spain) between February 2018 and March 2020. Participants were eligible to participate if they were the following conditions: (i) between 65 to 75 years, (ii) able to carry out the instrumental ADL, (iii) do not suffer any injury-avoiding participants from doing physical activity, and (iv) do not be involved in doing supervised physical activity greater than 20 minutes/day and 3 days/week. We excluded participants with the following conditions: (i) acute or terminal disease, (ii) severe depression, (iii) unstable cardiovascular disease, dementia, or Alzheimer's disease, (iv) medical history of ictus, epilepsy, or brain cancer, (v) severe visual problems, and (vi) alcohol and drug abuse. The final sample consisted of 92 participants (41 females) who had a valid measure of depressive symptoms and at least one measure of physical fitness test or body composition test at baseline (**Supplementary figure S1**).

Ethical considerations

All participants provided written informed consent before enrolment. The study protocol was designed in accordance with the 2013 Declaration of Helsinki (152) and approved by the Human Ethics and Research Committee of the research in Cádiz and the Andalusian Coordinating Committee on Biomedical Research Ethics (codes: 0667-M1-17 and 04/2018, respectively).

Outcomes measures

Sociodemographic characteristics

A sociodemographic questionnaire was used to collect information on age, antidepressant medication, economic stress, smoking status, alcohol intake, educational

level, marital status, and number of comorbidities. Antidepressant medication and economic stress were coded as "yes" or "no" (49,153). Smoking status and alcohol intake were coded as "current", "former" or "never" smoker and alcohol intake (154). Educational level was coded as "up primary education" or "higher education" (154). Marital status was coded as "without" or "with couple" (69). Finally, the number of comorbidities was coded as "none to 2" or "3 to more diseases" (69). The Pittsburgh Sleep Quality Index (155) was used to assess sleep quality, with a score from 0 to 21; the higher the score on the index, the worse the quality of sleep.

Body composition

Body composition variables such as weight, height, BMI, fat mass, fat free mass and muscle mass percentages, and waist and hip circumferences, were measured. Specifically, participants were barefoot and wearing underwear.

Body weight was measured with a multifrequency bioimpedance (TANITA-MC780MA) (156,157), and height was measured in the Frankfurt plane with a stadiometer (Type SECA 225; range, 60–200 cm; precision, 1 mm) (158). Once the Frankfurt plane was ensured, the evaluator stood in front of the participant and asked him to place his feet and legs together with his head firmly positioned against the back plane of the stadiometer. The participant was then held by the hands, with the thumbs under the jaw and the rest of the fingers at the sides of the head. Finally, the participant was asked to take a deep breath and exhale, at which precise height was taken. The average of the two measurements of height variable was used for the analyses.

BMI was calculated as weight divided by height squared (kg/m^2) (110). BMI was also collapsed into 4 categories: underweight ($<18.5 \text{ kg/m}^2$), normal-weight ($18.5\text{--}24.9 \text{ kg/m}^2$), overweight ($25\text{--}29.9 \text{ kg/m}^2$) and obese ($\geq 30 \text{ kg/m}^2$) (110). Moreover, BMI was also dichotomized as fat (overweight and obese) and not fat (underweight and normal weight) groups.

The waist and hip circumferences (cm) were assessed using a metallic non-extensible tape (Lufkin W606PM, Washington, United States) in accordance with the International Society for the Advancement of Kinanthropometry (ISAK) guidelines standard techniques (159). More exactly, waist circumference was taken at the midpoint between the lower

lateral costal border (10th rib) and the iliac crest, perpendicular to the longitudinal axis of the trunk. The participant adopted a relaxed standing position with arms crossed at the thorax and the measurement was angled after normal expiration. For hip circumference, it was taken at the level of the maximum posterior prominence of gluteus, perpendicular to the longitudinal axis of the trunk. The participant adopted a standing position with arms crossed at the thorax, feet together and gluteus relaxed. The mean of two measurements was recorded, except if there was a higher difference than 0.5 cm a third assessment was performed, and the mean of the two closest measurements was used in the analysis. Waist circumference was categorised as low risk of obesity or not fat (<99 cm for women and <106 cm for men) and high risk of obesity or fat ($\geq$ 99 cm for women and $\geq$ 106 cm for men) based on cut-off for older adults (111).

Fat mass, fat free mass and muscle mass percentages were obtained using a multifrequency bioimpedance (TANITA-MC780MA) (156,157). The older adult participants were grouped into four categories (underfat, healthy, overfat and obese) based on the sex- and age- specific cut-off points of fat mass, namely 60 years and older, as detailed in a previous study (113). These categories were dichotomised into “not fat” (including underfat and healthy) and “fat” (including overfat and obese) groups, as shown in **Table 1**.

Table 1. Sex- and age-ranges cut-off points of fat mass (%) adapted from Gallagher et al. (113).

Sex	Years	NOT FAT		FAT	
		Underfat	Healthy	Overfat	Obese
Men	20-39	<8	8-19.9	20-24.9	$\geq$ 25
	40-59	<11	11-21.9	22-27.9	$\geq$ 28
	$\geq$ 60	<13	13-24.9	25-29.9	$\geq$ 30
Women	20-39	<21	21-32.9	33-38.9	$\geq$ 39
	40-59	<23	23-33.9	34-39.9	$\geq$ 40
	$\geq$ 60	<24	24-35.9	36-41.9	$\geq$ 42

Physical fitness components

Physical fitness was assessed using the Senior Fitness Test (SFT), Short Physical Performance Battery (SPPB), handgrip, gait speed, and CPET tests.

SFT (160) included the following tests:

Back scratch test sought to evaluate upper-limbs flexibility. The standing participant passed one hand (palm down) over the shoulder and tried to reach as far as possible to contact the opposite hand (palm up) which was placed around the back. The distance between the two third fingers was recorded, and a negative score was given if the participant could not touch the measurement point and if going beyond a positive score. Two attempts were performed for each arm and the average of the best attempts in cm was used.

Chair sit and reach test aimed to assess lower-limbs flexibility. The seated participant extended one leg, and with the knee unbent, they tried to reach the toes of the extended leg with both hands. The distance between their fingers and toes was recorded, and a negative score was given if the participant could not touch the measurement point and going beyond a positive score. Two attempts were performed for each leg and the average of the best attempts in cm was used.

Chair stand test intended to appraise lower-limbs muscle strength. The participant seated and with arms folded across the chest, stood up and sat in the chair as many times as possible within 30 seconds. A single attempt was performed, and the number of repetitions was recorded.

Arm curl test aimed to determine upper-limbs muscle strength. The participant seated performed arm extension-flexion with a full range of motion, as many times as possible in 30 seconds holding a weight (2.3 kg for women and 3.6 kg for men) in the hand. A single attempt was performed for each arm and the number of repetitions for each arm was recorded. The sum of the repetitions of both arms was used.

8-ft up-and-go test is meant to ascertain agility. The participant got up from a chair, walked 2.44 m, turns around a cone and returned to sit down again, as quickly as possible. Performed 2 times and the best time in seconds was used.

6 minutes walking test purposed to assess cardiorespiratory fitness. The participant walked for 6 minutes as fast as possible along a flat 60-m circuit. It was allowed to stop and rest when needed during the test, but the time was still ticking. A single attempt was performed, and the maximum distance (m) was recorded within the time.

SPPB (38,39) aimed to assess functional capacity, and it is composed of the following test divided into 3 domains:

4-m walking aimed to evaluate gait speed at normal or usual pace. The participant walked a marked distance of 4-m at a usual speed. The time in seconds walking the distance was recorded.

Foot positions side by side, semi tandem (one foot slightly further ahead than the other) and tandem stand (one foot directly in front of the other) were meant to gauge balance. In that order, each position must be held for 10 seconds. The possibility of having done it, or the time the participant was able to hold it, was recorded.

Chair stand tests (1 and 5 repetitions) were carried out to measure lower-limbs muscle strength (possibility of performing 1-repetition and seconds in 5-repetitions chair stand). The seated participant performed a single stood-up from the chair, and then, if successful, performed 5 repetitions as fast as possible. The time in seconds taken to perform 5 repetitions was recorded.

All tests of SPPB were performed only once. Based on the performance in each test explained above, a score between 0 (highly dependent) and 12 (totally independent) was established to determine the functional capacity of the participant (38). In short, the sum of the results (ranging from 0 to 12 points) and independent performance registered in 4-m walking and 5-repetitions chair stand tests were used for these analyses.

The handgrip test (89,90) aimed to assess upper-limb muscle strength using a digital dynamometer (TKK 5101 Grip-D, Tokyo, Japan). For a correct grip, the dynamometer was adjusted at 5.5 size for males, and for females, the optimal grip was adjusted according to the size of the hand (161). All participants performed two attempts with each hand and the mean of the best attempts from each hand was recorded in kilograms.

Gait speed tests (72,77) comprised walking 6-m at usual pace and maximal pace, and the time required to walk the distance at each pace was measured to calculate gait speed in m/s.

An incremental CPET until exhaustion was conducted on a treadmill (Lode Valiant, Groningen, Netherlands) using the modified Bruce protocol (162), which has been previously used in a similar sample and designed for a geriatric population (163,164). Only test attempts that met the maximality criteria explained previously (165) were considered. Oxygen consumption was measured breath-by-breath using indirect calorimetry through a gas analyser of open circuit, Jaeger MasterScreen CPX® (CareFusion, San Diego, USA) and VO_{2peak} was considered the highest observed value of oxygen consumption obtained in the last three intervals of 10 seconds. VO_{2peak} absolute and VO_{2peak} relative were used for the analysis.

For analyses, each fitness test variable mentioned was divided into unfit (the lowest 30%) and fit (the highest 70%) groups, based on sex.

Depressive symptoms

Depressive symptoms were assessed using the short version of the Geriatric Depression Scale (GDS-15)(166). The scale was developed for use among older people (167), including people with cognitive impairment (168). GDS-15 was validated previously in Spanish participants over 65 years old (169). The questionnaire contains 15 items structured by yes/no responses and scores range from 0 to 15, with higher scores indicating the presence of more depressive symptoms. The cut-off score of ≥ 5 , for possible depression screening, has a sensitivity of 0.80 and a specificity of 0.79 (170). GDS-15 was administered in interviews to facilitate completion by older people.

Confounding variables

The following variables were explored as potential confounders: sex, antidepressant medication (yes/no), depression diagnosis (yes/no), smoking status (current, former, and never smokers), alcohol intake (current, former, and never intake), comorbidities (none to 2 and 3 or more), educational level (no formal education or primary school and secondary school or more), economic stress (yes/no), marital status (with couple and without couple), sleep quality and fat mass percentage.

Statistical analyses

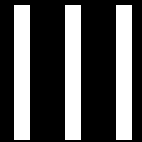
Study sample characteristics are presented as mean $\pm$ standard deviation (SD) for continuous variables or percentages for categorical variables. All variables were checked for normality using both graphical (normal probability plots) and statistical (Shapiro-Wilk test) procedures. T-test and chi-square were used to analyse sex differences in continuous and categorical variables, respectively.

Multiple linear regression analyses were performed using four different models to analyse the association of physical fitness components and body composition (independent variables) with depressive symptoms (dependent variable). The first model was unadjusted (Model 1), while second and third models (Models 2 and 3) were adjusted based on statistical and scientific criteria. Model 4 used stepwise selection methods among the confounders previously obtained by statistical and scientific criteria. Particularly, the statistical criteria used for Models 2 and 3 determined whether the individual association of each potential confounder and its modifying effect on the unadjusted coefficient was higher of 10%. The resulting adjusted models were sex and antidepressant medication (Model 2); sex, antidepressant medication and fat mass percentage (Model 3, except for body composition variables); and antidepressant medication (Model 4). For confounding variables included, the interaction was verified by generating virtual dummy variables in STATA (independent * confounder). As a result, no significant interactions were found for any of the studied variables in the regression models ($p > 0.05$).

Ordered logistic regression analyses were applied to analyse the associations of fitness levels (categorized as unfit and fit) and fatness levels (categorized as fat and not-fat) with depressive symptoms. Dichotomized objectively measured fitness and body composition variables, including BMI, fat mass percentage and waist circumference, were combined to establish fitness and fatness level groups. These groups were categorized as fit and not fat (used as reference group), fit and fat, unfit and not fat, and unfit and fat. The same adjusted models were performed.

Regression model diagnostics were carried out to check the assumptions (linearity, homoscedasticity, and normality), at least one of them had to be fulfilled in order to keep

the model. All the analyses were performed using the STATA software for Windows version 13.0. The level of significance was set at $p < 0.05$ in the statistical model.



STUDY III. Independent and combined associations of physical fitness and body composition with depressive symptoms in adults with diagnosed mild to moderate depression: SONRIE STUDY.

Study III. Independent and combined associations of physical fitness and body composition with depressive symptoms in adults with diagnosed mild to moderate depression: SONRIE STUDY.

Participants and selection criteria

The present study is a part of the SONRIE Study, a RCT (registered in "ClinicalTrials.gov", Identifier: NCT05849792) designed to analyse the effect of 12-week online physical exercise program on depression in adults with mild-to-moderate depression aged 25-65 years from Spain. The current study analysis focuses on the cross-sectional baseline data of the SONRIE study which was collected between September 2019 and March 2020. One hundred seventy-one participants were recruited from Mental Health Clinical Management Unit in the province of Cadiz and were eligible to participate if they had a psychiatric diagnosis of mild-to-moderate depression according to International Classification of Diseases 10th Revision (ICD-10) criteria (4), and no physical disability or health problems, which could prevent them from practising physical exercise. We excluded participants with the following conditions: (i) acute or terminal disease, (ii) severe depression, (iii) unstable cardiovascular disease, (iv) medical history of ictus, epilepsy, or brain cancer, and (v) severe hearing and visual impairment. The final sample of the present study consisted of 82 participants (69 women) with a valid measure of depressive symptoms and at least one measure of fitness test or body composition test at baseline (**Supplementary figure S2**).

Ethical considerations

All participants provided written informed consent before enrolment. The SONRIE study protocol was designed in accordance with the 2013 Declaration of Helsinki (38) and approved by the Ethics and Research Committee of the "Hospital Universitario de Puerta del Mar" (Cadiz, Spain) (code: 1875-N-18).

Outcome measurements

Sociodemographic characteristics

A sociodemographic questionnaire was used to collect information on age, antidepressant medication, economic stress, smoking status, alcohol intake, educational level, marital status, and number of comorbidities. The 36-Item Short Form Survey question "Pain interference with your normal work?" (171) was used to assess trouble with body pain. Additionally, mental health medical history was recorded to assess the persistence of depression diagnosis. Antidepressant medication and economic stress were coded as "yes" or "no" (49,153). Trouble with body pain was coded as "no", "moderately", or "quite to extremely" (69). The persistence of depression was registered as years post-diagnosis (172,173). Smoking status and alcohol intake were coded as "current", "former" or "never" smoker and alcohol intake (154). Educational level was coded as "up primary education" or "higher education" (154). Marital status was coded as "without" or "with couple" (69). Finally, the number of comorbidities was coded as "none to 2" or "3 to more diseases" (69).

Body composition variables

The body composition assessment was similar to the methods applied in Study II, but with different cut-off points for waist circumference and percentage fat mass for adults.

Waist circumference was categorised as low risk of obesity or not fat (<88 cm for women and <102 cm for men) and high risk of obesity or fat (≥88 cm for women and ≥102 cm for men) based on cut-off for adults (112).

The adults participants were grouped into four categories (underfat, healthy, overfat and obese) based on the sex- and age- specific cut-off points of fat mass, as detailed in a previous study (113). These categories were dichotomised into "not fat" (including underfat and healthy) and "fat" (including overfat and obese) groups, as shown in **Table 1**.

In this Study III, hip circumference was also categorised as low risk of obesity or not fat (the lowest 50%) and high risk of obesity or fat (the highest 50%) groups, based on age group (divided by tertiles) and sex (174,175).

Physical fitness component

The fitness tests have been explained above, in the methods of the Study II, except for the following tests:

Unipedal stance test (176) purposed to evaluate balance. The participant stood on one leg with open eyes and hands on the hips and held a maximum of 1 min. Time was stopped when the foot contacted the ground again, the standing foot moved, or the hands left the hip. All participants performed two attempts with each leg and the mean of the best attempts from each leg was recorded in seconds.

Standing long jump test (177) aimed to assess lower-limbs muscle strength. The participant behind the starting line jumped forward with feet together as far as possible. The distance from the starting line to the point where the back of the heel was closest to the starting line was considered. All participants performed two attempts and the best attempt was recorded in cm.

Lastly, this study also measured fitness subjectively. Self-reported fitness was measured using the adapted Spanish version of International Fitness Scale validated in youth and older adults (178,179). The item of general fitness with 5 statements (very poor/ poor/ average/ good/ very good), was collected. Self-reported fitness was divided into unfit (very poor to poor) and fit (average to very good) groups.

For analyses, each fitness test variable mentioned was divided into unfit (the lowest 50%) and fit (the highest 50%) groups, based on sex and age group (divided by tertiles).

Depressive symptoms

Depressive symptoms were measured using the Beck Depression Inventory II (BDI-II) (180,181), adapted version for Spain (182), which has been validated in Spanish adults with several psychopathological disorders. This self-reported scale does not diagnose depression but reports the severity of depressive symptoms. The BDI-II is composed of 21 items with 4 statements describing the severity of depressive symptoms. The range of scores is 0-63 and a higher score indicates depressive symptoms.

The severity of depressive symptoms has been categorized, as in previous studies (183,184), into four ordering levels based on sensitivity (0.76-0.89) and specificity (0.73-

0.82) cut-offs (185). These ordered levels were defined by a score of 0-13 (minimal), 14-19 (mild), 20-28 (moderate), and 29-63 (severe). Moreover, the severity of depressive symptoms was also dichotomized as lower (minimal to moderate symptoms: <29) and upper categories (severe symptoms: ≥30).

Confounding variables

The following variables were considered as potential confounders: age, antidepressant medication (yes/no) (153), economic stress (yes/no) (49), trouble with body pain (no to moderately/quite to extremely) (69), the persistence of depression (years' post-diagnosis) (172,173), smoking status (current, former, and never smokers), alcohol intake (current, former, and never intake) (154), comorbidities (none to 2 and 3 or more) (69), educational level (no formal education or primary school and secondary school or more) (154), marital status (with couple and without couple) (69), and BMI (69).

Statistical analyses

Normal distributions were ascertained, and homogeneity of variances was confirmed, after visual assessment of the frequency histogram and Shapiro–Wilk's, respectively. Participant characteristics are presented as mean and SD for continuous variables and frequencies for categorical variables. Differences between participants according to sex, i.e., men vs women, and severity of depressive symptoms, i.e., lower vs upper category, were analyzed by paired T-test for continuous variables and chi-square tests for categorical variables.

Multiple linear regression analyses were used to examine the association of fitness and body composition variables (independent variables) with depressive symptoms (dependent variable). Three models were applied: an unadjusted model (Model 1), and two adjusted models (Models 2 and 3) that were developed based on both statistical and scientific criteria. To construct the adjusted models, the individual association of each potential confounding variable and its modifying effect on the coefficient (>10%) from the pure model were analysed. Model 2 included age, BMI (except for body composition variables), the persistence of depression, economic stress, and trouble with body pain as confounding variables, while Model 3 added antidepressant medication as an additional variable but removed the persistence of depression. No significant interactions were

found for any of the studied variables in the regression models ($p>0.05$). Additionally, multicollinearity was not found in any of the models used in this study, as the variance inflation factor was below 10 and averaged variance inflation factor was close to 1 (186).

Logistic regression analyses were conducted on those variables that showed a significant association in the linear regression analyses. Specifically, it was applied to examine the associations between dichotomized fitness (unfit and fit groups) and body composition (fat and not fat) variables with the severity of depressive symptoms (upper and lower depressive symptoms categories). For Model 2 and 3, age was excluded as a predictor for objectively measured fitness and hip circumference variables; and BMI was dropped for the hip circumference variable. Firth's penalized maximum likelihood estimation was employed in the following logistic regression models to address potential bias caused by the small sample size and limited total information available, thereby enhancing the accuracy and robustness of the obtained results (187). Model 2 focused on examining the association between self-reported fitness and depressive symptoms, taking into account the potential biases associated with self-reported fitness. In Model 3, all associations were analysed to mitigate biases resulting from the small sample size and limited total information. The significance of predictor variables was assessed using Wald tests, and odds ratios with corresponding 95% confidence intervals were calculated.

Ordered logistic regression analyses were applied to explore the relationship of fitness levels (categorized as unfit and fit) and fatness levels (categorized as fat and not-fat) with the severity of depressive symptoms (categorized as minimal, mild, moderate, and severe) on those variables that showed a significant association in the previous regression analyses. Dichotomized objectively measured fitness and body composition variables, including BMI, fat mass percentage and waist and hip circumferences, were combined to establish fitness and fatness level groups. These groups were categorized as fit and not fat (used as reference group), fit and fat, unfit and not fat, and unfit and fat. Model 2, which excluded age and BMI, was used to analyze the relationship between fitness and fatness level groups and the severity of depressive symptoms.

To examine the independence of the association of self-reported fitness with depressive symptoms with respect to the objectively fitness level of the participant, adjusted multiple linear regression analyses were conducted with separate covariates of

objectively measured fitness variables (usual gait speed at 4-m, unipedal stance test, handgrip test and 6-min walking test).

All the analyses were performed using the STATA software for Windows version 13.0. The level of significance was set at $p < 0.05$ in the statistical model.

A summary of the methodologies of the included studies is shown in **Table 2**.

Table 2. General overview of the methodology followed in the studies included in this International Doctoral Thesis.

Study	Design	Participants	Independent (exposure) variables	Dependent (outcome) variables
I: Is physical fitness a key element to prevent depressive symptoms in healthy and depressed adults and elderly? A systematic review of cross-sectional and longitudinal studies.	Systematic review	247,483 adults and older adults (longitudinal studies) 230,174 adults and older adults (cross-sectional studies)	Fitness components	Depressive symptoms
II: Independent and combined associations of physical fitness components and body composition with depressive symptoms in older adults. INTERMAE STUDY.	Cross-sectional	92 older adults (44.5% women)	Fitness components Body composition	Depressive symptoms
III: Independent and combined associations of physical fitness and body composition with depressive symptoms in adults with diagnosed mild to moderate depression: SONRIE STUDY.	Cross-sectional	82 adults with depression diagnosed (84.15% women)	Fitness components Self-reported fitness Body composition	Depressive symptoms

RESULTS AND DISCUSSION

RESULTS

The results of the individual studies comprised in this International Doctoral Thesis are presented underneath.

STUDY I. Is physical fitness a key element to prevent depressive symptoms in healthy and depressed adults and elderly? A systematic review of cross-sectional and longitudinal studies.

Study 1. Is physical fitness a key element to prevent depressive symptoms in healthy and depressed adults and elderly? A systematic review of cross-sectional and longitudinal studies.

RESULTS

Study selection

A total of 14,252 studies (PubMed: 5,713; Web of Science: 8,539) were identified through the electronic database search. Additional records were found from other sources (n=3). Of these, 2,848 duplicated studies were eliminated before screening. After checking the title and abstract, 232 full-text studies were selected for further review. Finally, after applying the criteria for inclusion and exclusion, 102 studies were included and evaluated in the present work. See the flow diagram summarizing the selection process in **Figure 3** and, the number of studies published per year of these finally included, in **Supplementary Figure S3**.

Quality assessment and publication bias

To assess the "Ascertainment of the exposure", all studies were awarded the highest score (1 point for longitudinal studies and 2 points for cross-sectional studies) as they had to meet the inclusion criterion of using a validated measurement tool. Moreover, studies were considered to have controlled for the most important factor if they assessed at least 2 covariates. If they included more covariates, they were deemed to have controlled for additional variables.

Furthermore, since all outcome instruments were self-reported and referred to depressive symptoms, each study received the maximum score (1 point for longitudinal and 2 points for cross-sectional studies) for the "Assessment of the outcome", following the specific NOS criteria for this item. As a result, the total score for longitudinal studies was 8 instead of 9, and 9 points instead of 10 for the cross-sectional studies.

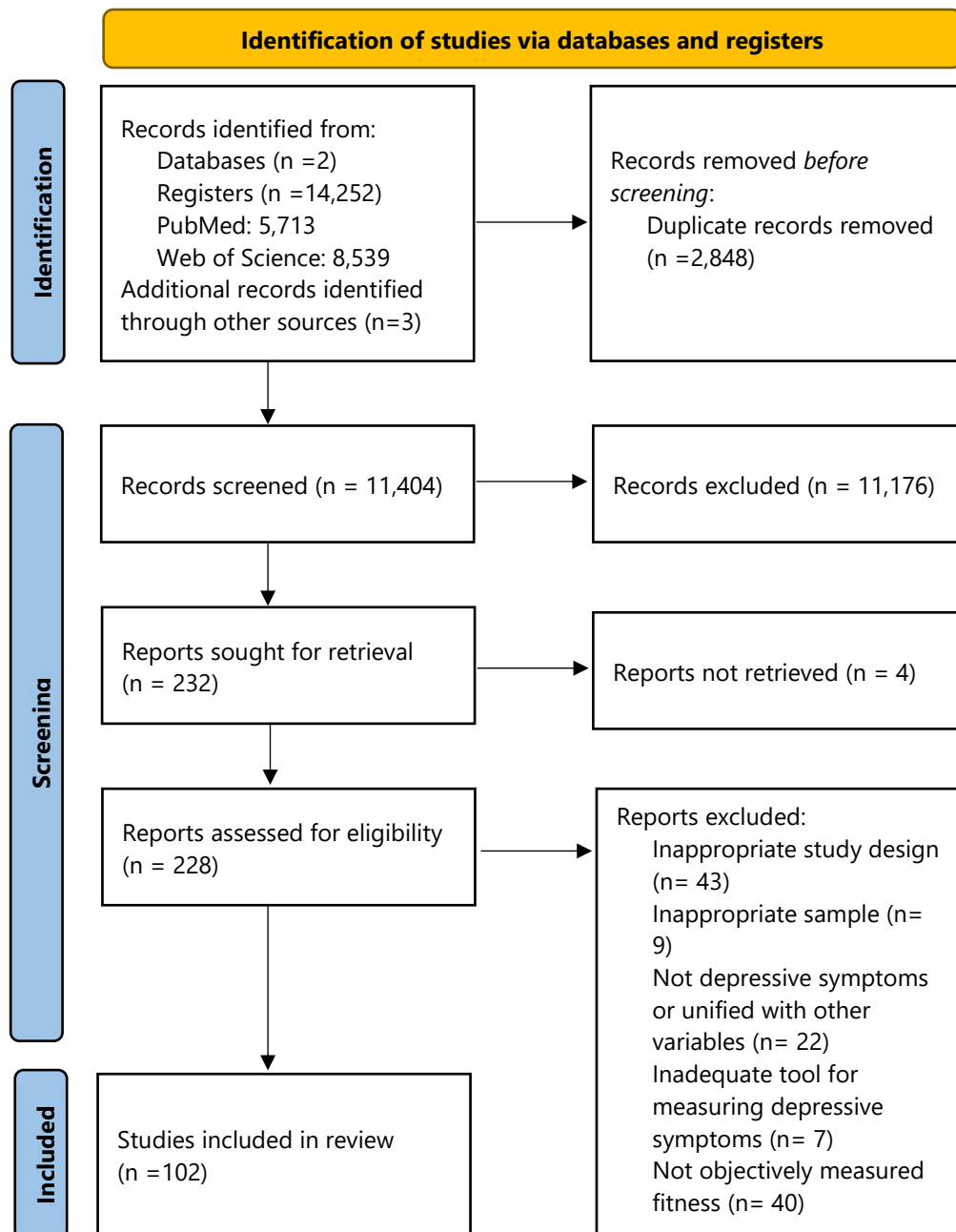


Figure 3. PRISMA flow chart of the selection process.

The results related to the risk of bias assessment are detailed in **Tables 3 and 4**. According to NOS for longitudinal studies, 17 studies (54%) were identified as “high quality”, 13 studies (46%) as “moderate quality”, and none as “low quality”. Regarding cross-sectional studies, according to the adapted NOS scale, 74 studies (90%) were identified as “high quality”, 8 studies (10%) as “moderate quality” and none as “low quality”. Therefore, all studies included in this study had low or moderate risk of bias.

Table 3. Quality assessment with NOS of the longitudinal studies included in this systematic review.

First author, publication year	SELECTION				COMPARATIBILITY		OUTCOME			Total quality scores	Classification of quality
	Representative present cohort	Selection of non-exposed	Ascertainment of the exposure [†]	Outcome not present at start	The study controls for the most important factor ^{††}	The study control for any additional factor ^{†††}	Assessment of the outcome ^{†††}	Adequate follow-up length	Adequate follow-up		
Baumeister et al., 2017 (63)	*	*	*	*	*	*	-	*	-	7	Moderate
Becofsky et al., 2015 (138)	*	*	*	*	*	*	-	*	*	8	High
Bertoni et al., 2018 (188)	*	*	*	*	*	*	-	*	-	7	Moderate
Briggs et al., 2018 (189)	*	*	*	-	*	*	-	*	*	8	High
Carvalho et al., 2019 (190)	*	*	*	-	*	*	-	*	-	7	Moderate
Chen et al., 2019 (191)	-	*	*	*	*	*	-	-	*	6	Moderate
Chu et al., 2020 (70)	*	*	*	*	*	*	-	-	*	7	Moderate
Conradsson et al., 2013 (53)	*	*	*	-	*	*	-	*	*	7	Moderate
Fukumori et al., 2015 (192)	*	*	*	*	*	*	-	-	*	7	Moderate

Table 3 (continued)

Gianfredi et al., 2021 (153)	*	*	*	*	*	*	-	*	*	8	High
Hamer et al., 2015 (193)	*	*	*	*	*	*	-	*	*	8	High
Hollenberg et al., 2003 (60)	*	*	*	*	*	*	-	*	*	8	High
Kandola et al., 2020 (194)	*	*	*	*	*	*	-	*	*	8	High
Kim et al., 2019 (195)	*	*	*	*	*	*	-	*	*	8	High
Krishnamurth et al., 2006 (196)	*	*	*	*	*	*	-	*	*	8	High
Lever-van Milligen et al., 2017 (68)	*	*	*	*	*	*	-	*	*	8	High
Lys et al., 2019 (197)	*	*	*	-	*	*	-	*	*	7	Moderate
McDowell et al., 2018 (91)	*	*	*	*	*	*	-	*	*	8	High
Patino et al., 2021 (198)	*	*	*	*	*	*	-	*	*	8	High
Payette et al., 2011 (199)	*	*	*	-	*	*	-	*	*	7	Moderate
Penninx et al., 1998 (200)	*	*	*	*	*	*	-	*	*	8	High
Rantanen et al., 2000 (201)	*	*	*	-	*	*	-	*	-	6	Moderate

Table 3 (continued)

Stessman et al., 2017 (71)	*	*	*	-	*	*	-	*	*	7	Moderate
Sui et al., 2009 (202)	*	*	*	*	*	*	-	*	*	8	High
Taekema et al., 2010 (203)	*	*	*	-	*	*	-	*	-	7	Moderate
Tomey et al., 2010 (49)	*	*	*	*	*	*	-	*	-	7	Moderate
Veronese et al., 2017 (64)	*	*	*	-	*	*	-	*	*	8	High
Zhao et al., 2020 (69)	*	*	*	*	*	*	-	*	*	8	High

^{*} For this index, one star was given to all studies since fitness was defined in the method section according to a validated measurement tool. ^{**} For this index, one star was given if two confounding factors were evaluated. ^{***} For this index, one star was given if additional factor was evaluated. ^{****} For this index, no star, out of a maximum of 1 star, was given to any study since depressive symptoms were measured by self-reported questionnaire. **NOS**, Newcastle-Ottawa Scale; * One star or point on the criteria met; - Criteria not met.

Table 4. Quality assessment with NOS of the cross-sectional studies included in the systematic review.

First author, publication year	SELECTION				COMPARATIBILITY		OUTCOME		Total quality Scores	Classification of quality
	Representative sample	Sample size	Non-respondents	Ascertainment of the exposure (risk factor) [†]	The study controls for the most important factor ^{††}	The study control for any additional factor ^{†††}	Assessment of the outcome ^{††††}	Statistical test		
Avila-Funes et al., 2008 (76)	*	*	*	**	*	*	*	*	9	High
Boström et al., 2014 (94)	*	*	*	**	*	*	*	*	9	High
Brandon and Loftin, 1991 (204)	-	*	*	**	*	-	*	*	8	High
Briggs et al., 2018 (189)	*	*	*	**	*	*	*	*	9	High
Brooks et al., 2018 (90)	*	*	-	**	*	*	*	*	8	High
Brown et al., 2014 (205)	*	*	*	**	*	*	*	*	9	High

Table 4 (continued)

Brown et al., 2020 (93)	-	*	*	**	*	*	*	*	9	High
Buchman et al., 1991 (206)	-	*	-	**	*	-	*	*	6	Moderate
Carvalho et al., 2019 (190)	*	*	*	**	*	*	*	*	9	High
Castaneda-Sceppa et al., 2010 (77)	*	*	*	**	*	*	*	*	9	High
Chen et al., 2017 (207)	*	*	*	**	*	*	*	*	9	High
Chen et al., 2020 (78)	*	*	*	**	*	*	*	*	9	High
Chu et al., 2020 (70)	*	*	*	**	*	*	*	*	9	High
De Souza-Vasconcelos et al., 2016 (208)	*	*	*	**	*	*	*	*	9	High
Enright et al., 2003 (209)	*	*	*	**	*	*	*	*	9	High
Fried et al., 1990 (210)	-	*	*	**	*	-	*	*	7	Moderate

Table 4 (continued)

Fukumori et al., 2015 (192)	*	*	*	**	*	*	*	*	9	High
Galper et al., 2006 (211)	*	*	*	**	*	*	*	*	9	High
Gerber et al., 2013 (56)	*	*	*	**	*	*	*	*	9	High
Giuliani et al., 2008 (79)	*	*	*	**	*	*	*	*	9	High
Goins, Innes and Dong, 2012 (212)	*	*	*	**	*	*	*	*	9	High
Gu et al., 2021 (154)	*	*	*	**	*	*	*	*	9	High
Gurina et al., 2011 (213)	*	*	-	**	*	*	*	*	8	High
Hamacher et al., 2018 (51)	*	*	-	**	*	*	*	*	8	High
Hamer et al., 2011 (214)	*	*	*	**	*	*	*	*	9	High
Kyu-Man et al., 2019 (215)	*	*	*	**	*	*	*	*	9	High

Table 4 (continued)

Hayashi et al., 2019 (216)	*	*	*	**	*	*	*	*	9	High
Herman et al., 2005 (217)	-	*	*	**	*	*	*	*	8	High
Jeoung, 2020 (67)	*	*	-	**	*	-	*	*	7	Moderate
Jin et al., 2017 (57)	-	*	*	**	*	*	*	*	9	High
Kim et al., 2019 (195)	*	*	*	**	*	*	*	*	9	High
Kirk et al., 2020 (218)	*	*	*	**	*	*	*	*	9	High
Kose et al., 2005 (219)	-	*	-	**	*	-	*	*	6	Moderate
Kvelde et al., 2010 (80)	*	*	*	**	*	*	*	*	9	High
Laredo-Aguilera et al., 2019 (220)	*	*	*	**	*	-	*	*	8	High
Lee and Hong, 2016 (81)	*	*	*	**	*	*	*	*	9	High
Lee and Ryan., 2020 (221)	*	-	*	**	*	*	*	*	8	High

Table 4 (continued)

Lee, 2015 (59)	*	*	*	**	*	-	*	*	8	High
Lee, 2018 (92)	*	*	*	**	*	*	*	*	9	High
Levinger et al., 2012 (50)	-	*	*	**	*	*	*	*	8	High
Lin et al., 2017 (222)	*	*	-	**	*	*	*	*	8	High
Ling et al., 2010 (223)	*	*	*	**	*	*	*	*	9	High
Lord et al., 2002 (224)	*	*	-	**	*	*	*	*	8	High
Marconcin et al., 2020 (225)	*	*	*	**	*	*	*	*	9	High
Marques et al., 2020 (226)	*	*	*	**	*	*	*	*	9	High
McDowell et al., 2018 (91)	*	*	*	**	*	*	*	*	9	High
Michel- Pellegrino et al., 2007 (227)	-	*	-	**	*	*	*	*	7	Moderate
Mollaoglu et al., 2012 (52)	*	*	*	**	*	-	*	*	8	High

Table 4 (continued)

Moy et al., 2011 (228)	-	*	-	**	*	*	*	*	7	Moderate
Noguerón et al., 2020 (229)	*	*	*	**	*	*	*	*	9	High
Olgun- Yazar et al., 2019 (230)	*	*	*	**	*	-	*	*	8	High
Park et al., 2019 (89)	*	*	*	**	*	*	*	*	9	High
Patino- Hernandez et al., 2017 (231)	*	*	*	**	*	*	*	*	9	High
Rice et al., 2010 (55)	*	*	-	**	*	*	*	*	8	High
Rodríguez- Hernández et al., 2014 (54)	-	*	*	**	*	-	*	*	7	Moderate
Roth and Holmes, 1985 (232)	*	*	*	**	*	-	*	*	8	High
Russo et al., 2007 (73)	*	*	*	**	*	*	*	*	9	High
Sáez- Padilla et al., 2020 (82)	*	*	*	**	*	*	*	*	9	High

Table 4 (continued)

Sallinen, et al., 2011 (233)	*	*	*	**	*	*	*	*	9	High
Seino et al., 2013 (83)	*	*	*	**	*	*	*	*	9	High
Serrano-Checa et al., 2020 (96)	*	*	-	**	*	*	*	*	8	High
Singhal et al., 2020 (84)	*	*	*	**	*	*	*	*	9	High
Smith et al., 2018 (75)	*	*	*	**	*	*	*	*	9	High
Smith et al., 2019 (234)	*	*	-	**	*	*	*	*	8	High
Staples et al., 2020 (74)	*	*	-	**	*	-	*	*	7	Moderate
Stessman et al., 2017 (71)	*	*	*	**	*	*	*	*	9	High
Suija et al., 2013 (41)	*	*	*	**	*	*	*	*	9	High
Szlejf et al., 2019 (235)	*	*	*	**	*	*	*	*	9	High
Taani et al., 2018 (85)	*	*	*	**	*	-	*	*	8	High

Table 4 (continued)

Taekema et al., 2010 (203)	*	*	*	**	*	*	*	*	9	High
Takahashi et al., 2006 (236)	-	*	*	**	*	*	*	*	8	High
Thapa et al., 1994 (237)	*	*	*	**	*	*	*	*	9	High
Tiihonen et al., 2018 (86)	*	*	*	**	*	*	*	*	9	High
Tolmunen et al., 2006 (238)	*	*	*	**	*	*	*	*	9	High
Vanoh et al., 2016 (58)	*	*	*	**	*	*	*	*	9	High
Venant et al., 2019 (183)	*	*	*	**	*	*	*	*	9	High
Viana et al., 2013 (239)	*	*	*	**	*	*	*	*	9	High
Wang et al., 2018 (72)	*	*	*	**	*	*	*	*	9	High
Woo et al., 2016 (240)	*	*	*	**	*	*	*	*	9	High
Wu et al., 2017 (128)	*	*	*	**	*	*	*	*	9	High

Table 4 (continued)

Yanagita et al., 2006 (87)	*	*	*	**	*	*	*	*	9	High
Youssef, 2005 (241)	*	*	*	**	*	*	*	*	9	High

*[†] For this index, two stars were given to all studies since fitness was defined in the method section according to a validated measurement tool. ^{††} For this index, one star was given if two confounding factors were evaluated. ^{†††} For this index, one star was given if an additional factor was evaluated. ^{††††} For this index, one star out of a maximum of 2 was given to all studies since depressive symptoms were measured by self-reported questionnaires. **NOS**, Newcastle-Ottawa Scale; * One star or point on the criteria met; - Criteria not met.*

Data extraction: study sample characteristics

The characteristics of the 102 unique studies included (8 of them duplicated for both designs) are provided in **Table 5** (longitudinal studies) and **Table 6** (cross-sectional studies). Longitudinal studies were 28 (49,53,138,153,188–195,60,196–203,63,64,68–71,91) (n= 247,483 participants) and cross-sectional studies were 82 (41,50,67,70–78,51,79–87,89,52,90–94,96,128,154,183,189,54,190,192,195,203–209,55,210–219,56,220–229,57,230–239,58,240,241,59) (n=230,174 participants). The number of participants per study ranged from 17 to 152,978 and the percentage of women participants varied from 18.4% to 87%. Concretely, 4 studies studied only men (50,87,201,238) and 8 studied only women (49,59,60,81,83,96,220,229). Regarding age, 9 studies were found on individuals aged 50 years and over (55,60,91,190,193,212,226,234,235), 15 studies on adults up to 60 years (41,49,202,204,206,232,238,50,52,56,57,68,69,154,183), 67 studies on those over 60 years (51,53,74–76,78–84,54,85–87,89,90,93,94,96,128,188,58,189,191,196–201,203,205,59,207–210,213–218,64,219–225,227–229,70,231,233,236,237,239–241,71–73), and 11 studies that included both adults and older people (63,67,230,77,92,138,153,192,194,195,211).

On the other hand, 2 studies included only overweight and obese study participants (50,183), 2 studies had 56 and 60% older participants with dementia diagnosis (53,79), 4 studies included participants with a diagnosis of depression but represented less than 10% of the sample (64,90,91,196), 3 studies had 13% (86), 19.8% (63) and 20.7% (92) of their sample diagnosed with depression, and 3 studies (53,68,93) reported that more than 50% of their sample had a diagnosis of depressive disorders.

Study measurements

Fitness component

The most frequently investigated fitness component was upper-limbs muscle strength present in 61% of both longitudinal (n=17 out of 28) (49,64,192–195,197,201,203,68–71,91,188,190,191) and cross-sectional studies (n=50 out of 82) (41,50,73–75,77–79,81–83,85,54,87,89–93,128,154,183,190,57,192,195,203,205,207,208,214–216,220,58,221,223,225,226,228,230,231,234,235,239,59,67,70–72). The second more

relevant component was gait, studied in 18% (5 out of 28) of longitudinal (49,64,191,196,199) and 32% (26 out of 82) cross-sectional studies (50,51,85,87,93,96,205,208,210,216,217,229,72,230,233,237,239,240,73,74,76–79,83). Additionally, CRF was included in 25% (n=7 out of 28) of longitudinal (60,63,64,138,153,194,202) and 22% (n=18 out of 82) of cross-sectional studies (41,50,82,204,206,209,211,224,232,238,52,54–59,67). Lower-limbs muscle strength was studied in only 3 out of 28 longitudinal (11%)(49,64,199) and 18 out of 82 cross-sectional studies (22%)(50,54,81–87,237,58,59,67,76–80). The percentages of each of the fitness components are shown in **Figure 4**.

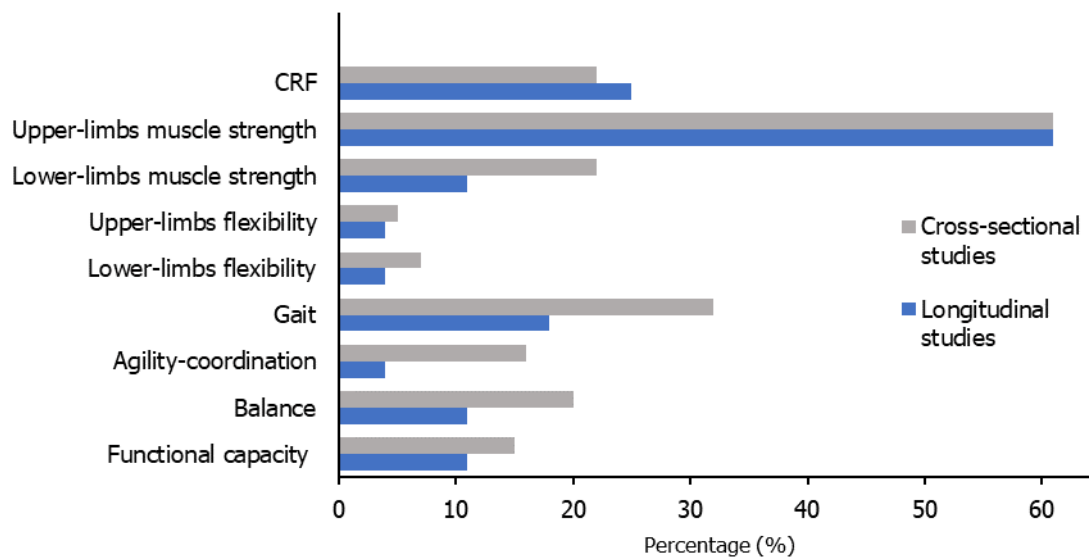


Figure 4. Proportion of fitness components by study design. Several of the articles studied multiple components, resulting in overlapping percentages. **CRF**, cardiorespiratory fitness.

Regarding CRF, the predominant test was submaximal or maximal exercise cycle ergometer (50,52,56,63,153,194,204,232,238) or treadmill testing (55,57,60,138,202,211). In the case of upper-limbs strength, the predominant test used was the hand-held dynamometer, whereas, for lower-limbs strength, chair stand tests prevailed over the other tests. Finally, for gait speed, normal speed walking between 3 to 12 m was the most commonly used test as opposed to fast speed walking which was only used in 3 studies of middle-aged to older people (50,77,233). The frequency of tests per fitness component is listed in **Supplementary Table S3**.

Depressive symptoms

The most commonly depressive symptoms scale used was Geriatric Depression Scale 15 items (n=27 out of 102; 27%) (53,58,196,203,208,210,213,214,216,218,220,221,70,222,223,228,231,236,237,241,72,74,81,85,86,89,94) and 30 items (19%) (54,59,199,209,217,219,224,227,229,230,240,64,67,76,78,80,82,128,191), followed by Centre for Epidemiologic Studies Depression Scale 20 items (15%) (49,60,205,206,211,212,233,77,83,91,189,190,197,198,202), Beck Depression Inventory 21 items (7%) (52,55,57,63,183,204,232), and Patient Health Questionnaire 9 items (6%) (75,90,92,153,194,215). The remaining studies used other scales, such as Hamilton Depression Rating Scale, Self-Rating Depression Scale, or Inventory of Depression Symptomatology, however, their application is minimal.

Table 5. Main characteristics of the longitudinal studies included in the systematic review.

Author, year	Follow-up	Sample characteristics (N, sex, age)	Independent and dependent variables	Main results
Baumeister et al., 2017 (63)	4.5 ys	n=1080 (50.9% women) 25-83 ys 10.7% incident and 9.1% recurrent MDD	Fitness component (test) CRF (maximal exercise cycle ergometer testing) Depressive symptoms scale-items: BDI II-21	(-) CRF was inversely associated with depressive symptoms.
Becofsky et al., 2015 (138)	9.9 ys	n=12,599 (18.4% women) Women: 44.5±10.2 ys Men: 44.9 ± 9.3 ys (20-100 ys)	Fitness component (test) CRF (maximal exercise treadmill testing) Depressive symptoms scale-items: CESD-10	(-) Women in higher CRF groups had 41 and 48% decreased risk of having elevated depressive symptoms. (-) Men in higher CRF groups had 60 and 54% decreased risk of having elevated depressive symptoms.
Bertoni et al., 2018 (188)	2 and 4 ys	n=6,526 (56% women) 76.0±4.8 ys (≥70 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: EURO-D-12	(-) Depressed group had a 34% increased risk of having low muscle strength. (Ø) Low muscle strength group was not associated with having elevated depressive symptoms.
Briggs et al., 2018 (189)	2 ys	n=2,638 (52.5% women) Nondepressed and normal gait: 67.9 ys Depressed: 66.3 ys Gait disturbance: 76.8 ys Depressed and gait disturbance: 73.2 ys (≥60 ys) Community-dwelling older adults	Fitness component (test) Agility (timed up and go test) Depressive symptoms scale-items: CESD-20	(-) Agility was inversely associated with depressive symptoms. (-) Low agility group had 100% increased risk of having elevated depressive symptoms. (-) Depressive symptoms were associated with low agility. (-) Depressed group at baseline had 68% increased risk of having low agility.

Table 5 (continued)

Carvalho et al., 2019 (190)	2 ys	n= 5,271 (51.1% women) 63.2±9.0 ys (≥50 ys)		Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-20	(-) Nondepressed group with low muscle strength was associated with increased odds of having elevated depressive symptoms. (-) Low muscle strength group had 44 and 61% increased risk of having incident and persistent elevated depressive symptoms, respectively.
Chen et al., 2019 (191)	1 year	n=691 (56% women) 67.5±5.7 ys (≥60 ys) Community-dwelling older adults		Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (4-m walking at normal pace) Depressive symptoms scale-items: GDS-30	(-) Nondepressed group showed higher muscle strength but not gait speed. (-) High muscle strength group was associated with a 60% decreased risk of having elevated depressive symptoms, but not for gait speed.
Chu et al., 2020 (70)	1.5 ys	n=1,264 (52.7% women) 76.7 ± 3.9 ys (70-87 ys)		Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-15	(-) The lowest grip strength group had a 56% increased risk of having elevated depressive symptoms.
Conradsson et al., 2013 (53)	3 months	n=206 (74.3% women) 84.3 ys (≥65 ys) Dependent on ADL and living in residential care facilities. 59% depression and 56% dementia diagnosis		Fitness component (test) Balance (Berg Balance Scale) Depressive symptoms scale-items: GDS-15	(Ø) Balance was not associated with depressive symptoms.
Fukumori et al., 2015 (192)	1 year	n= 4,314 (58.5% women) 63.9±9.0 ys (40-79 ys)		Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: MHI-5	(-) Lower muscle strength groups had 73, 17 and 11% increased risk of having elevated depressive symptoms.

Table 5 (continued)

Gianfredi et al., 2021 (153)	5 ys	n=1,730 (50.8% women) 59.9±8.0 (40-75 ys)	Fitness component (test) CRF (submaximal exercise cycle ergometer testing) Depressive symptoms scale-items: PHQ-9	(-) CRF was inversely associated with depressive symptoms. (-) In sample without antidepressant medication, higher CRF groups had 48 and 55% decreased risk of having elevated incident depressive symptoms. (-) In sample without individuals with a lifetime history of MDD, the highest CRF group had 42% decreased risk of having elevated depressive symptoms.
Hamer et al., 2015 (193)	4 ys	n=3,862 (53.4% women) 64.6 ± 8.3 ys	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-8	(-) Obese adults in the lowest muscle strength group had 79% increased risk of having depressive symptoms. (-) In obese adults, reporting a decreased muscle strength had 97 increased risk of having depressive symptoms.
Hollenberg et al., 2003 (60)	2 and 4 ys	n=663 (100% women) Nondepressed: 67 ys Depressed: 65 ys (≥55 ys)	Fitness component (test) CRF (submaximal exercise treadmill testing) Depressive symptoms scale-items: CESD-20	(-) Depressive symptoms were inversely associated with CRF.
Kandola et al., 2020 (194)	7 ys	n=152,978 (~54.4% women) 40-69 ys	Fitness component (test) CRF (6-min submaximal exercise test on a stationary bike) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: PHQ-9	(-) Lower CRF groups had 60 and 15% increased risk of having elevated depressive symptoms. (-) Lower muscle strength groups had 41 and 13% increased risk of having elevated depressive symptoms. (-) Lower combined groups of CRF and muscle strength had 98 and 43% increased risk of having elevated depressive symptoms.
Kim et al., 2019 (195)	10 ys	n=9,279 (55.5% women) ≤54 ys (34%); 55-64 ys (27.9%); ≥65 ys (38.1%). (≥45 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-10	(-) The lowest muscle strength group showed higher depressive symptoms.

Table 5 (continued)

Krishnamurthy et al., 2006 (196)	3 ys	n=201 90-98 ys (nondisabled nonagenarians): 31 (54.8% women) 91.87±2.4 ys 70-85 ys (controls): 270 (n/a % women) 77.4±3.8 ys 2 nonagenarians had depression diagnosis	Fitness component (test) Gait speed (walking at normal pace on an instrumented mat) Depressive symptoms scale-items: GDS-15	(-) Depressive symptoms were inversely associated with gait speed in nondisabled nonagenarians.
Lever-van Milligen et al., 2017 (68)	6 ys	n=2,480 (65.7% women) 41.9±13.1 56% current depressive or anxiety disorders and 22% history of depressive or anxiety disorder.	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: IDS-30	(-) Depressive symptoms were inversely associated with muscle strength in women, but not men.
Lys et al., 2019 (197)	4 ys	n=1,161 (52.9% women) 69 ys (65-74 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-20	(-) Muscle strength was inversely associated with depressive symptoms.
McDowell et al., 2018 (91)	2 ys	n=4104 (56.5% women) 50-59 ys (40.3%); 60-69 ys (34.6%); 70-79 ys (19.6%); ≥80 ys (5.5%). (≥50 ys) 9% depression diagnosis (Cross-sectional).	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-20	(-) Higher muscle strength groups had 68 and 67% decreased risk of having elevated depressive symptoms. (-) By sex, only the highest grip strength group in men had 58% decreased risk of having elevated depressive symptoms.

Table 5 (continued)

Patino et al., 2021 (198)	20 ys	n=1,545 (54.9% women) 72±6.1 ys (≥65 ys) Community-dwelling older adults	Fitness component (test) <u>Functional capacity (SPPB):</u> Balance (Side by side, semi tandem and tandem stand during 10 sec) Gait speed (4-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: CESD-20	(-) Depressed group was associated with 53% increased risk of having lower functional capacity.
Payette et al., 2011 (199)	3 ys	n=1,741 (52.4% women) 74.5±4.3 ys (68-82 ys)	Fitness component (test) Balance (60-sec unipedal stance) Gait speed (4-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: GDS-30	(-) Depressed group showed lower balance, gait speed and muscle strength.
Penninx et al., 1998 (200)	4 ys	n=1,286 (69% women) 77.7±4.9 ys (≥71 ys)	Fitness component (test) <u>Functional capacity (SPPB):</u> Balance (Side by side, semi tandem and tandem stand during 10 sec) Gait speed (4-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: CESD-11	(-) Nondepressed group showed higher functional capacity. (-) Depressive symptoms were inversely associated with functional capacity. (-) Depressed group was associated with 55% increased risk of decline functional capacity.
Rantanen et al., 2000 (201)	3 ys	n= 2,275 (100% men) 77.1±3.8 ys (71-92 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-11	(-) Depressive symptoms were inversely associated with muscle strength. (-) Elevated depressive symptoms in the BMI<20 group were associated with 4.5 times the risk of steep strength decline. (-) Elevated depressive symptoms in the BMI 20-24.99 group had 2 times the risk of steep strength decline.

Table 5 (continued)

Stessman et al., 2017 (71)	8, 7 or 5 ys	n= 327 aged 70 ys, 384 aged 78, 1187 aged 85 and 406 aged 90 (52.7% women) (70-90 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: BSI-53 (depression subscale)	(-) Only those aged 85 at baseline in low grip strength group had 2.36 times the risk of having elevated depressive symptoms in the follow-up (aged 90).
Sui et al., 2009 (202)	12 ys	n=14,343 (21.5% women) Women: 44.6±10.3 ys Men: 45.0±9.5 ys	Fitness component (test) CRF (maximal exercise treadmill testing) Depressive symptoms scale-items: CESD-20	(-) Women in higher CRF groups had 60 and 59% decreased risk of having elevated depressive symptoms. (-) Men in higher CRF groups had 73 and 53% decreased risk of having elevated depressive symptoms.
Taekema et al., 2010 (203)	1 year	n= 555 (65% women) 85 ys	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-15	(-) Muscle strength was inversely associated with depressive symptoms.
Tomey et al., 2010 (49)	5 ys	n=377 (100% women) 50±5 ys (42-52 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Lower-limbs muscle strength (5-rep chair stand, isometric quadriceps strength in chair) Gait speed (walk 12.20-m at normal pace) Flexibility (Forward reach) Balance (stair climb and 0.90-kg lift from the floor to a plane) Depressive symptoms scale-items: CESD-20	(-) Balance, gait speed and lower-limbs muscle strength (only 5 rep-chair stand test) were associated with depressive symptoms.

Table 5 (continued)

Veronese et al., 2017 (64)	4 ys	n= 3,099 (59.8% women) 72.5±6 ys (65-96 ys) 6.6% depression diagnosis	Fitness component (test) CRF (6-min walking test) Upper-limbs muscle strength (hand-held dynamometer) Lower-limbs muscle strength (knee extensor and hip flexor by dynamometer) <u>Functional capacity (SPPB):</u> Balance (Side by side, semi tandem and tandem stand during 10 sec) Gait speed (4-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: GDS-30	(-) The lowest physical performance group was inversely associated with depressive symptoms for all tests and functional capacity, except gait speed. Balance was not reported.
			Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-10	
Zhao et al., 2020 (69)	3.75 ys	n=8,480 (49.2% women) 55-60 ys	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-10	(-) Higher muscle strength groups had 87 and 74% for relative performance and 71 and 59% for absolute performance decreased odds of having elevated depressive symptoms.

ADL, Activities of daily living; **BDI**, Beck Depression Inventory; **BSI**, Brief Symptom Inventory; **CDS**, Cardiac Depression Scale; **CESD**, Centre for Epidemiologic Studies Depression Scale; **CISR**, Clinical Interview Scheduled Revised; **CRF**, Cardiorespiratory Fitness; **CSDD**, Cornell Scale for Depression in Dementia; **GDS**, Geriatric Depression Scale; **HADS**, Depression Subscale of the Hospital Anxiety and Depression Scale; **HPL**, Human Population Laboratory; **HRSD**, Hamilton Depression Rating Scale; **HSCL**, Hopkins' Symptom Checklist; **IDS**, Inventory of Depression Symptomatology; **MDD**, Major Depressive Disorder; **MHI**, Mental Health Inventory; **PHQ**, Patient Health Questionnaire; **rep**, repetition; **SDS**, Self-Rating Depression Scale; **SPPB**, Short Physical Performance Battery; **ys**, years. (Ø), Association was no reported. (-), Association was reported.

Table 6. Main characteristics of the cross-sectional studies included in the systematic review.

Author, year	Sample characteristics (N, sex, age)	Independent and dependent variables	Main results
Avila-Funes et al., 2008 (76)	n=1,755 (52% women) 74.0±4.2 ys (67-84 ys) Community-dwelling older adults	Fitness component (test) <u>Functional capacity (Physical performance scale):</u> Balance (60-sec unipedal stance) Gait speed (4-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Agility (timed up and go test) Depressive symptoms scale-items: GDS-30	(-) Those without elevated nutritional risk or mild depressive symptoms (both or separately) showed better performance (each test and total score of scale). (-) Depressive symptoms were independently associated with functional capacity.
Boström et al., 2014 (94)	n=392 (72% women) 86.2±6.0 ys (65-103 ys) Community and residential care facilities older adults	Fitness component (test) Balance (Berg Balance Scale) Depressive symptoms scale-items: GDS-15	(-) Balance was independently associated with depressive symptoms.
Brandon and Loftin, 1991 (204)	n=17 (47.1 %women) 32.1±4.9 ys Recreational cyclists	Fitness component (test) CRF (maximal cycle ergometer testing) Depressive symptoms scale-items: BDI-21	(-) Depressive symptoms were inversely associated with CRF.

Table 6 (continued)

Briggs et al., 2018 (189)	n= 2,972 (52.5% women) Nondepressed and normal gait: 67.9 ys Depressed: 66.3 ys Gait disturbance: 76.8 ys Depressed and gait disturbance: 73.2 ys (≥60 ys) Community-dwelling older adults	Fitness component (test) Agility (timed up and go test) Depressive symptoms scale-items: CESD-20	(-) Low agility group had 77 % increased risk of having elevated depressive symptoms.
Brooks et al., 2018 (90)	n=3,421 (51.5% women) 69.9±6.9 ys (≥60 ys) Community-dwelling older adults and 4.3% depression diagnosis	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: PHQ-9	(-) Muscle strength was inversely associated with depressive symptoms.
Brown et al., 2014 (205)	n=1,027 (57.6% women) 75 ys	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (10-m walking at normal pace) Depressive symptoms scale-items: CESD-20	(-) Nondepressed and mildly depressed groups showed higher performance in all fitness components.
Brown et al., 2020 (93)	n=134 (66.4 % women) 69.9±7.43 ys (≥60 ys) Sample with depressive disorder diagnosis	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (walking at normal pace) Depressive symptoms scale-items: HRSD-24	(-) Muscle strength was inversely associated with depressive symptoms, but not gait speed.

Table 6 (continued)

Buchman et al., 1991 (206)	n=207 (26.1% women) Women: 23.6±2.9 ys Men: 23.2±2.2 ys Medical students	Fitness component (test) CRF (submaximal 5 min step testing) Depressive symptoms scale-items: CESD-20	(-) Depressive symptoms were inversely associated with CRF in men, but not women.
Carvalho et al., 2019 (190)	n= 5,271 (51.1% women) 63.2±9.0 ys (≥50 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-20	(-) Depressed group showed higher odds of having low muscle strength.
Castaneda-Sceppa et al., 2010 (77)	n=1,357 (70.4% women) Women: 57.4±7.5 ys Men: 56.7±7.9 ys (45-75 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Lower-limbs muscle strength (1 and 5-rep chair stand) Gait speed (walk 3.05-m at normal and faster pace) Balance (tandem stand during 10 sec) Coordination (time in 10-foot tapping) Depressive symptoms scale-items: CESD-20	(-) The lowest upper-limbs muscle strength group and low gait speed group had 46% and 63%, respectively, increased risk of having elevated depressive symptoms. (-) Lower-limbs muscle strength and coordination were inversely associated with depressive symptoms, but not balance.
Chen et al., 2017 (207)	n= 1,081 (59.4% women) 76.3±6.1 ys (≥65 ys) Community-dwelling older adults	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: HADS-7	(-) Nondepressed group showed higher muscle strength.

Table 6 (continued)

Chen et al., 2020 (78)	n=250 (59.6% women) Women: 67.69±6.20 ys Men: 69.82±6.84 ys (≥60 ys) Community-dwelling older adults	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) <u>Functional capacity (SPPB):</u> Lower-limbs muscle strength (5-rep chair stand) Gait speed (4-m walking at normal pace) Balance (Side by side, semi tandem and tandem stand during 10 sec) Depressive symptoms scale-items: GDS-30	(-) All fitness components and functional capacity were inversely associated with depressive symptoms, similarly in women and men.
Chu et al., 2020 (70)	n=1,264 (52.7% women) 76.7 ± 3.9 ys (70-87 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-15	(-) Nondepressed group showed higher muscle strength. (Ø) The lowest muscle strength group had no risk of having elevated depressive symptoms.
De Souza- Vasconcelos et al., 2016 (208)	n= 1,374 (64.4% women) 73.4±6.4 ys Community-dwelling older adults	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (4.6-m walking at normal pace) Depressive symptoms scale-items: GDS-15	(Ø) Low muscle strength or/and gait speed groups showed similar depressive symptoms. (-) Depressed group had 53% increased risk of having lower both muscle strength and gait speed.
Enright et al., 2003 (209)	n=2,281 (60.2% women) Completed test: 77±4 ys Partial test: 78±5 ys	Fitness component (test) CRF (6-min walking test) Depressive symptoms scale-items: CESD-30	(-) Lower CRF groups showed elevated depressive symptoms. (-) CRF was inversely associated with depressive symptoms.
Fried et al., 1990 (210)	n=36 (75% women) 73 ys (63-90 ys) Community-dwelling older adults	Fitness component (test) Gait speed (5-m walking at normal pace) Depressive symptoms scale-items: GDS-15	(-) Depressed group showed lower gait speed.
Fukumori et al., 2015 (192)	n= 4,314 (58.5% women) 63.9±9.0 ys (40-79 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: MHI-5	(-) Lower muscle strength groups had 35 and 20% increased odds of having elevated depressive symptoms to baseline.

Table 6 (continued)

Galper et al., 2006 (211)	n=6,728 (19% women) Women: 48.1±11.1 ys Men: 49.5±10.4 ys (20-88 ys)	Fitness component (test) CRF (maximal exercise treadmill testing) Depressive symptoms scale-items: CESD-20	(-) CRF was inversely associated with depressive symptoms in men and women. (-) Higher CRF groups showed lower depressive symptoms in men and women.
Gerber et al., 2013 (56)	n=197 (49.2% women) 39.2±8.1 ys (25-50 ys)	Fitness component (test) CRF (submaximal exercise cycle ergometer testing) Depressive symptoms scale-items: HADS-7	(-) Low CRF group showed higher depressive symptoms. (-) CRF was inversely associated with depressive symptoms.
Giuliani et al., 2008 (79)	n=1,791 (75.6% women) 84.6±7.8 ys 60% dementia diagnosis Nursing home population	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) <u>SPPB:</u> Balance (Side by side, semi tandem and tandem stand during 10 sec) Gait speed (4-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: CSDD-19	(-) Depressed group had 62 and 58 decreased risk of having high upper-limbs and lower-limbs muscle strength, respectively, but not balance and gait speed.
Goins, Innes and Dong, 2012 (212)	n=328 (64.3% women) 69.5±9.6 ys (≥55 ys) Members of a tribe	Fitness component (test) <u>Functional capacity (SPPB):</u> Balance (Side by side, semi tandem and tandem stand during 10 sec) Gait speed (4-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: CESD-20	(-) Nondepressed group showed higher functional capacity.
Gu et al., 2021 (154)	n= 24,109 (46% women) 41.5±11.9 ys	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: SDS-20	(-) The highest muscle strength group had 90 for males and 80% for women decreased risk of having elevated depressive symptoms.

Table 6 (continued)

Gurina et al., 2011 (213)	n=611 (71.7% women) Women: 75.7±6.1 Men: 73.6±5.3 (65-91 ys) Community-dwelling older adults	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) <u>Functional capacity (Physical performance scale):</u> Gait speed (2.44-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Agility (putting on and taking off a cardigan) Balance (tandem position) Depressive symptoms scale-items: GDS-15	(-) Functional capacity was inversely associated with depressive symptoms.
Hamacher et al., 2018 (51)	n=102 (51% women) 72 ± 4.5 ys	Fitness component (test) Gait performance (foot stability and variability of stride length and time in single task condition [walk 4-min at normal pace] and dual-task condition [adding reciting serial three subtractions]) Depressive symptoms scale-items: CESD-n/a	(Ø) Gait performance was not associated with depressive symptoms.
Hamer et al., 2011 (214)	n=1,007 (48.2% women) 76.4±7.3 ys (≥65 ys) Community-dwelling older adults	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-15	(-) Nondepressed group showed higher performance in muscle strength. (-) Low muscle strength group was associated with 11% increased risk of having elevated depressive symptoms.
Kyu-Man et al., 2019 (215)	n=3,169 (54.2% women) 69.55±6.25 ys (≥60 ys) Community-dwelling older adults	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: PHQ-9	(-) The lowest grip strength group had 85% increased odd of having elevated depressive symptoms. (-) Depressive symptoms were inversely associated with muscle strength.
Hayashi et al., 2019 (216)	n=432 (46. % women) 72.5±4.7 ys	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (5-m walking at normal pace) Depressive symptoms scale-items: GDS-15	(-) All fitness components were inversely associated with depressive symptoms.

Table 6 (continued)

Herman et al., 2005 (217)	n=25 with gait problems and 28 healthy (68% women). Gait problems: 78.2±5 ys Healthy: 78.4±5.6 ys	Fitness component (test) Gait performance (stride time variability in 2-min walking at normal pace in 25 m long) Depressive symptoms scale-items: GDS-30	(-) In gait problems group, depressive symptoms were inversely associated with gait performance.
Jeoung, 2020 (67)	n=160 (76.3 % women) 54.2±8.4 ys (40-70 ys)	Fitness component (test) CRF (20-m shuttle run test) Upper-limbs muscle strength (hand-held dynamometer and sit up) Lower-limbs muscle strength (standing long jump) Agility (10-m shuttle run test) Flexibility (sit and reach) Depressive symptoms scale-items: GDS-30	(-) Upper-limbs muscle strength was associated with depressive symptoms, but not the other tests.
Jin et al., 2017 (57)	n=514 (35 % women) Nondepressed men and women: 45.6 and 42.1 ys Mild-depressed men and women: 48.1 and 42.2 ys Moderate-depressed men and women: 51.7 and 44.2 ys (≥30 ys) Office workers	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer and 1-min sit up) Flexibility (sit and reach) CRF (maximal exercise treadmill testing) Depressive symptoms scale-items: BDI-21	(-) Nondepressed group of men and women showed higher CRF. (Ø) Neither men nor women showed differences in muscle strength and flexibility according to depressive symptoms groups. (-) Lower CRF groups had 162 for men and 60% for women, and 26 for men and 11% for women increased risk of having elevated depressive symptoms.
Kim et al., 2019 (195)	n=9,279 (55.5% women) ≤54 ys (34%); 55-64 ys (27.9%); ≥65 ys (38.1%). (≥45 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-10	(-) The lowest muscle strength group showed higher depressive symptoms.

Table 6 (continued)

Kirk et al., 2020 (218)	n=356 (75% women) 79 ys (≥ 65 ys) Community-dwelling older adults	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (4-m walking at normal pace) Depressive symptoms scale-items: GDS-15	(-) High muscle strength and gait speed group (joined) had 4 times the risk of elevated depressive symptoms.
Kose et al., 2005 (219)	n=30 (36.7% women) 75.9 $\pm$ 5.5ys (70-82 ys) Nursing home population	Fitness component (test) Agility (timed up and go) Balance (Berg Balance Scale) Depressive symptoms scale-items: GDS-30	(-) Agility and balance were inversely associated with depressive symptoms.
Kvelde et al., 2010 (80)	n=280 (84.3% women) 79.0 $\pm$ 6.5 ys (62-95 ys)	Fitness component (test) Lower-limbs muscle strength (maximal isometric knee extension) Balance (sway in standing position with open eyes) Depressive symptoms scale-items: GDS-30	(-) Nondepressed group showed higher balance but not muscle strength. (-) All fitness components were inversely associated with depressive symptoms.
Laredo-Aguilera et al., 2019 (220)	n= 38 (100% women) 72.29 $\pm$ 5.21 ys (≥ 65 ys) Active older women	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-15	(-) High muscle strength group showed lower depressive symptoms. (-) Muscle strength was inversely associated with depressive symptoms.
Lee and Hong, 2016 (81)	n=6,169 (100% women) 74.22 $\pm$ 6.3 ys (65-105 ys)	Fitness component (test) Lower-limbs muscle strength (5-rep chair stand) Upper-limbs muscle strength (lifting 8 kg and reaching above the head) Depressive symptoms scale-items: GDS-15	(-) Nondepressed group showed higher muscle strength. (-) Low muscle strength groups were associated with 71% for lower-limbs and 34% for upper-limbs, increased risk of having depressive symptoms.

Table 6 (continued)

Lee and Ryan., 2020 (221)	n= 1,863 (~58.4% women) ~72.8±5.8 ys Healthy participants	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-15	(-) High muscle strength group had 51% decreased risk of having elevated depressive symptoms. (-) High muscle strength group had 52 for men, and 43% for women, decreased risk of having elevated depressive symptoms.
Lee, 2015 (59)	n= 173 (100% women) 74.01±5.6 ys (65-80 ys)	Fitness component (test) CRF (3-min walking test) Upper-limbs muscle strength (hand-held dynamometer and 30-sec arm curl) Lower-limbs muscle strength (30-sec chair stand) Balance (unipedal stance) Flexibility (sit and reach and back scratch) Agility (8-ft up and go) Depressive symptoms scale-items: GDS-30	(-) All fitness components were inversely associated with depressive symptoms, but not flexibility (back scratch test) and balance. (-) Nondepressed group showed higher performance in all fitness components, but not in flexibility (back scratch test). (-) The highest groups of all fitness components had decreased risk of having elevated depressive symptoms, but not in balance and flexibility (back scratch test).
Lee, 2018 (92)	n= 4,252 (56.8% women) 44 ys 19-39 ys: 1,320 40-59 ys: 1,561 60-80 ys: 1,417 20.7%depression diagnosis	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: PHQ-9	(-) Nondepressed group showed higher muscle strength, in each age group. (-) Depressive symptoms were inversely associated with muscle strength in entire sample. (-) Lower muscle strength groups had increased risk of having elevated depressive symptoms entire sample and each aged group.
Levinger et al., 2012 (50)	n= 19 with diabetes and 38 healthy (100% men) Nondiabetic: 51.1±6.8 ys Diabetic: 54.2±7.4 ys Overweight and obese	Fitness component (test) CRF (maximal exercise cycle ergometer testing) Upper-limb muscle strength (1RM chest press) Lower-limb muscle strength (1-rep chair stand and 1 RM leg press) Gait speed (15-m walking at fast pace) Agility (timed up and go) Balance (stair climb and descend) Depressive symptoms scale-items: CDS-26	(Ø) Fitness components were not associated with depressive symptoms in the diabetic and non-diabetic groups.

Table 6 (continued)

Lin et al., 2017 (222)	n= 413 (55.5% women) 76.10±7.25 ys (≥65 ys)	Fitness component (test) Agility (timed up and go test) Depressive symptoms scale-items: GDS-15	(-) Depressive symptoms were inversely associated with agility.
Ling et al., 2010 (223)	n= 555 (65% women) 85 ys	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-15	(-) Higher muscle strength groups showed lower depressive symptoms.
Lord et al., 2002 (224)	n=515 (85.2% women) 79.5±6.4 ys (62-95 ys)	Fitness component (test) CRF (6-min walking test) Depressive symptoms scale-items: GDS-30	(-) Depressive symptoms were inversely associated with CRF.
Marconcin et al., 2020 (225)	n=20,520 (54.9% women) 66.3±6.6 ys	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: EUROD-12	(-) The highest muscle strength group had 58% decreased risk of having elevated depressive symptoms.
Marques et al., 2020 (226)	n=60,380 (55.7% women) 67.42±9.7 ys (50-103 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: EUROD-12	(-) Men in higher muscle strength groups had 69, 65 and 57% decreased risk of having elevated depressive symptoms. (-) Women in higher muscle strength groups had 76, 66 and 59% decreased risk of having elevated depressive symptoms. (-) In middle age, higher muscle strength groups had 80, 78 and 70% decreased risk of having elevated depressive symptoms. (-) In older adults, higher muscle strength groups had 69, 60 and 53% decreased risk of having elevated depressive symptoms.

Table 6 (continued)

McDowell et al., 2018 (91)	n=4505 (56.5% women) 50-59 ys (40.3%); 60-69 ys (34.6%); 70-79 ys (19.6%); ≥80 ys (5.5%). (≥50 ys) 9% depression diagnosis (Cross-sectional).	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-20	(-) Higher muscle strength groups had 75 and 62% decreased risk of having elevated depressive symptoms. (-) By sex, only the highest muscle strength group had 49 for men and 69% for women, decreased risk of having elevated depressive symptoms.
Michel-Pellegrino et al., 2007 (227)	n=19 (73.7% women) Fallers: 85.5±7.9 ys Non-fallers: 84.0±10.7 ys (8 women and 4 men).	Fitness component (test) Balance (biomechanical parameters using the single-step protocol of Dietrich and Brenière) Depressive symptoms scale-items: GDS-30	(-) Depressive symptoms were inversely associated with balance.
Mollaoglu et al., 2012 (52)	n= 60 obese and 60 healthy (50% women) Men healthy and obese: 39.6±8.4 and 41.2±9.5 ys Women healthy and obese: 35.2±4.9 and 36.8±8.1 ys	Fitness component (test) CRF (submaximal exercise cycle ergometer testing) Depressive symptoms scale-items: BDI-21	(Ø) CRF was not associated with depressive symptoms for men or women.
Moy et al., 2011 (228)	n= 434 (49.1 % women) 67.9±6.3 ys Free Living Elderly in Rural	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-15	(-) Depressive symptoms were inversely associated with muscle strength for men but not women. (-) Depressive symptoms were a predictor of muscle strength for males.
Noguerón et al., 2020 (229)	n=129 (100% women) 79±8 ys (≥70 ys) Previous fall in the last year	Fitness component (test) Gait performance (stride speed and variability walking at normal, fast, and slow pace) Depressive symptoms scale-items: GDS-30	(-) Depressive symptoms were inversely associated with the majority of gait performance parameters.

Table 6 (continued)

Olgun-Yazar et al., 2019 (230)	n=116 depressed ≥65 ys (56.9% women); 165 nondepressed ≥65 ys (43% women); 136 nondepressed 18-39 ys (49.3% women) Women nondepressed and depressed ≥65 ys: 72.4±6.5 and 75.9±7.0 ys Men nondepressed and depressed ≥65 ys: 72.3±6.5 and 74.1±7.9 ys Women and men nondepressed 18-39 ys: 33.4±5.1 and 33.6±4.1 ys	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (4-m walking at normal pace) Depressive symptoms scale-items: HRSD-24 (youth group) and GDS-30	(-) Depressed older group showed lower muscle strength and gait speed, similarly for men and women. (-) In depressed older group, those with higher depressive symptoms showed lower muscle strength and gait speed (joined) for men, but not women.
Park et al., 2019 (89)	n= 13,901 (57% women) 69.5±7.06	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-15	(-) Low grip strength group showed higher depressive symptoms in men and women, although with a higher ratio in men.
Patino-Hernandez et al., 2017 (231)	n= 2,000 (46.9% women) 70.69±7.65 ys (≥60 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (2.4-m walking at normal pace) Depressive symptoms scale-items: GDS-15	(-) Gait speed was inversely associated with depressive symptoms, but not muscle strength.
Rice et al., 2010 (55)	n=131 (37 %women) 66.3±6.6 ys (54-83 ys)	Fitness component (test) CRF (submaximal exercise treadmill testing) Depressive symptoms scale-items: BDI-21	(-) CRF was inversely associated with depressive symptoms in women, but not in men.

Table 6 (continued)

Rodríguez-Hernández et al., 2014 (54)	n= 138 (87% women) 67.94±5.26 ys Active participants	Fitness component (test) <u>Senior Fitness Test:</u> CRF (6-min walking test) Upper-limbs muscle strength (30-sec arm curl) Lower-limbs muscle strength (30-sec chair stand) Flexibility (sit and reach and back scratch) Agility (8-ft up and go) Depressive symptoms scale-items: GDS-30	(-) Depressive symptoms were inversely associated with performance in muscle strength, agility, upper-limbs flexibility. (-) All fitness components were inversely associated with depressive symptoms, but not CRF and lower-limbs flexibility.
Roth and Holmes, 1985 (232)	n=112 (64.3% women) 18.9±2.4 ys (17-31 ys)	Fitness component (test) CRF (submaximal exercise cycle ergometer testing) Depressive symptoms scale-items: BDI-21	(Ø) Depressive symptoms were not associated with CRF.
Russo et al., 2007 (73)	n=364 (67% women) 85.8±4.8 ys (80-102 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) <u>Functional capacity (SPPB):</u> Balance (Side by side, semi tandem and tandem stand during 10 sec) Gait speed (4-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: MDSHC-9	(-) Nondepressed group showed higher gait speed and functional capacity, but not for upper-limbs muscle strength.

Table 6 (continued)

Sáez-Padilla et al., 2020 (82)	n=63 sedentary (77.8% women); 66 non-sedentary (80.3% women) Sedentary: 71.2±5.81 ys Non-sedentary: 69.7±6.1 ys (60-87 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) <u>Senior Fitness Test:</u> CRF (6-min walking test) Upper-limbs muscle strength (30-sec arm curl) Lower-limbs muscle strength (30-sec chair stand) Flexibility (sit and reach and back scratch) Agility (8-ft up and go) Depressive symptoms scale-items: GDS-30	(-) Muscle strength and Senior Fitness Tests unified were inversely associated with depressive symptoms in sedentary and non-sedentary groups. (-) Muscle strength was inversely associated with depressive symptoms in sedentary and non-sedentary group. (-) Flexibility was inversely associated with depressive symptoms in sedentary womens' group. (-) Balance, CRF and upper and lower-limbs muscle strength were inversely associated with depressive symptoms in non-sedentary group.
Sallinen, et al., 2011 (233)	n=605 (75% women) 77.1±1.9 ys (75-81 ys) Community-dwelling older adults	Fitness component (test) Gait speed (10-m walking at fast pace) Depressive symptoms scale-items: CESD-20	(-) The lowest gait speed group showed higher depressive symptoms. (-) Depressive symptoms were inversely associated with gait speed.
Seino et al., 2013 (83)	n= 340 (100% women) 80±4.6 ys (≥75 ys) Community-dwelling older adults	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (5-m walking at normal pace) <u>Functional capacity (Physical performance score):</u> Lower-limbs muscle strength (5-rep chair stand) Balance (tandem stand during 30 sec and 8-rep alternate step) Agility (timed up and go test) Depressive symptoms scale-items: CESD-20	(-) All fitness parameters and functional capacity were inversely associated with depressive symptoms. (-) Low upper-limbs muscle strength, gait speed, agility and functional capacity groups had 2.8, 2.8, 2.7 and 2.9 times, respectively, the risk of having elevated depressive symptoms.

Table 6 (continued)

Serrano-Checa et al., 2020 (96)	n=271 (100% women) 69.2 ± 5.7 ys	Fitness component (test) Agility (timed up and go test) Balance (3- meter timed tandem walk) Gait speed (walk 30-sec in treadmill) Depressive symptoms scale-items: HADS-7	(-) Agility, balance and gait speed were inversely associated with depressive symptoms. (-) Depressive symptoms were inversely associated with agility and balance.
Singhal et al., 2020 (84)	n= 100 (30.1% women) 72.5±6.4 ys (≥65 ys)	Fitness component (test) Lower-limbs muscle strength (1 RM knee extension) Depressive symptoms scale-items: GDS-5	(-) Nondepressed group showed higher muscle strength. (-) Low muscle strength was associated with moderate to severe depressive symptoms in women, but not in men.
Smith et al., 2018 (75)	n=2,812 (54% women) Men: 68.9±0.3 ys Women 69.5±0.3 ys (≥60 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: PHQ-9	(Ø) In normal weight group, muscle strength was not associated with depressive symptoms severity groups in women and men. (-) In overweight group, low muscle strength was associated with mild depressive symptoms in men. (-) In obesity group, low muscle strength was associated with moderate to severe depressive symptoms in men and women.
Smith et al., 2019 (234)	n=3,741 (66.4% women) 68.4 ys (≥50 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CESD-8	(-) Muscle strength was inversely associated with depressive symptoms.
Staples et al., 2020 (74)	n=111 (78.4% women) Men: 74.9±7.2 ys Women: 77.1±3.8 ys (≥60 ys) Community-dwelling older adults	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (10-m walking at normal pace) Agility (timed up and go) Depressive symptoms scale-items: GDS-15	(-) Gait speed and agility were inversely associated with depressive symptoms, but not muscle strength.

Table 6 (continued)

Stessman et al., 2017 (71)	n= 327 aged 70 ys, 384 aged 78, 1187 aged 85 and 406 aged 90 (52.7% women) (70-90 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: BSI-53 (depression subscale)	(-) Low grip strength group showed higher depressive symptoms in all age groups, but not in 70 years. (-) Those aged 78, 85 and 90 years in low grip strength group had 2.38, 1.22 and 2.04 times, respectively, the risk of having elevated depressive symptoms compared to normal group, but not in 70 years.
Suija et al., 2013 (41)	n= 5,497 (51% women) 31 ys	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer and isometric trunk extension) CRF (4-min step test) Depressive symptoms scale-items: HSCL-25 (depression subscale)	(-) The lowest upper-limbs strength group (dynamometer) had 64% increased risk of having elevated depressive symptoms in men, but not in women. (-) The lowest upper-limbs strength group (isometric trunk extension) was associated with 58 for men and 43% for women, increased risk of having elevated depressive symptoms. (Ø) CRF was not associated with depressive symptoms.
Szlejf et al., 2019 (235)	n=5,927 (54.4% women) 62.7±5.9 ys (≥55 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: CISR-n/a	(-) Nondepressed group showed higher muscle strength compared to depressed group.
Taani et al., 2018 (85)	n= 31 (71% women) 87.5±6 ys (≥70 ys) Residential Care Apartment Complex Residents	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Lower-limbs muscle strength (Jumping mechanigraphy) <u>Functional capacity (SPPB):</u> Balance (Side by side, semi tandem and tandem stand during 10 sec)	(-) Nondepressed group showed higher upper-limbs and lower-limbs muscle strength, gait speed, and functional capacity.

Table 6 (continued)

Taekema et al., 2010 (203)	n= 555 (65% women) 85 ys	Gait speed (4-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: GDS-15 Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-15	(-) Higher muscle strength groups showed lower depressive symptoms.
Takahashi et al., 2006 (236)	n=383 (77.2 %women) 78.6±5.9 ys (≥65 ys) Community-dwelling older adults	Fitness component (test) Balance (functional reach test: maximal distance beyond arm's length in standing position to the front (anterior) and to the right and left sides (lateral)) Depressive symptoms scale-items: GDS-15	(-) Depressed group showed higher balance performance in lateral functional reach test, but not in anterior functional reach test.
Thapa et al., 1994 (237)	n=303 (71.9% women) 81.0±7.5 ys	Fitness component (test) Balance (Tinetti Scale and 10-sec in different positions and functional reach test: maximal distance beyond arm's length in standing position) Lower-limbs muscle strength (3-rep chair stand) Gait speed (3.05-m walking at normal pace) Depressive symptoms scale-items: GDS-15	(-) Depressive symptoms were inversely associated with balance (only Tinetti Scale) but no other fitness components.
Tiihonen et al., 2018 (86)	n=267 (66.3% women) Able to complete chair stand test: 83.8±4.5 ys Unable to complete chair stand test: 85.1±6.0 ys (≥75 ys) Older home-care clients and 13% depression diagnosis.	Fitness component (test) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: GDS-15	(-) Unable group had 18% increased risk of having elevated depressive symptoms compared to able group.

Table 6 (continued)

Tolmunen et al., 2006 (238)	n=1,519 (100% men) Depressed: 52.4±5.3 Nondepressed: 52.0±5.5 (42-61 ys)	Fitness component (test) CRF (maximal exercise cycle ergometer testing) Depressive symptoms scale-items: HPL depression scale – 18	(-) Higher CRF groups had 3.42 and 2.45 times the risk of having elevated depressive symptoms.
Vanoh et al., 2016 (58)	n= 2,264 (52.2% women) Nondepressed: 68.9 ± 6.2 ys Depressed: 69.8 ± 6.4 ys Community-dwelling older adults	Fitness component (test) CRF (2-min step test) Upper-limbs muscle strength (hand-held dynamometer) Lower-limbs muscle strength (30-sec chair stand) Flexibility (sit and reach and back scratch) Agility (timed up and go test) Depressive symptoms scale-items: GDS-15	(-) Nondepressed group showed higher performance in all fitness components. (-) Low upper-limbs flexibility group had 3% increased risk of having elevated depressive symptoms.
Venant et al., 2019 (183)	n=373 (70.8 %women) 44±16 ys Obese	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) <u>Functional capacity (SPPB):</u> Balance (Side by side, semi tandem and tandem stand during 10 sec) Gait speed (4-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: BDI II-21	(-) Upper-limbs muscle strength and functional capacity were inversely associated with depressive symptoms. (-) Low upper-limbs muscle strength and/or functional capacity group showed higher depressive symptoms.

Table 6 (continued)

Viana et al., 2013 (239)	n=53 (75.5% women) 76.7±5.9 ys (≥65 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (walk 4.6-m at normal pace) Depressive symptoms scale-items: GDS-5	(-) Muscle strength was inversely associated with depressive symptoms, but not gait speed.
Wang et al., 2018 (72)	n=865 (50.6% women) 68.7±6.5 ys (≥60 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (6-m walking at normal pace) Depressive symptoms scale-items: GDS-15	(-) Nondepressed group showed higher gait speed, but not muscle strength.
Woo et al., 2016 (240)	n= 4,000 (50% women) Faster walkers: 69.8±3.7 ys Slower walkers: 72.6±5.2 ys (≥65 ys)	Fitness component (test) Gait speed (6-m walking at normal pace). Depressive symptoms scale-items: GDS-30	(Ø) Faster gait speed group showed similar depressive symptoms to slower group.
Wu et al., 2017 (128)	n=1,046 (53.5% women) Nondepressed and depressed women: 66 ys (63-71 ys) and 69 ys (64-78 ys) Nondepressed and depressed men: 69 ys (64-75 ys) and 71 ys (65-77 ys) (≥60 ys) Elderly suburb dwelling residents	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Depressive symptoms scale-items: GDS-30	(-) The lowest muscle strength group had 2.55 for men, and 4.18 for women times the risk of having elevated depressive symptoms.

Table 6 (continued)

Yanagita et al., 2006 (87)	n=2,856 (100% men) Nondepressed: 76.8±3.4ys Depressed: 77±3.4ys (71-93 ys)	Fitness component (test) Upper-limbs muscle strength (hand-held dynamometer) Gait speed (3.05-m walking at normal pace) Lower-limbs muscle strength (5-rep chair stand) Depressive symptoms scale-items: CESD-11	(-) Nondepressed group showed higher muscle strength and gait speed compared to depressed group. (-) High gait speed group had 66 decreased risk of having elevated depressive symptoms. (-) High muscle strength group had 72 for lower-limbs and 80% for upper-limbs, decreased risk of having elevated depressive symptoms.
Youssef, 2005 (241)	n=300 (53.3% women) Men: 70.4±9.1 ys Women: 68.9±8.6 ys (60-100 ys)	Fitness component (test) <u>Functional capacity:</u> Balance, gait speed and muscle strength (Nagi physical disability scale). Depressive symptoms scale-items: GDS-15	(-) Low functional capacity group had 2.51 times the risk of having elevated depressive symptoms.

ADL, Activities of daily living; **BDI**, Beck Depression Inventory; **BSI**, Brief Symptom Inventory; **CDS**, Cardiac Depression Scale; **CESD**, Centre for Epidemiologic Studies Depression Scale; **CISR**, Clinical Interview Scheduled Revised; **CRF**, Cardiorespiratory Fitness; **CSDD**, Cornell Scale for Depression in Dementia; **GDS**, Geriatric Depression Scale; **HADS**, Depression Subscale of the Hospital Anxiety and Depression Scale; **HPL**, Human Population Laboratory; **HRSD**, Hamilton Depression Rating Scale; **HSCL**, Hopkins' Symptom Checklist; **IDS**, Inventory of Depression Symptomatology; **MDD**, Major Depressive Disorder; **MHI**, Mental Health Inventory; **PHQ**, Patient Health Questionnaire; **RM**, Repetition Maximum; **rep**, repetition; **SDS**, Self-Rating Depression Scale; **SPPB**, Short Physical Performance Battery; **ys**, years. (Ø), Association was not reported. (-), Association was reported.

Synthesis qualitative of main outcomes

The current evidence on fitness component in relation to depressive symptoms, as supported by available studies, is detailed below. In addition, findings on sex, age and population with diagnosed depression are included. The age groups considered are as follows: 19-24 years (young adult), 19-44 years (adult), 45-64 years (middle aged), 65-79 (older adult), and 80 years and above (aged). For more details on the qualitative analyses, see **Table 7**.

Cardiorespiratory fitness

Our analysis of longitudinal studies on CRF and depressive symptoms showed consistent negative association across the 7 studies available (60,63,64,138,153,194,202), 6 of them considered high quality (60,64,138,153,194,202). One study included only females (60). Likewise, 2 studies found a stronger association between CRF and depressive symptoms in men compared to women (138,202). In terms of age, 2 studies (63,138) had a general sample ranging from young adults to aged, 3 studies (60,153,194) covered adults to older adults, 1 study (202) on adults and 1 (64) on older adults. Finally, 2 studies (63,64) reported a percentage of their sample with diagnosed depression, but it was less than 20%. However, the association between CRF and depressive symptoms in this specific population was not detailed in either study.

With respect to cross-sectional studies, 11 high quality studies (55,56,238,57–59,82,204,209,211,224) out of 12 (206) found a consistent negative relationship between CRF and depressive symptoms. However, 8 other studies (41,50,52,54,55,67,206,232) found no association between CRF and depressive symptoms with 2 of these studies having previously reported favourable results. These studies examining both sexes and found significant differences in either the women's (55) or men's group (206). Two studies examined only women (59) or men (238), and 1 study (57) showed a stronger relationship between CRF and depressive symptoms in men than in women. In term of age, 1 study (211) covered a general sample from young adults to aged, 4 studies (50,56,57,238) examined adults to middle-aged, 2 studies (55,67) adults to older adults, 4 studies (59,82,209,224) examined older adult to aged, and 5 studies (41,52,204,206,232) studied adults only, and 2 studies (54,58) examined only older adults.

Upper-limbs muscle strength

The longitudinal association between upper-limbs muscle strength and depressive symptoms showed a consistent inverse association across 15 studies (64,68,193–195,197,201,203,69–71,91,188,190–192). Of these, 7 (64,68,69,91,193–195) were considered of high quality and 8 (70,71,188,190–192,197,201,203) had moderate quality. Conversely, 4 studies (49,68,91,188) reported no association between upper-limbs muscle strength and depressive symptoms, with three of them having previously reported favourable results. Precisely, 1 study (68) only found an association in women in their sample, and another (91) reported an association in the overall sample and only in men when split by sex. In addition, 1 study was based only on women (49). In terms of age, the studies covered a range of ages, with 3 studies (49,68,69) including adults to middle-aged, 2 studies from adults to older adults (192,194), 5 (91,190,191,193,195) from middle-aged to older adults, 6 studies (64,70,71,188,197,201) from older adults to aged, and 1 (203) only including aged participants. Regarding the sample with depression, 1 study (68) reported that 56% of their sample suffered from depressive and anxiety disorders, and another (64) reported that 6.6% of their sample had a diagnosis of depression.

In the same line, evidence from cross-sectional studies showed a consistent and negative relationship between upper-limbs muscle strength and depressive symptoms. Specifically, 44 studies (80% of results) (41,54,79,81–83,85,87,89–92,58,93,128,154,183,190,192,195,203,205,207,59,208,214–216,220,221,223,225,226,228,67,230,234,235,239,70,71,75,77,78) reported this inverse association, and most of these studies were considered of high quality, with the exception of 3 (54,67,228) studies. By contrast, 11 studies (41,50,231,57,70,72–75,208,228) showed results of no association, 5 of which (41,70,75,208,228) were also mentioned above with favourable results. On the side, 12 studies (41,57,228,230,75,78,89,91,128,154,221,226) analysed this association by sex of the sample, 4 of them (41,57,78,154,230) reported similar results for both sexes, 3 (89,154,221) found a stronger association between upper-limbs muscle strength and depressive symptoms in men than in women versus 3 (91,128,226) that found a stronger association in women, and 2 (41,228) that only showed an association in men versus 1 (75) that only showed an association in women.

Furthermore, 4 studies (59,81,83,220) were based only on women, and 2 were based on men. Concerning age groups, most of the studies covered older adults to aged, or focused on one of these two age groups. In addition, 2 studies (221,230) ranged from young adults to aged, 1 study (67) from adults to older adults, and 9 studies (46,77,91,190,192,195,225,234,235) from middle-aged to older adults or aged. Another 2 studies focused on specific age groups of adults (41) and middle-aged (50). In relation to the depressed population, 3 studies reported 4.3% (90), 9% (91) and 20.7% (92) of their sample with a diagnosis of depression, and only 1 study (93) had a complete sample of people with depressive disorders.

Lower-limbs muscle strength

Insufficient evidence was observed for the longitudinal association between lower-limbs muscle strength and depressive symptoms. The three studies found for this fitness component (49,64,199) an inverse association being only 1 of them of high quality (64). Of these, 1 (49) showed 2 opposite results, being at the same time the only 1 examining women (49). In relation to age, 1 study (49) covered adults to middle age, and 2 (64,199) covered older adults to the aged. Regarding to depression, only 1 study (64) reported that 6.6% of the sample had a diagnosis of this disorder.

Evidence from cross-sectional studies showed consistent negative evidence between lower-limbs muscle strength and depressive symptoms. Indeed, 15 studies (54,58,83–87,59,76–82), out of a total of 18 (50,54,81–87,237,58,59,67,76–80), found an inverse relationship between the two parameters. All of them were considered as high quality but 1 (54) was considered as moderate quality. Likewise, 4 studies (50,67,80,237) found no association between lower-limbs muscle strength and depressive symptoms, one of them (67) previously reported favourable result. One study (78) analyzed this association by sex and reported similar results for men and women. Three studies (59,81,83) were based only on women and 2 (50,87) on men. Regarding age, 1 study (67) examined adults to older adults, 3 studies (77,78,82) from middle-aged to older adults, 11 studies (54,58,237,59,76,80,81,83,85–87) from older adults to aged, and only 1 study (50) studied middle-aged, 1 (84) older adults and, 1 (79) on aged. Finally, only 1 study (86) reported that 13% of its sample was diagnosed with depression.

Flexibility

Insufficient evidence was found for a longitudinal association between upper and lower limbs flexibility and depressive symptoms. Only 1 moderate quality study (49) analysed lower limbs flexibility and found no relationship between this and depressive symptoms. No papers on upper limbs flexibility and depressive symptoms were found in the literature. It is worth noting that the study that studied lower limb flexibility was based only on women and adults and middle-aged people.

On the other hand, evidence from cross-sectional analysis for upper-limbs flexibility and depressive symptoms was of 3 studies (54,58,82) reporting a negative relationship out of total of 4 (54,58,59,82) and one of them (82) showing 2 opposite results. Precisely, the last study (82) reported its results differentiating by sex and showed only association in women. In addition, 1 study (59) was based only on women. In relation to age, 2 studies (59,82) ranged from older adults to aged, and 2 (54,58) focused only on older adults.

The cross-sectional evidence regarding the association between lower-limbs flexibility and depressive symptoms is mixed. Three studies (54,57,67) out of total of 5 (54,57–59,67) reported no association between lower-limbs flexibility and depressive symptoms. One study (59) reported results for women only, and the other study (57) reported no association in either sex. Regarding age, 1 paper (57) included adults to middle-aged, 1 paper (67) covered adults to older adults, 1 paper (59) covered older adults to aged, and 2 papers (54,58) focused only on older adults. We did not find any cross-sectional studies that examined the relation between lower-limbs flexibility and depressive symptoms in people diagnosed by depression.

Gait: speed and other performance variables

A negative association was evidenced between gait speed and depressive symptoms in the longitudinal studies across 3 studies (49,196,199) out of total of 5 (49,64,191,196,199). Of these, only 1 study (196) was considered of high quality and the rest moderate. Therefore, the association between gait speed and depressive symptoms was not consistent. Further, 1 study examined adults to middle-aged women (49), 3 studies (64,196,199) covered older adults to aged and, 1 study (191) focused on older adults.

Evidence from cross-sectional studies showed consistent negative evidence between gait speed and depressive symptoms across 16 papers (72,73,205,208,210,230,231,233,74,76–78,83,85,87,96), of these, only 2 (74,210) were considered of moderate quality. Eight papers (50,79,93,208,216,237,239,240) showed no association between gait speed and depressive symptoms, with one of them (208) showing also favourable results. Moreover, 1 study (78) analysed by sex showed similar relationships between the two parameters in both men and women. Two studies (83,96) examined only women, and other 2 studies (50,87) only men. In relation to the age group examined, most of the studies ranged from older adults to aged (72,78,93,96,205,216,231,240), with a few exceptions. One study (230) ranged from young adults to aged and 1 (77) from middle-aged to older adults. In addition, 1 study (50) focused on middle-aged adults, 8 studies examined older adults, and 1 study (73) on aged. Finally, only 1 study (93) assessed a whole sample diagnosed with depression.

Other variables related to gait performance were only examined in 3 cross-sectional studies (51,217,229). Of these, 2 studies (217,229) demonstrated an association between gait performance and depressive symptoms. However, due to not meeting the minimum number of required studies, this category was considered insufficient. One of these studies (229) focused exclusively on women, while all of these studies included older adults to aged as part of their samples.

Agility-coordination

The longitudinal association of agility-coordination and depressive symptoms was insufficient due to a lack of studies. Only 1 study (189) focusing on older adults, reported no relationship between the two parameters.

On the other hand, the cross-sectional association evidenced a consistent negative relationship between agility-coordination and depressive symptoms across 11 studies (54,58,222,59,74,76,77,83,96,189,219) out of total of 13 studies (50,54,189,219,222,58,59,67,74,76,77,83,96). Only 2 studies (54,74) were of moderate quality. Likewise, 3 studies (59,83,96) were based only on women and 1 study on men (50). In terms of age on this evidence, 1 study (67) ranged from adults to older adults, 1 study (77) from middle-aged to older adults, 1 study (74) from middle-aged to aged and

5 studies (59,76,83,219,222) from older adults to aged. In addition, 1 study (50) focused only on middle-aged adults and 4 studies (54,58,96,189) on older adults. No studies were found that examined the relationship between agility-coordination and depressive symptoms in people diagnosed by depression.

Balance

Insufficient evidence was reported in the longitudinal association between balance with depressive symptoms across 3 studies of moderate quality (49,53,199), showing one of them no association (53). Moreover, 1 study (49) was focused on women. As for age, 2 studies (53,199) ranged from older adults to aged, and 1 from adults to middle-aged (49). Finally, only 1 study (53) with 59%, a considerable percentage of the population with depression, studied balance alongside depressive symptoms.

Otherwise, cross-sectional analysis evidenced a consistent negative association between balance with depressive symptoms across 12 studies (59,76,236,237,78,80,82,83,94,96,219,227), of which 10 of high quality (59,76,78,80,82,83,94,96,236,237) and 2 of moderate quality (219,227) reported association between balance and depressive symptoms. In contrast, 7 studies (50,59,77,79,82,236,237) showed no association, 4 of them (59,82,236,237) also with favourable results as mentioned above. In addition, 1 study (78) analysed segregating by sex and found similar results for both; 3 studies (59,83,96) only examined women and 1 study (50) was focused on men. In terms of sample age, all studies ranged from older adults to aged, except 1 study (77) which ranged from middle-aged to older adults, 1 study (50) of only middle-aged and 1 study (78) of only older adults.

Functional capacity

The longitudinal analysis of functional capacity and depressive symptoms was insufficient to evidence an association between the two parameters because only 3 studies (64,198,200) investigated this relationship. Despite this, all of them demonstrated an inverse association between functional capacity and depressive symptoms. In relation to age, all of them focused on older adults and aged. In addition, 1 study (64) reported that 6.6% of their sample had a diagnosis of depression.

Concerning the cross-sectional association between functional capacity and depressive symptoms, a consistent negative was identified across the 12 studies (73,76,230,241,78,82,83,85,183,212,213,218) of high quality for this fitness component. However, one of them (230) also reported no association. Notably, this study separated the sample by sex in its analyses and found an association between functional capacity and depressive symptoms in men but not in women. In contrast, another study (78) also conducted separate analyses for men and women and found similar results for both sexes. Moreover, 1 study (83) was based only on women. Organised according to age, 1 study (230) ranged from young adults to aged, 1 study (183) from adults to middle-aged, 1 study (212) from middle-aged to older adults, and 7 studies (76,82,83,85,213,218,241) from older adults to aged. In addition, 1 study (78) focused only on older adults and 1 study (73) focused only on aged. Scientific literature was not found examining the relation between functional capacity and depressive symptoms in people diagnosed by depression.

Table 7. Longitudinal and cross-sectional evidence synthesis of physical fitness and depressive symptoms in general population, including article references.

Fitness component	N studies	Sample size	Negative significant difference		No significant difference		Consistency (%)	Level of evidence
			High quality	Moderate quality	High quality	Moderate quality		
Longitudinal studies (N=28)								
CRF	7 (60,63,64,138,153,194,202)	186492	6 (60,64,138,153,194,202)	1 (63)			100	Consistent negative
Upper-limbs muscle strength	17 (49,64,192–195,197,201,203,68–71,91,188,190,191)	209020	7 (64,68,69,91,193–195)	8 (70,71,188,190–192,197,201,203)	2 (68,91)	2 (49,188)	79	Negative
Lower-limbs muscle strength	3 (49,64,199)	5217	1 (64)	2 (49,199)		1 (49)	75	Insufficient
Upper-limbs flexibility	0							Insufficient
Lower-limbs flexibility	1 (49)	377				1 (49)	100	Insufficient
Gait (speed)	5 (49,64,191,196,199)	6109	1 (196)	2 (49,199)	1 (64)	1 (191)	60	Negative
Agility	1 (189)	2.638	1 (189)				100	Insufficient
Balance	3 (49,53,199)	2324		2 (49,199)		1 (53)	75	Insufficient
Functional capacity	3 (64,198,200)	5930	3 (64,198,200)				100	Insufficient
Cross-sectional studies (N=82)								
CRF	18 (41,50,82,204,206,209,211,224,232,238,52,54–59,67)	20527	11 (55,56,238,57–59,82,204,209,211,224)	1(206)	5 (41,50,52,55,232)	3 (54,67,206)	60	Consistent negative
Upper-limbs muscle strength	50 (41,50,73–75,77–79,81–83,85,54,87,89–93,128,154,183,190,57,192,195,203,205,207,208,214,215,216)	204422	41 (41,58,82,83,85,87,89–93,128,59,154,183,190,192,195,203,205,207,208,214,215,216)	3 (54,67,228)	11 (41,50,231,57,70,72–75,208,228)		80	Consistent negative

	7,208,214– 216,220,58 ,221,223,2 25,226,228 ,230,231,2 34,235,239 ,59,67,70– 72) 18		,220,221,2 23,225,226 ,230,234,2 35,71,239, 75,77– 79,81)					
Lower-limbs muscle strength	(50,54,81– 87,237,58, 59,67,76– 80)	19454	14 (58,59,84– 87,76–83)	1 (54)	3 (50,80,23 7)	1 (67)	79	Consistent negative
Flexibility (Upper- limbs)	4 (54,58,59,8 2)	2638	2 (58,82)	1 (54)	2 (59,82)		60	Negative
Flexibility (Lower- limbs)	5 (54,57– 59,67)	3312	2 (58,59)		1 (57)	2 (54,67)	60	No association
	23 (50,72,87,9 3,96,205,2 08,210,216 ,230,231,2 33,73,237, 239,240,74 ,76– 79,83,85)		14 (72,73,208, 230,231,23 3,76– 78,83,85,8 7,96,205)	2 (74,210)	8 (50,79,93 ,208,216, 237,239, 240)		67	Consistent negative
Gait (speed)		20294						
Gait (other parameters)	3 (51,217,22 9)	283	2 (217,229)		1 (51)		67	Insufficient
Agility- coordinatio n	13 (50,54,189, 222,58,59, 67,74,76,7 7,83,96)	10041	8 (58,59,76,7 7,83,96,18 9,222)	3 (54,74,21 9)	2 (50,67)		85	Consistent negative
Balance	15 (50,59,96,2 19,227,236 ,237,76– 80,82,83,9 4)	7767	10 (59,76,78,8 0,82,83,94, 96,236,237)	2 (219,227)	7 (50,59,77 ,79,82,23 6,237)		63	Consistent negative
Functional capacity	12 (73,76,230, 241,78,82, 83,85,183, 212,213,21 8)	5052	12 (73,76,230, 241,78,82, 83,85,183, 212,213,21 8)		1 (230)		92	Consistent negative

CRF, Cardiorespiratory fitness. **N studies**, number of studies reporting depressive symptoms and fitness component or scale. **Consistency** was calculated by dividing the number of study results reporting negative significant or nonsignificant differences by the total number of study results reporting depressive symptoms and fitness.

DISCUSSION

The purpose of this systematic review was to synthesize the evidence available on the associations of fitness components with depressive symptoms in healthy and depressed adults and elderly. Foremost, there is consistent evidence for the role of high CRF in reducing depressive symptoms both longitudinally and cross-sectionally. Upper-limbs muscle strength and gait speed have also shown to reduce symptoms, but there is no consistent evidence longitudinally. At the cross-sectional level, there is strong evidence for the association of upper and lower-limbs muscle strength, gait speed, agility, balance, and functional capacity with depressive symptoms. However, the evidence for upper-limbs flexibility is inconsistent, and for the lower limbs, there is no association. On the contrary, there is insufficient research on the longitudinal association between other components and depressive symptoms, as well as on other parameters of gait performance at the cross-sectional level.

Moreover, most of the research on the association between fitness and depressive symptoms has focused on older adults or the general population, leaving a gap in our understanding of these relationships during adulthood, when depressive symptoms tend to emerge with greater severity (3). Meanwhile, of those fitness components considered as inversely related to depressive symptoms, CRF and upper-limbs muscle strength have shown sex-specific results. Specifically, CRF was more strongly associated with lower depressive symptoms in men than women, both longitudinally and cross-sectionally. Upper-limbs muscle strength, on the other hand, was found to be inversely associated with depressive symptoms in both men and women, but there is limited research on other components, with fewer than four studies per component. The sex differences are relevant as previous studies have suggested that the aetiology of depressive symptoms may differ by sex (3,242).

Another important aspect is the lack of research on the relationship between fitness and depressive symptoms in people with depression. In most cases, studies reported the percentage of participants with depression (64,86,90–92,196) but not all participants were included, and only 1 study (93) analysed a complete sample of individuals with depressive disorders. Therefore, no conclusions can be drawn for this population. In fact,

the distinction between depressive symptoms and depression has been complicated by unclear terminology in the studies and the misuse of symptom questionnaires to diagnose depression. It is possible that participants were sometimes considered to have depression because they exceeded the cut-off point of the questionnaires (243). However, what they mostly exhibited were relevant depressive symptoms and not necessarily clinical depression (3,242).

As far as fitness is concerned, CRF and muscle strength have been the main components considered for their potential health benefits (26), which may have overshadowed other fitness components that may provide relevant information, especially in adulthood where the variety of studies on fitness was limited. A previous review found an inverse association of CRF, measured using CPET, with depressive symptoms (45). Our findings support this association and also suggest that men have a stronger inverse relationship than women. Moreover, unlike the previous review was focused on older population, our review includes studies that used field tests in addition to CPET. Although CEPT is considered the gold standard for assessing CRF (244), and proper protocols are available to reduce the potential risks in this population (245), other studies opted for the use of field tests instead of CEPT.

As for muscle strength, its inverse relationship with depressive symptoms has been systematically reviewed and meta-analysed. Two reviews specifically studied the manual dynamometry test (66,88), while another examined the overall strength of upper and lower limbs (46). In contrast to a previous review by Huang et al. (66), which showed a greater association in men, our review reported the same level of association between men and women. However, it should be noted that Huang et al. (66) only covered a smaller number of studies, all of which were longitudinal.

In the case of gait speed, a systematic review studied the relationship between depressive symptoms, executive dysfunction and gait speed impairment in older adults (246), showing an increased risk of falls, impairment of daily activities and quality of life, and overall increased morbidity and mortality (246). Many studies have also found that those with a higher comfortable walking speed had fewer depressive symptoms. As gait speed is related to performance and functionality, its declines in aging, could lead to depressive symptoms, while severe depressive symptoms and depression could lead to deterioration

of gait speed (247). However, our review has gathered that most evidence was based on normal gait speed tests, whereas fast walking speed, which is related to mobility and daily activities (248), was not investigated in association with depressive symptoms.

The limited number of studies on agility, balance and functional capacity have mainly focused on older adults, as mentioned earlier. However, despite the small quantity of research, there is consistent evidence reporting an inverse association between these fitness components and depressive symptoms in cross-sectional studies. Most of the studies show that better agility, balance and functional capacity are associated with a lower risk of depressive symptoms. In the case of functional capacity, a systematic review of institutionalised elderly people concluded that depression is a longitudinal factor of decline in functional capacity in this population (249).

As a consequence of the present review, gaps in the literature and future lines of research are presented:

- Most of the studies had cross-sectional design and few conclusions could be drawn from the longitudinal studies for each component. Therefore, scientific evidence needs to be oriented towards longitudinal studies.
- More studies focused on the association between independent fitness components (i.e., flexibility and other gait performance parameters) and depressive symptoms are needed.
- More studies that allow obtaining decisions by sex, especially in those fitness components with consistent findings.
- There is a need for research in young adulthood and different age groups. Most of the included studies cover the middle-aged and older population.
- Studies analysing the role of fitness on depressive symptoms, well-identified, in people diagnosed with depression are needed.

Finally, our systematic review makes a significant contribution to the field by synthesising the association between physical fitness and depressive symptoms in healthy and depressed adults and older adults. The results indicate that CRF, strength, and gait speed show such an inverse relationship with depressive symptoms longitudinally, while all fitness components except flexibility and other gait parameters show an inverse

relationship with depressive symptoms cross-sectionally. However, there is no evidence regarding the specific population with diagnosed depression. These results highlight the need to provide supervised physical exercise that focuses on improving modifiable health-related factors, such as fitness, to reduce depressive symptoms in the adult and older population, especially in those at risk of depression.



STUDY II. Independent and combined associations of physical fitness components and body composition with depressive symptoms in older adults. INTERMAE STUDY.

Study II. Independent and combined associations of physical fitness components and body composition with depressive symptoms in older adults. INTERMAE STUDY.

RESULTS

Descriptive characteristics of the participants are shown in **Table 8** for both, all participants together (n=92) and separately by sex (n=42 women, 45.65%). Participants showed significant differences between sexes in all body composition variables ($p<0.001$), except BMI and hip circumference. On the other hand, men had higher physical fitness levels than women (all $p<0.05$), except for the sit and reach test, in which women showed significantly better performance ($p=0.04$). Arm curl and back scratch tests reported no differences. Moreover, significant differences were observed for depressive symptoms ($p<0.001$) and antidepressant medication, being higher in women (31.71% vs 10.42%, $p=0.01$) than men. According to the GDS-15 cut-off point (≥ 5), 12 older adults had mild-moderate depressive symptoms. In addition, 10 of the participants (10.87%) had been diagnosed with depression and 18 (19.97%) were routinely taking antidepressants.

The associations of physical fitness and body composition components with depressive symptoms are shown in **Table 9**. Particularly, for physical fitness components negative associations with depressive symptoms were found for usual and maximal gait speed, handgrip, arm curl, and 6-min walking tests, and for VO_{2peak} absolute and relative variables assessed by laboratory test (all $p<0.05$). Positive associations between 8-ft up-and-go test ($p<0.02$) and depressive symptoms were also observed. Concerning the body composition variables, fat mass was positively associated with depressive symptoms, while fat free mass and muscle mass were negatively associated with depressive symptoms. After applying the adjusted models (models 2 to 4), these associations were attenuated and only the associations of usual gait speed at 4 and 6-m with depressive symptoms were maintained. Sensitivity analyses for model 3 were performed where fat mass percentage was replaced by BMI and results were similar [values for usual gait speed at 4 m: Unstandardized Regression Coefficient (b)= -2.52; Standardized Regression Coefficient (β)=-0.26; $p=0.016$, and values for usual gait speed at 6-m: b = -2.98; β =-0.28;

p=0.005]. Exceptionally, usual gait speed was the only component that remained significant independently of all confounders.

Figure 5 displays the significant associations of combined fitness-fatness with the likelihood of increasing depressive symptoms in older adults. The independent combination of each of the 5 fitness tests (back scratch, usual gait speed at 6-m, arm curl, 6-min walking test and VO_{2peak} relative tests) and BMI identified a significant association between the unfit and fat group and higher depressive symptoms in older adults. Specially, unfit and fat participants had higher odds of experiencing worse depressive symptoms, with ORs ranging from 4.29 to 9.17, compared to fit and not fat participants. Additional results using combinations of other physical fitness and body composition variables can be found in the **Supplementary Table S4**. No significant associations were observed after adjustment for confounding factors.

Table 8. Descriptive characteristics of the INTERMAE study sample.

	All		Male		Female		P- value
	N	Mean $\pm$ SD	N	Mean $\pm$ SD	N	Mean $\pm$ SD	
<u>Sociodemographic variables</u>							
Age (years)	92	68.95 $\pm$ 2.98	50	69.12 $\pm$ 2.97	42	68.75 $\pm$ 3.01	0.551
Smoking status (% current/former/never)	89	13.48/49.44/37.08	49	22.45/63.27/14.29	40	2.50/32.50/65.00	<0.001
Alcohol intake (% current/former/never)	89	73.03/6.74/20.22	49	83.67/8.16/8.16	40	60.00/5.00/35.00	0.007
N Comorbidities (% $\geq$ 3/ none to 2)	89	56.18/43.82	49	40.82/59.18	40	75.00/25.00	0.001
Educational level (% up primary education/ higher education)	90	45.56/54.44	49	36.73/63.27	41	56.10/43.90	0.066
Marital status (% without/ with couple)	90	21.11/78.89	49	16.33/83.67	41	26.83/73.17	0.224
Economic stress (% yes/no)	90	33.33/66.67	49	28.57/71.43	41	39.02/60.98	0.295
Sleep quality (score)	90	6.37 $\pm$ 3.29	49	5.59 $\pm$ 3.19	41	7.29 $\pm$ 3.20	0.014
<u>Body composition</u>							
Weight (kg)	91	74.19 $\pm$ 13.73	50	80.06 $\pm$ 13.70	41	67.02 $\pm$ 9.92	<0.001
Height (cm)	91	160.86 $\pm$ 9.56	50	166.69 $\pm$ 7.42	41	153.74 $\pm$ 6.62	<0.001
BMI (kg/m ²)	91	31.05 $\pm$ 8.00	50	28.80 $\pm$ 4.45	41	28.44 $\pm$ 4.65	0.710
Fat mass (%)	91	31.04 $\pm$ 7.92	50	25.92 $\pm$ 5.84	41	37.30 $\pm$ 5.44	<0.001
Fat free mass (%)	91	68.97 $\pm$ 8.00	50	74.09 $\pm$ 5.84	41	62.72 $\pm$ 5.43	<0.001
Muscle mass (%)	91	65.48 $\pm$ 7.62	50	70.38 $\pm$ 5.54	41	59.52 $\pm$ 5.16	<0.001
Waist circumference (cm)	91	99.07 $\pm$ 11.68	50	103.09 $\pm$ 10.94	41	94.16 $\pm$ 10.74	<0.001
Hip circumference (cm)	91	104.26 $\pm$ 9.23	50	102.92 $\pm$ 9.05	41	105.88 $\pm$ 9.31	0.128
Obesity by BMI (%no/yes)	91	18.68/81.32	50	18.00/82.00	41	19.51/80.49	0.854
Obesity by fat mass (%no/yes)	91	41.30/58.70	50	44.00/56.00	41	38.10/61.90	0.567
Obesity by waist circumference (%no/yes)	91	70.33/29.67	50	68.00/32.00	41	73.17/26.83	0.591

Physical fitness tests

Chair sit and reach test (cm)	92	-8.46 ± 12.38	50	-10.84 ± 12.52	42	-5.64 ± 11.73	0.044
Back scratch test (cm)	92	-11.68 ± 9.87	50	-13.40 ± 9.31	42	-9.63 ± 10.24	0.067
Usual gait speed at 4-m (m/s) [†]	83	1.31 ± 0.24	43	1.37 ± 0.24	40	1.24 ± 0.24	0.022
Usual gait speed at 6-m (m/s)	92	1.29 ± 0.21	50	1.35 ± 0.21	42	1.23 ± 0.20	0.008
Maximal gait speed at 6-m (m/s)	92	1.85 ± 0.32	50	1.96 ± 0.29	42	1.72 ± 0.32	<0.001
8-ft up-and-go test (s)	92	6.38 ± 1.46	50	5.89 ± 1.17	42	6.96 ± 1.57	<0.001
Handgrip test (kg)	91	27.18 ± 8.58	50	33.23 ± 6.58	41	19.81 ± 3.36	<0.001
Arm curl test (rep)	89	29.79 ± 7.16	49	30.53 ± 6.80	40	28.90 ± 7.58	0.281
Chair stand test (rep)	90	11.01 ± 2.76	49	12.12 ± 2.11	41	9.68 ± 2.89	<0.001
5-rep chair stand (s) [†]	78	12.98 ± 2.63	42	11.93 ± 1.88	36	14.20 ± 2.86	<0.001
SPPB-score (points) [†]	78	10.65 ± 1.09	42	10.98 ± 1.12	36	10.28 ± 0.95	<0.004
6-min walking test (m)	92	553.75 ± 83.12	50	582.15 ± 89.19	42	519.93 ± 61.60	<0.001
VO _{2peak} absolute (l/min) ^{††}	67	1937.55 ± 462.76	41	2166.73 ± 423.34	26	1576.15 ± 237.98	<0.001
VO _{2peak} relative (ml/kg/min) [†]	67	26.31 ± 4.81	41	27.66 ± 5.04	26	24.18 ± 3.55	0.003

Depression variables

Depressive symptoms (score)	92	1.68 ± 2.11	50	1.12 ± 1.66	42	2.36 ± 2.39	0.004
Antidepressant medication (% yes/no)	89	20.22/79.78	38	10.42 / 89.58	31	31.71 / 68.29	0.013
Depression diagnosis (% yes/no)	89	11.24/88.76	49	6.12/93.88	40	17.50/82.50	0.091

Data are presented as mean ± standard deviation or percentages. Differences between sexes were examined by independent t-test and chi-square. Statistically significant differences are highlighted in bold. BMI, body mass index; rep, repetition; SPPB, Short Physical Performance Battery. Obesity by BMI: ≥25 kg/m². Obesity by fat mass was according to Gallagher et al. criteria (113). Obesity by waist circumference: ≥99 cm for women and ≥106 cm for men.[†]Tests belonging to the SPPB. ^{††}Only data from participants who met the maximality criteria of the CPET.

Table 9. Associations of physical fitness tests and body composition variables with depressive symptoms in older adults.

	Model 1			Model 2			Model 3			Model 4		
Variable	B	β	P	B	β	P	B	β	P	B	β	P
<u>Physical fitness components</u>		(n= 92)			(n= 89)			(n=88)			(n= 89)	
Sit and reach test (cm)	-0.01	-0.07	0.536	-0.03	-0.17	0.106	-0.03	-0.19	0.072	-0.02	-0.12	0.218
Back scratch test (cm)	-0.02	-0.11	0.285	-0.04	-0.19	0.062	-0.05	-0.22	0.030	-0.03	-0.15	0.138
Usual gait speed at 4-m (m/s) [†]	-3.22	-0.36	0.001	-2.37	-0.25	0.022	-2.48	-0.25	0.018	-2.58	-0.27	0.012
Usual gait speed at 6-m (m/s)	-3.68	-0.37	<0.001	-2.79	-0.27	0.008	-2.92	-0.28	0.006	-3.04	-0.29	0.003
Maximal gait speed at 6-m (m/s)	-1.52	-0.23	0.026	-0.56	-0.09	0.418	-0.80	-0.12	0.281	-0.85	-0.13	0.198
8-ft up-and-go test (s)	0.34	0.23	0.025	0.15	0.10	0.328	0.21	0.14	0.185	0.21	0.15	0.143
Handgrip test (kg)	-0.07	-0.30	0.004	-0.03	-0.13	0.413	-0.03	-0.13	0.403	-0.04	-0.17	0.105
Arm curl test (rep)	-0.07	-0.25	0.017	-0.04	-0.15	0.130	-0.05	-0.16	0.108	-0.05	-0.16	0.119
Chair stand test (rep)	-0.07	-0.09	0.411	0.05	0.06	0.565	0.02	0.03	0.827	-0.01	-0.01	0.959
5-rep chair stand (s) [†]	0.12	0.14	0.216	0.05	0.06	0.620	0.05	0.06	0.601	0.09	0.11	0.311
SPPB- score (points) [†]	-0.24	-0.12	0.284	-0.07	-0.04	0.737	-0.08	-0.04	0.718	-0.15	-0.08	0.475
6-min walking test (m)	-0.01	-0.31	0.003	-0.01	-0.14	0.186	-0.01	-0.18	0.119	-0.01	-0.18	0.078
VO _{2peak} absolute (l/min) ^{††}	-0.01	-0.33	0.007	-0.01	-0.24	0.108	-0.01	-0.24	0.107	-0.01	-0.21	0.082
VO _{2peak} relative (ml/kg/min) ^{††}	-0.14	-0.32	0.009	-0.72	-0.17	0.176	-0.10	-0.24	0.113	-0.08	-0.18	0.134
<u>Body composition</u>		(n=91)			(n=88)						(n=88)	
BMI (kg/m ²)	0.01	0.01	0.948	-0.01	-0.01	0.889	-	-	-	-0.01	-0.03	0.810
Fat mass (%)	0.06	0.21	0.049	-0.01	-0.04	0.759	-	-	-	0.03	0.10	0.327
Fat free mass (%)	-0.06	-0.21	0.049	0.01	0.04	0.752	-	-	-	-0.03	-0.10	0.330

Muscle mass (%)	-0.06	-0.21	0.048	0.01	0.04	0.758	-	-	-	-0.03	-0.10	0.325
Waist circumference (cm)	-0.01	-0.07	0.490	0.01	0.02	0.880	-	-	-	-0.01	-0.05	0.588
Hip circumference (cm)	0.01	0.03	0.806	-0.01	-0.03	0.735	-	-	-	-0.01	-0.01	0.953

Data are presented for all sample as unstandardized regression coefficient (b), standardized regression coefficient (β), and P-value (P). Model 1 was unadjusted; model 2 was adjusted for sex and antidepressant medication; model 3 for covariates of model 2 and fat mass percentage; model 4 for antidepressant medication (stepwise regression criteria). Statistically significant associations are in bold. BMI, body mass index; rep, repetition; SPPB, Short Physical Performance Battery. [†]Different n for usual gait speed at 4-m of SPPB (n=83, model 1, and n=80, model 2 and 3), 5-rep chair stand of SPPB and SPPB-score (n=78, model 1, and n=75, model 2 and 3) variables data. ^{**}Only data from participants who met the maximality criteria of the CPET.

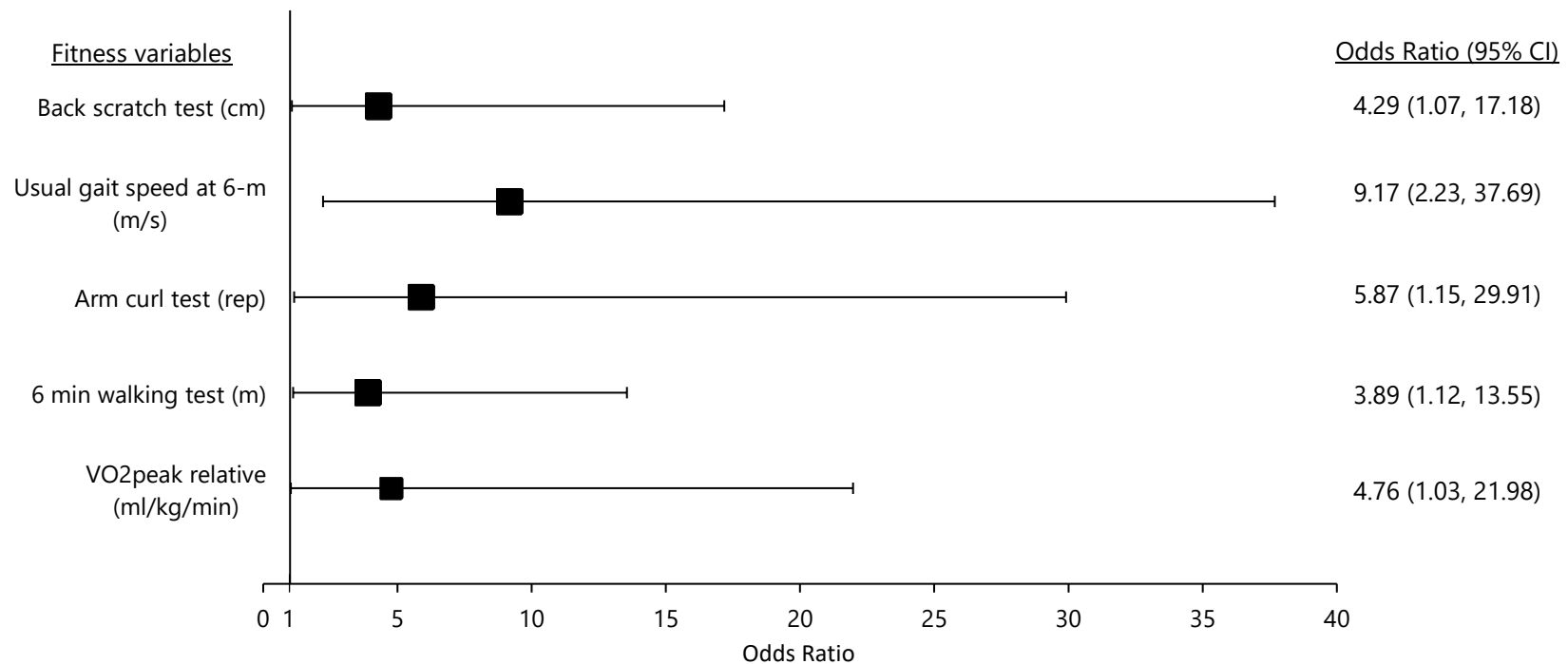


Figure 5. Associations of unfit and fat group with the odds of increasing depressive symptoms in older adults, compared with fit and not fat group (referent). Fit was defined as the 70% top of the overall study sample and unfit as the bottom 30%, showed in Back scratch, Usual gait speed at 6-m, Arm curl, and 6 min walking tests, and VO_{2peak} relative. Fat was defined as overweight and obesity status and not fat as normal weight, depending on BMI criteria. Odds ratios were unadjusted. CI, confidence interval.

DISCUSSION

The present study aimed to analyse the associations of physical fitness components and body composition with depressive symptoms in older adults. Our study found that older people who were more physically fit and had lower body fat had fewer depressive symptoms at both independent and combined levels. Firstly, people with higher performances in gait speed, agility, upper-limb muscular strength or CRF, as well as, better fat or muscle composition, showed lower depressive symptoms. However a clear confounding role of sex, antidepressant medication and fat mass percentage have been identified for these associations. To highlight that the normal walk speed is the unique component associated with depressive symptoms independently of all the confounders. Secondly, the analysis of combined fitness fatness showed those unfit (i.e., performance in upper-limbs flexibility, gait speed, upper-limbs strength and CRF) and fat (i.e. BMI and fat mass percentage) older adults were much more likely to have higher depressive symptoms compared to their fit and not fat peers.

Physical fitness components

A large number of cross-sectional and longitudinal scientific articles support the inverse association between CRF and depressive symptoms in the elderly (45,58,59,64,209,250). Recent articles (59,64) reported that older adults between 65 to 96 years with higher levels of CRF, evaluated by means of 6-min walking test, were associated with decreased odds of having elevated depressive symptoms compared to the lower CRF levels population. Equally, another recent paper (58), found a similar result in a sample of 62 to 76 years community-dwelling older adults. In consonance with these previous studies (58,59,64), the present work corroborates this association in a similar age group and also using the 6-min walking test. However, previous studies using CPET, were focused in general population from age 20 (63,138) or middle aged (153,194) and did not report such associations in older adults. To our knowledge, only the articles of Hollenberg et al. (60) and Rice et al. (55) analysed this association between VO_{2peak} and depressive symptoms in older women with a mean age of 65 years, supporting our current findings. However, we add and extra value to previous studies providing evidence of the association for both men and women.

Likewise, several articles reported that the greater the handgrip strength, the fewer the depressive symptoms in the elderly, as reported in the aforementioned systematic review and meta-analysis of Zasadzka et al. (88), and as also is supported by our results. Similarly, we have observed that better performance in the arm curl test is associated with fewer depressive symptoms, in concordance with previous studies (54,59,82). Although the sample of these articles was mostly made up of women (80, 87, 100%) compared to the present work, which was well-balanced by sex (up of 45% of women). On the other hand, our findings reflected no association between lower-limbs strength and depressive symptoms, in line with other articles (49,50,80). However, previous literature, using chair stand tests, has also reported a negative association in community dwelling older (58,59,78,198).

For the flexibility component, we did not observe an association between lower-limbs flexibility and depressive symptoms, in line with previous findings in middle-aged population (57). In contrast, other studies in older adults (54,58,59) found an inverse association. Methodological differences in population selection (i.e only women) among studies could partially explain the contradictory results. Thus, more studies are needed to clarify the association between these two variables. On the other side, upper-limb flexibility has not been related to depressive symptoms in several articles in the scarce scientific evidence (54,59,82), in agreement with our results.

Gait speed is mainly studied in elderly population because of its relation to sarcopenia and frailty detection (251). Our results strongly suggest that those older with greater performance in usual paced walking showed fewer depressive symptoms independently of confounders. This is in concordance with previous literature on people over 60 years living in the community (72,74,78,83,216,230,231) where the mostly used tests were between 4 and 6-m as did the present study. Likewise, when we studied walking speed at a maximal pace, we also found an inverse association with depressive symptoms, although this relationship disappeared after adjusting for covariates. Sallinen et al. (233) observed that in community-dwelling older adults aged 77 years, maximal walking speed over 10 m was inversely associated with depressive symptoms. Studies with mixed samples of middle-aged and older adults showed both inverse (77) and no associations

(50), probably due to the expected higher relevance of such tests in older adults than in middle-aged.

Findings from our study about agility agreed with the results of several articles (54,58,74,96), which demonstrated those older adults, with a mean age very similar to our sample, had fewer depressive symptoms if they performed better on the 8-ft up-and-go or timed up and go tests. Even though gait speed and agility seem to be consistently related to depressive symptoms in the older people of this study, surprisingly no association was observed between the SPPB battery, which focuses on performance on similar tests of physical functioning, and depressive symptoms. This may be due to the lack of association between the 5-repetitions chair test with depressive symptoms or non-sensitivity to this population group, which is living in the community and are independently functional. In fact, the studies (73,79,85) that reported an association between SPPB score and depressive symptoms had a population sample of elderly octogenarians or from residential care which is a clearly different population group from our study.

Body Composition Components

In relation to body composition, the percentage of fat, fat-free and muscle mass were associated with depressive symptoms, while BMI and waist and hip circumferences did not. Considering that our participants were predominantly overweight-obese, the percentage of mass may provide a more accurate indication of the individual's level of fatness. Therefore, our results support the trend that the higher the fatness and the lower the muscle mass, the greater the depressive symptoms suffer by older adult (123,127,128). The well known limitation of BMI into discriminate whether high or low BMI is due fat mass or fat free mass could be one of reasons explaining why the separate analysis of fat and fat-free masses resulted in a more accurate association with depressive symptoms.

Combined group of physical fitness and fatness

The novel finding of the current study is related to the analysis of these factor not only independently but also from a combined approach. It is the analysis of the role of combined group of physical fitness and fatness components with depressive symptoms

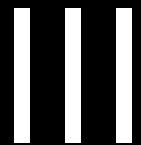
in older adults. To the best of our knowledge, this is the first study applying this combined approach in a specific population of older people. Consistent with our results, the research by Becofsky et al. (138) on the general population (age range 20 to 100) showed that people considered unfit (CRF based), and fat (BMI, waist circumference or percentage of adiposity based) had more depressive symptoms than those who were healthier. In addition, this relevant study also observed that those in the fit and fat group showed fewer symptoms than those in the unfit and not fat group, supporting the argument that physical fitness level is more relevant to depressive symptoms than body composition, as in other studies (142,252). In our case, both conditions seem to complement each other, and we were unable to investigate the relevance of one variable over the other because of the smaller number of participants per group that avoid us to make additional sensitivity analysis.

All present findings discussed, except usual gait speed, reported association with depressive symptoms that are not independent of the confounding effects of sex, antidepressant medication and fat mass percentage. These variables are relevant confounders as detailed in the scientific evidence, due to sex differences in the aetiology of depressive symptoms (3,242), the association between obesity and depressive disorders (117), and the stimulating effect of antidepressants on patients by increasing serotonin levels (253). Nevertheless, the sample was not divided according to them as they showed no interaction in our study and either the sample size could become a limitation. Thus, the mentioned confounders should highly be monitored in future studies when researchers evaluate the relationships between fitness, fatness and depressive symptoms.

On the other side, usual gait speed, become the only component among all those studied, which is independent of all these confounding factors, which makes it a fitness component that seems have a key role. This simple walking test over 4 and 6-m at normal speed is easy to apply and widely used in the elderly population to detect frailty (251). Its poor performance could also be useful in screening depressive symptoms, having a relevant clinical application.

In the end, higher levels of physical fitness, notably gait speed, and muscle mass and lower fatness seem to contribute to having fewer depressive symptoms in older adults.

Higher performances in gait speed, agility, upper-limb muscular strength and CRF, as well as, more appropriate fat and muscle levels, appear to have a beneficial impact, individually, on depressive symptoms. Furthermore, unfit and fat older people might have increased odds of higher depressive symptoms compared to their fit and not fat peers.



STUDY III. Independent and combined associations of physical fitness and body composition with depressive symptoms in adults with diagnosed mild to moderate depression: SONRIE STUDY.

Study III. Independent and combined associations of physical fitness and body composition with depressive symptoms in adults with diagnosed mild to moderate depression: SONRIE STUDY.

RESULTS

The characteristics of the sample included in this study are shown in **Table 10** for all participants together (n=82), by sex (84.15% female) and, by the severity of depressive symptoms (85.4% upper category). Regarding the sex difference, the age of men was mainly concentrated in the 54-65 years age group (69.23%) showing a less equal distribution compared to women (p=0.01). Alcohol intake also differed between sexes, with a higher percentage for men in former intake (53.85%) and for women in current intake (52.24%) (p=0.018). In terms of body composition, all variables differed significantly between men and women (P<0.05), except for BMI, hip circumference, and obesity according to BMI and fat mass percentage. Specifically for fitness, men performed significantly better than women in handgrip and standing long jump (both P<0.001). Comparing the sample by severity of depressive symptoms, non-significant differences in body composition, fitness, antidepressant medication, or persistence of depression between the lower and upper categories were found (P>0.05). On the contrary, significant differences were observed in self-reported fitness levels between the two groups (p=0.01), with the lower category reporting a higher average level (66.67%) compared to the upper category, which reported (60.87%) very poor-poor level. Regarding socio-demographic variables, participants in the upper category reported significantly more troubled with body pain (p=0.03) and economic stress (p=0.04) compared to participants in the lower category.

Associations of fitness (objectively and subjectively measured) and body composition variables with depressive symptoms in all study sample are shown in **Table 11**. Linear regression analyses reported inverse significant associations between performance in unipedal stance test and depressive symptoms (values: b= -0.14; β =-0.26), but only for Model 1. There were also significant inverse associations between self-reported fitness (higher values for very good statement) and depressive symptoms for both Model 1 and 2 (values range: b= -4.70 to -5.11; β =-0.39 to -0.40). In addition, a direct association was

found between hip circumference and depressive symptoms for all Models (values range: $b = 0.19$ to 0.29 ; $\beta = 0.24$ to 0.33). Furthermore, in Model 3, significant positive associations appeared for both 4-m walking speed and the number of metres walked in 6-min.

The associations between those variables that showed a significant association previously of body composition variable (i.e., hip circumference), fitness objectively (i.e., SPPB-4m walk, unipedal stance, and 6-min walking tests) and subjectively measured with the odds of severe depressive symptoms in the entire study sample are shown in **Table 12**. Logistic regression analyses indicated a significant inverse association between the performance in unipedal stance test and depressive symptoms. Specifically, the risk of severe depressive symptoms in unfit participants was 579% higher compared with those fit participants [Odd ratio (OR) 95% confidence interval (95% CI) for Model 1: 6.79 (1.38-33.43)]. It also found significant associations between self-reported fitness and severe depressive symptoms in both Model 1 and 2, with those in the unfit group having 678% and 2.683%, respectively, increased risk of severe depressive symptoms compared to those in the fit group [OR (95% CI) for Model 1: 7.78 (1.58, 38.27); and for Model 2: 27.83 (1.25, 617.23)].

Lastly, the combined balance fitness-fatness analyses, considering fatness as hip circumference, indicated that participants in the “unfit and not fat” and “unfit and fat” groups had higher odds of experiencing severe depressive symptoms compared to fit and not fat participants [OR (95% CI): 4.44 (1.17, 16.87) and 6.90 (1.87, 25.38), for unfit and not fat, and unfit and fat group, respectively]. Similarly, the combined self-reported fitness-fatness analyses, considering fatness as hip circumference, showed higher odds the same groups [OR (95% CI): 6.03 (1.67, 21.75) and 8.76 (2.28, 33.75), for unfit and not fat, and unfit and fat group, respectively]. **Figure 6**.

Additionally, **Supplementary Table S5** provides further details when the analyses were performed combining balance fitness-fatness analyses, considering fatness as either as BMI or fat mass percentage. Participants in the unfit and fat groups had higher odds of experiencing severe depressive symptoms compared to fit and not fat participants [OR (95% CI): 4.57 (1.23, 16.99) and 6.78 (1.86, 24.70), for BMI and fat mass, respectively]. Moreover, the analyses performed combining self-reported fitness-fatness analyses, considering fatness as either as BMI or fat mass percentage, indicated that participants

in the unfit and not fat and unfit and fat groups, respectively, had higher odds of experiencing severe depressive symptoms compared to fit and not fat participants [Unfit and not fat group= OR (95% CI): 6.27 (1.06, 37.18) and 6.28 (1.88, 21.05); Unfit and fat group= OR (95% CI): 5.61 (1.37, 22.91) and 6.28 (1.88, 21.05), for BMI and fat mass, respectively]. However, when fatness was calculated using waist circumference, in both fitness variables of balance and self-reported fitness, the unfit and not fat group had higher risk odds of having depressive symptoms [Unipedal stance test= OR (95% CI): 3.85 (1.24, 11.93); Self-reported fitness= OR (95% CI): 5.05 (1.65, 15.42)]. Similar associations were observed in the adjusted models (data not shown).

Finally, analyses were conducted to examine the relationship between self-reported fitness and depressive symptoms, considering the objectively measured fitness, in the overall population. The results showed that this association remained statistically significant even after controlling for objectively measured fitness variables. Specifically, after adjusting for usual gait speed at 4-m ($\beta = -5.97$; 95%CI= -8.60- -3.34; $p < 0.001$), or unipedal stance test ($\beta = -4.60$; 95%CI= -7.35, -1.85; $p = 0.001$), or handgrip test ($\beta = -0.40$; 95%CI= -7.91, -2.50; $p < 0.001$), or 6-min walking test ($\beta = -0.50$; 95%CI= -8.73, -3.46; $p < 0.001$), the association between self-reported fitness and depressive symptoms persisted.

Table 10. Descriptive characteristics of the SONRIE study sample.

					Sex		Severity of depressive symptoms			
	All		Women		Men		Lower		Upper	
	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
<i>Sociodemographic variables</i>										
Sex (%)	82		69	84.15	13	15.85	12	83.33/16.67	70	84.29/15.71
Age (years)	82	48.94±9.55	69	48.23±9.53	13	52.73±9.14	12	51.61±7.85	70	48.49±9.79
Age groups (% 25-43/ 44-53/54-65 years)	82	30.49/ 30.49/ 39.02	69	34.78/31.88/33.33	13	7.69/23.08/69.23*	12	16.67/ 50.00/ 33.33	70	32.86/ 27.14/ 40.00
Troubled with body pain (% no to moderately/ quite to extremely)	82	39.02/60.98	69	36.23/63.77	13	53.85/46.15	12	66.67/33.33	70	34.29/65.71*
Economic stress (% no/yes)	81	39.51/60.49	68	42.65/57.35	13	23.08/76.92	12	66.67/33.33	69	34.78/65.22*
Smoking status (% current/former/never)	81	34.57/25.93/39.51	68	33.82/25.00/41.18	13	38.46/30.77/30.77	12	25.00/25.00/50.00	69	36.23/26.09/37.68
Alcohol intake (% current/former/never)	80	47.50/23.75/28.75	67	52.24/17.91/29.85	13	23.08/53.85/23.08*	12	66.67/16.67/16.67	68	44.12/25.00/30.88
Educational level (% up primary education/ higher education)	81	58.02/41.98	68	61.76/38.24	13	38.46/61.54	12	58.33/41.67	69	57.97/42.03
Marital status (% without/ with couple)	81	33.33/66.67	68	35.29/64.71	13	23.08/76.92	12	16.67/83.33	69	36.23/63.77
N Comorbidities (% ≥3/ none to 2)	81	51.85/48.15	68	54.41/45.59	13	/61.54	12	33.33/66.67	69	55.07/44.93

Body composition

Weight (kg)	80	75.63±17.75	67	73.18±16.06	13	88.23±21.21**	12	72.68±12.39	68	76.15±18.56
Height (cm)	80	161.65±8.73	67	159.00±5.88	13	175.38±8.27***	12	163.06±8.06	68	161.40±8.88
BMI (kg/m ²)	80	28.85±6.00	67	28.88±5.89	13	28.68±6.76	12	27.28±3.90	68	29.13±6.28
Fat mass (%)	80	34.95±7.99	67	36.69±6.90	13	26.01±7.42***	12	33.31±7.97	68	35.24±8.02
Fat free mass (%)	80	65.05±7.99	67	63.31±6.90	13	73.99±7.42***	12	66.69±7.97	68	64.76±8.02
Muscle mass (%)	80	61.75±7.59	67	60.0±6.54	13	70.32±7.02***	12	63.33±7.58	68	61.48±7.61
Waist circumference (cm)	81	90.42±15.87	68	88.89±15.28	13	98.39±17.15*	12	87.85±13.60	69	90.86±16.28
Hip circumference (cm)	81	105.91±14.49	68	106.06±14.86	13	105.06±12.92	12	101.25±8.18	69	106.72±15.22
Obesity by BMI (%no/yes)	80	23.75/76.25	67	23.88/76.12	13	23.08/76.92	12	25.00/75.00	68	23.53/76.47
Obesity by fat mass (%no/yes)	80	32.50/67.50	67	31.34/61.54	13	38.46/61.54	12	41.67/58.33	68	30.88/69.12
Obesity by waist circumference (%no/yes)	81	72.84/27.16	68	72.84/27.16	13	38.46/61.54**	12	75.00/25.00	69	72.46/27.54
Obesity by hip circumference (%no/yes)	81	51.85/48.15	68	51.47/48.53	13	53.85/46.15	12	66.67/33.33	69	49.28/50.72

Physical appraisal**Flexibility**

Chair sit and reach test (cm)	81	-5.50±13.69	68	-6.67±13.60	13	0.67±12.95	12	-6.94±15.82	69	-5.24±13.39
Back scratch test (cm)	82	-6.99±10.95	69	-7.64±10.90	13	-3.59±10.96	12	-7.19±11.48	70	-6.96±10.94

Gait speed

Usual gait speed at 4-m (m/s) [†]	82	1.38±0.29	69	1.36±0.30	13	1.48±0.26	12	1.33±0.18	70	1.39±0.31
Usual gait speed at 6-m (m/s)	82	1.38±0.45	69	1.38±0.48	13	1.35±0.15	12	1.31±0.18	70	1.39±0.48

Maximal gait speed at 6-m (m/s)	82	1.80±0.29	69	1.78±0.30	13	1.89±0.26	12	1.90±0.28	70	1.78±0.29
Agility										
8-ft up-and-go test (s)	82	6.49±1.25	69	6.58±1.32	13	6.00±0.70	12	5.99±1.03	70	6.57±1.28
Balance										
Unipedal stance test (s)	78	35.03±21.54	65	34.91±21.62	13	35.66±22.00	12	44.70±18.24	66	33.27±21.74
Upper-limbs muscle strength										
Handgrip test (kg)	82	24.96±9.21	69	22.27±6.43	13	39.25±8.70***	12	26.82±10.12	70	24.64±9.09
Arm curl test (rep)	79	34.28±8.72	67	33.93±8.67	12	36.25±9.15	11	35.45±8.51	68	34.09±8.80
Lower-limbs muscle strength										
Standing long jump (cm)	71	88.43±34.26	60	81.71±27.41	11	125.09±45.08***	11	99.59±35.75	60	86.39±33.88
Chair stand test (rep)	80	11.83±2.68	68	11.84±2.76	12	11.75±2.22	12	11.25±2.26	68	11.93±2.74
5-rep chair stand (s) [†]	80	12.30±3.74	67	12.34±3.98	13	12.10±2.27	12	11.90±2.70	68	12.37±3.91
Functional capacity										
SPPB-score (points) [†]	80	11.08±1.06	67	11.06±1.09	13	11.15±0.99	12	11.08±1.08	68	11.07±1.07
CRF										
6-min walking test (m)	80	539.60±78.50	67	533.05±79.08	13	573.39±68.58	11	557.2±48.36	69	536.79±82.20
Subjectively measured fitness										
Self-reported fitness (% very poor/poor/average/good/very good)	81	18.62/35.80/39.51/4.94/1.23	68	20.29/34.78/40.58/2.90/1.45	±	8.33/41.67/33.33/16.67/0.00	±	8.33/8.33/66.67/16.67/0.00	69	20.29/40.58/34.78/2.90/1.45*

Depression variables

Depressive symptoms (score)	82	32.27±11.36	69	32.30±11.50	13	32.08±11.04	12	14.08±6.37	70	35.39±8.81***
Antidepressant medication (% no/yes)	77	12.99/87.01	66	87.88/12.12	11	81.82/18.18	11	0.00/100.00	66	15.15/84.85
Persistence of depression (years)	61	1.86±2.26	53	2.07±2.35	8	0.51±0.74	10	1.14±1.19	51	2.01±2.40

Data are presented as mean ± standard deviation or percentages. Differences between sex and between depressive symptoms levels were examined by independent t-test and statistically significant differences are in bold and marked as * <0.05 ** <0.005 *** <0.001 . BMI, body mass index; rep, repetition; SPPB, Short Physical Performance Battery. Severity of depressive symptoms: lower group [minimal to moderate]: 0 to 28 points of Beck Inventory Scale; upper group [severe]: 29 to 63 points of Beck Inventory Scale. Obesity by BMI: ≥ 25 kg/m². Obesity by fat mass was according to Gallagher et al. criteria (113). Obesity by waist circumference: ≥ 88 cm for women and ≥ 102 cm for men. Obesity by hip circumference: the highest 50% sample group based on age and sex. *Tests belonging to the SPPB.

Table 11. Associations of physical fitness tests and body composition variables with depressive symptoms in adults with depression.

Variable	Model 1				Model 2				Model 3			
	N	B	β	IC 95%	N	B	β	IC 95%	N	B	β	IC 95%
<i>Physical fitness tests</i>												
<i>Flexibility</i>												
Chair sit and reach test (cm)	81	-0.01	-0.02	(-0.20-0.17)	58	<0.001	<0.001	(-0.21-0.21)	73	0.08	0.10	(-0.11-0.28)
Back scratch test (cm)	82	-0.02	-0.02	(-0.25-0.21)	59	0.01	0.01	(-0.26-0.29)	74	0.13	0.12	(-0.12-0.38)
<i>Gait speed</i>												
Usual gait speed at 4-m (m/s) [†]	82	6.59	0.17	(-1.94-15.13)	59	7.94	0.20	(-1.90-17.77)	74	13.26	0.33***	(5.00-21.52)
Usual gait speed at 6-m (m/s)	82	1.85	0.07	(-3.80-7.50)	59	4.11	0.16	(-2.01-10.23)	74	4.72	0.19	(-0.60-10.05)
Maximal gait speed at 6-m (m/s)	82	-4.18	-0.11	(-12.79-4.44)	59	-3.28	-0.08	(-15.08-8.51)	74	3.52	0.09	(-6.57-13.61)
<i>Agility</i>												
8-foot up and go test (s)	82	0.13	0.01	(-1.88-2.15)	59	0.78	0.08	(-1.95-3.51)	74	-0.95	-0.10	(-3.21-1.31)
<i>Balance</i>												
Unipedal stance test (s)	78	-0.14	-0.26*	(-0.26- -0.02)	57	-0.11	-0.23	(-0.27-0.39)	72	-0.10	-0.19	(-0.25-0.04)
<i>Upper-limbs muscle strength</i>												
Handgrip test (kg)	82	-0.01	-0.01	(-0.29-0.26)	59	-0.06	-0.05	(-0.41-0.28)	74	0.15	0.12	(-0.13-0.44)
Arm curl test (rep)	79	-0.01	-0.01	(-0.31-0.28)	57	0.26	0.20	(-0.10-0.62)	72	0.22	0.16	(-0.11-0.54)
<i>Lower-limbs muscle strength</i>												
Standing long jump (cm)	71	-0.03	-0.10	(-0.11-0.05)	52	-0.10	-0.25	(-0.22-0.03)	65	0.01	0.02	(-0.09-0.10)
Chair stand test (rep)	80	0.23	0.05	(-0.73-1.18)	59	0.58	0.14	(-0.54-1.69)	72	0.39	0.09	(-0.67-1.46)
5-rep chair stand (s) [†]	80	0.25	0.08	(-0.43-0.93)	58	-0.17	-0.04	(-1.18-0.85)	72	-0.12	-0.04	(-0.79-0.56)
<i>Functional capacity</i>												
SPPB-score (points)	80	-0.80	-0.08	(-3.17-1.58)	58	0.42	0.04	(-2.29-3.13)	72	0.21	0.02	(-2.24-2.66)
<i>CRF</i>												
6-min walking test (m)	80	-0.02	-0.12	(-0.05-0.02)	59	0.02	0.14	(-0.03-0.07)	72	0.04	0.28*	(0.00-0.08)
<i>Subjectively measured fitness</i>												

Self-reported fitness (score)	81	-5.11	-0.40***	(-7.76- -2.45)	58	-4.70	-0.39*	(-7.95- -1.45)	73	-3.05	-0.23	(-6.19-0.08)
<u>Body composition</u>												
BMI (kg/m ²)	80	0.36	0.19	(-0.6-0.79)	59	0.36	0.22	(-0.05-0.78)	74	0.40	0.20	(-0.05-0.85)
Fat mass (%)	80	0.24	0.16	(-0.08-0.56)	59	0.30	0.23	(-0.02-0.62)	74	0.18	0.12	(-0.15-0.51)
Fat free mass (%)	80	-0.24	-0.16	(-0.56-0.08)	59	-0.30	-0.23	(-0.62-0.02)	74	-0.18	-0.12	(-0.51-0.15)
Muscle mass (%)	80	-0.25	-0.16	(-0.58-0.09)	59	-0.31	-0.23	(-0.65-0.02)	74	-0.19	-0.12	(-0.54-0.16)
Waist circumference (cm)	81	0.09	0.13	(-0.07-0.25)	60	0.15	0.23	(-0.02-0.32)	75	0.12	0.17	(-0.06-0.31)
Hip circumference (cm)	81	0.19	0.24*	(0.02-0.36)	60	0.28	0.33*	(0.08-0.48)	75	0.29	0.30*	(0.09-0.50)

Data are presented for all sample as unstandardized regression coefficient (b), standardized regression coefficient (β), and confidence interval (CI). Model 1 was unadjusted; model 2 was adjusted for age, BMI, the persistence of depression, economic stress, and trouble with body pain; and model 3 for age, BMI, antidepressant medication, economic stress, and trouble with body pain. BMI was dropped in models 2 and 3 for the body composition variables. Statistically significant associations are in bold and marked as * <0.05 *** <0.001 . BMI, body mass index; rep, repetition; SPPB, Short Physical Performance Battery. *Tests belonging to the SPPB.

Table 12. Associations of physical fitness tests and body composition variables with the odds of increasing depressive symptoms in adults with depression.

Variable		Model 1			Model 2			Model 3		
	Level	N	OR	IC 95%	N	OR	IC 95%	N	OR	IC 95%
<u>Physical fitness tests</u>										
<i>Gait speed</i>										
Usual gait speed at 4-m [†]	Fit	41	1		34	1		39	1	
	Unfit	41	1.48	(0.43-5.12)	27	0.65	(0.12-3.52)	35	1.01	(0.24-4.16)
<i>Balance</i>										
Unipedal stance test	Fit	38	1		29	1		37	1	
	Unfit	40	6.79	(1.38-33.43)*	29	0.96	(0.20-4.56)	35	5.59	(0.87-36.09)
<i>CRF</i>										
6-min walking test	Fit	39	1		33	1		36	1	
	Unfit	41	0.86	(0.24-3.08)	28	0.29	(0.05-1.71)	36	0.27	(0.05-1.40)
<i>Subjectively measured fitness</i>										
Self-reported fitness	Fit	37	1		30	1		31	1	
	Unfit	44	7.78	(1.58-38.27)*	28	27.83	(1.25-617.23)*	29	3.43	(0.72-16.32)
<u>Body composition</u>										
Hip circumference	Not-fat	42	1		32	1		39	1	
	Fat	39	2.06	(0.57-7.48)	29	3.03	(0.58-15.88)	37	1.70	(0.42-6.81)

Data are presented as odd ratio (OR), and confidence interval (CI). Model 1 was unadjusted; model 2 was adjusted for age (only for self-reported fitness), BMI (except for hip circumference), the persistence of depression, economic stress, and trouble with body pain; and model 3 for age (only for self-reported fitness), BMI (except for hip circumference), antidepressant medication, economic comfort, and pain interference. Fit was defined as the 50% top of the age group (divided by tertiles) and sex, and unfit as the bottom 50%, showed in all physical fitness variables. Statistically significant associations are in bold and marked as * <0.05 . BMI, body mass index; rep, repetition; SPPB, Short Physical Performance Battery. [†]Tests belonging to the SPPB.

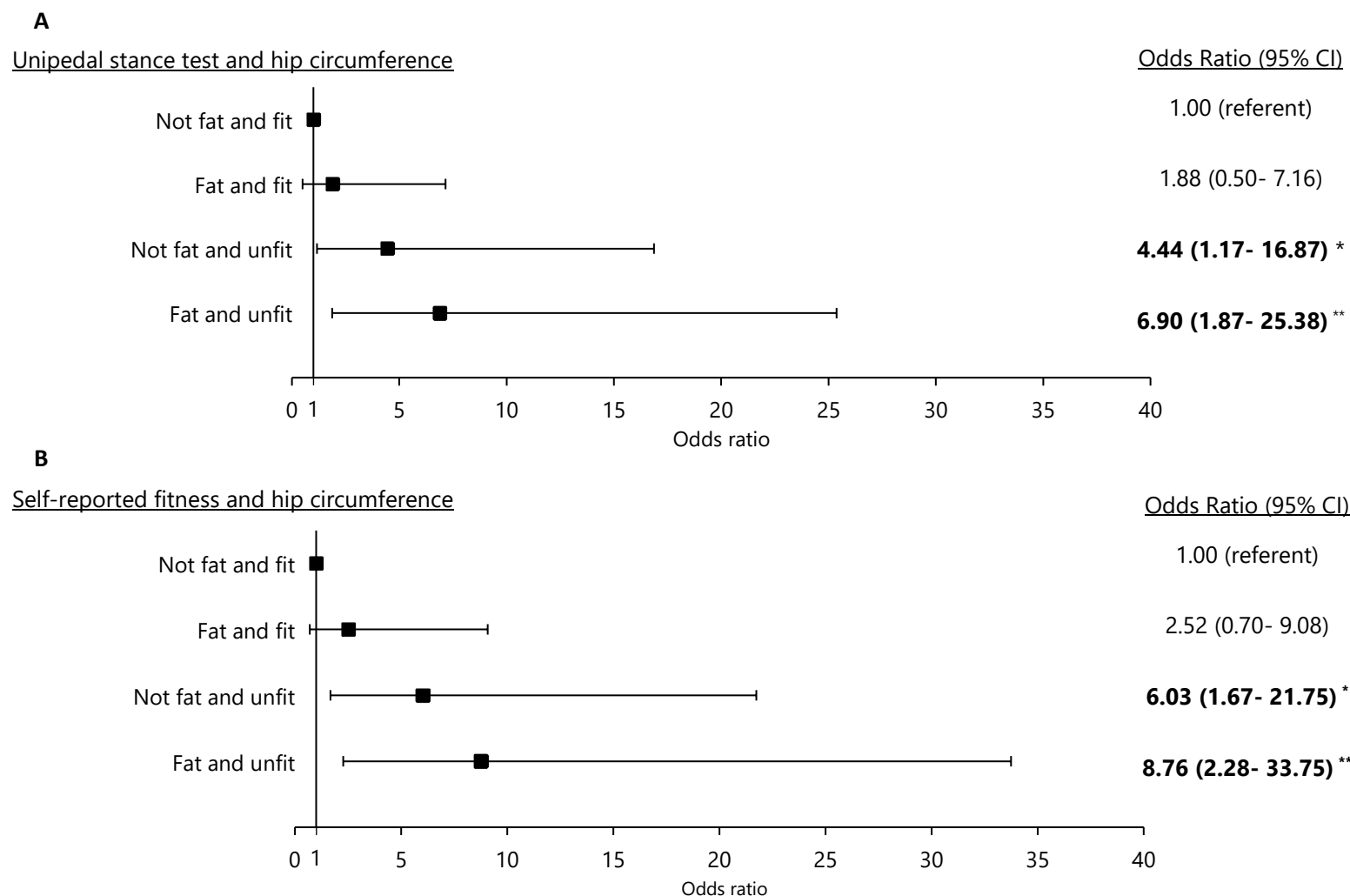


Figure 6. Associations of unfit/fit and not fat/fat groups with the odds of increasing depressive symptoms in adults with depression, compared with fit and not fat group (referent). Fit was defined as the 50% top of the age group (divided by tertiles) and sex, and unfit as the bottom 50%, showed in Unipedal stance test (balance) (A) and Self-reported fitness (B). Fat was defined as the 50% top of the age group (divided by tertiles) and sex for hip circumference, and not fat as the bottom 50%, for hip circumference. Statistically significant associations are in bold and marked as * <0.05 ** <0.005 . Odds ratios were unadjusted. CI, confidence interval.

DISCUSSION

The present paper examined the associations of fitness components and body composition with depressive symptoms in adults diagnosed with depression. Results suggested that both objective and subjective measures of fitness may have a role in reducing depressive symptoms. Specifically, for objectively measured fitness, our results revealed that better balance performance, as measured by the unipedal stance test, was associated with lower levels of depressive symptoms. Additionally, the results found that unfit participants in this variable, were at a significantly higher risk of developing severe depressive symptoms than those who were fit. However, it was only true for the unadjusted model. Regarding subjectively measured fitness, there was a significant link between self-reported fitness and depression since higher levels of self-reported fitness were associated with lower levels of depressive symptoms. Indeed, unfit participants also had a higher risk of severe depressive symptoms compared to fit ones. On the other hand, while the results of this study found a direct association between hip circumference and depressive symptoms, this association did not persist when examining the risk of depression in participants who were classified as fat versus not fat. Additionally, the association between fitness-fatness and depressive symptoms varied depending on the measure used, highlighting the importance of considering both fitness (objective and subjectively measured) and body composition factors in the management and prevention of depressive symptoms in adults with depression.

The finding about the link between balance performance and depressive symptoms are in accordance with previous studies performed in older adults (76,80,199) using the same unipedal stance test (76,199). However, a lack of association was reported in the only study that we found analysing balance and depressive symptoms in older adults diagnosed by depression (53). In fact, Conradsson et al. (53) found no relationship between balance and depressive symptoms in their sample of elderly, which contrasts with our results. To our knowledge, only two studies examined balance and depressive symptoms associations focus in adults, as we have done (49,50). However, their findings were inconsistent. One study reported an inverse association between balance and depressive symptoms, in line with ours (49), while the other did not find such association (50). Moreover, neither of these studies specifically focused on adults diagnosed with

depression, as we have done. Thus, our study provides important insights into the relationship between fitness components and depressive symptoms in adults diagnosed with depression, an area that remains understudied compared to other medical conditions (254–256).

The observed association between balance performance and depressive symptoms might be partially explained by the effect of depression on postural stability (257). Postural stability, also known as balance, refers to the ability to control the relationship between the center of mass and the base of support (258). Moreover, scientific literature has also shown patients with depression experience cognitive impairments (259,260). These impairments should be considered because the regulation of posture adaptation to the environment requires the involvement of the sensory-cognitive-motor system (258). This system involves complex neural networking, including dopaminergic pathways and circuits in the prefrontal cortex and basal ganglia (261). As a result, even slight changes in cognition may lead to postural instability and impaired balance (262–264). This suggests that depression may impact postural stability through the disruption of neuronal networks that regulate balance. Additionally, individuals with depression often exhibit motor manifestations such as abnormal and tense postures, slowness of movement, and motor stagnation, which may impair their postural control (257). Moreover, it is important to consider that multimorbidity and polypharmacy are biologically plausible factors which can lead to diminished balance (264). Overall, this highlights the need for a holistic approach to the management of depression that takes into account not only its mental health impact but also its physical manifestations, such as impaired balance and postural instability.

Interestingly, among all objectively measured fitness components, only balance has been found to be related to depressive symptoms in adults with depression. This suggests that publication bias may have influenced the evidence in the literature, leading to a potential underrepresentation of published studies reporting no association between physical fitness and depressive symptoms in people with depression. In addition, small studies that find no association are less plausible to be published than small studies that find significant associations (265). Therefore, it is important to take these factors into consideration when interpreting the existing research. On the other hand, the lack of

association between objectively measured fitness components, except for balance, and depressive symptoms in adults with depression may be attributed to several causes. Depression is a multifactorial disorder, and although the study controlled for various confounding factors and relied on existing literature, factors such as cognitive function may have been overlooked. Furthermore, depression is often characterized by a decreased level of physiological and psychological activation or readiness (266). In other words, arousal is reduced in people with depression (266), and this has been linked to poorer physical performance (267) and reduced physical activity (268). This may contribute to a lower level physical fitness and may explain the lack of a significant association between fitness and depressive symptoms observed in this target population.

Our findings regarding self-reported fitness are in line with previous studies that have shown it to be a strong predictor for mortality (97), cardiovascular disease risk,(98), and resilience to stress in adults (99). However, we did not find any studies that specifically investigated the association between self-reported fitness and depression in our population. Nonetheless, studies conducted in other populations such as pregnant women (42), perimenopausal women (43), and healthy adolescents (100), have observed an inverse association between self-perception of fitness and depressive symptoms, with is in line with our results. Furthermore, our findings demonstrated the independence of this relationship in terms of the objective fitness level of the sample.

Terms related to self-reported fitness, but not studied in our work, such as self-rated health (269), as well as self-esteem and self-efficacy (270), have been shown to be inversely related to depressive symptoms in population with chronic diseases (269) and disabilities (270). Self-rating of fitness is believed to be developed as part of a cognitive process that is inherently subjective and contextual. A previous study (271) introduced a theory that distinguished between different states in the process of self-reported health, which may also be applicable to understanding self-rated fitness. These stages involve the processing of information, *i.e.*, the meaning of health; interpretation of meanings, *i.e.*, the way in which those components should be considered; and finally, the selection, *i.e.*, which level on the given scale summarizes better (271).

Despite this, it is still relatively unknown how individuals evaluate their health status, and which cognitive, cultural and other processes are involved (272–275). Similarly, the same

circumstance may apply to self-rated fitness. Nonetheless, our study suggests that a simple question related to self-rated fitness could be a valuable addition to the evaluation of depressive symptoms in clinical settings. This subjective measure of fitness demonstrated an inverse association with depressive symptoms, even independently of objective measured fitness.

On the other hand, several reviews have suggested that a good body composition is relevant for better mental health and vice versa (276,277). However, in our study, we only observed a relationship with hip circumference, which disappeared when dichotomised by the 50th percentile. There is not yet a clear explanation for why hip circumference is positively related to depressive symptoms. Some studies have suggested that the accumulation of fat in the hip region, known as gynoid fat (278), may be related to the production of certain hormones that affect mood, such as oestrogen and progesterone (279). In addition, it has been proposed that high abdominal fat, measured through BMI or waist circumference, is related to chronic high-grade inflammation, which in turn is related to depression (280). Despite this, hip circumference is not a commonly used scientifically validated variable like waist circumference and BMI. Nonetheless, a study on a healthy population (281) reported a positive correlation between hip circumference and depressive symptoms, which is consistent with our findings. However, another study (278) that included individuals with psychological illnesses other than depression found no such association. Therefore, more studies are needed to establish the exact relationship between hip circumference and depressive symptoms in people with depression.

Moreover, when fatness, according to hip circumference, was combined with balance or self-reported fitness variables, both not fat and fat low fitness profiles, showed increased odds of severe depressive symptoms against the ideal group (fit and not fat). The higher odds for the second profile were noteworthy. This may be due to the important role of fitness, which in combination with fatness has a stronger impact on depressive symptoms than both independently. This view could also be supported by similar findings when fatness was considered by BMI, fat percentage and waist circumference, due to the same groups were also much more likely to have increased depressive symptoms compared to the fit and not fat group. In this line, the landmark paper by Becofsky et al. (138) on

healthy population, provided concrete results on the role of fitness, specifically of CRF, combined with fatness measured by BMI, fat mass and waist circumference. Overall, their sample revealed that again, the groups most likely to have increased depressive symptoms were the same as those in this study. Thus, both studies seem to show the greater influence of fitness on depressive symptoms in general population, and also in its combination with body composition.

Ultimately, better perceived fitness and higher performance in balance may have a protective effect against depressive symptoms in adults with depression. Additionally, a larger hip circumference may be related to more depressive symptoms, while low fitness combined with high body fat might further increase depressive symptoms compared to their high-fitness and low-fat peers. Self-rated fitness is a simple and quick tool that can be used in clinical settings to assess an individual's perception of their own fitness level, and it may provide useful information for evaluating the relationship between physical fitness and depressive symptoms, particularly in settings where more comprehensive assessments may not be possible.

LIMITATIONS AND STRENGTHS

LIMITATIONS AND STRENGTHS

The findings presented in this International Doctoral Thesis have some general and specific limitations that should be considered when interpreting the results. Nevertheless, this International Doctoral Thesis also has several strengths. Therefore, these limitations are presented below along with the main strengths.

Limitations

- In **Study I**, the sample was very heterogeneous in terms of having a totality of healthy people, despite excluding disease-specific elements.
- The samples of the included studies with larger age ranges and the lack of studies that distinguished by age made it difficult to further divide the qualitative analysis in **Study I**. Similarly, this was the case for sex distinction.
- Another limitation found in **Study I** was discerned whether the population had been diagnosed as depressed or had a severity of depressive symptoms that referred to depression was complicated by the terminology and categorisation used in the scientific evidence.
- Eventually in **Study I**, there was only a qualitative analysis of the included studies, albeit based on refereed reviews (150,151).
- The cross-sectional design of the **Studies II and III** does not provide insight into the causal relationship of fitness and body composition with depressive symptoms.
- The limited sample size should be taken into account. In **Study II**, the sample was mostly overweight and showed depressive symptoms concentrated in low values. Nevertheless, showing depressive symptoms below the depressive threshold is quite common in older people and not benign (282). In **Study III**, the small number of men sample did not allow us to identify relationships in this sex, due to the lower percentage of the population of men with diagnosed depression (3).
- The sample of **Study II** included exclusively people between the ages of 65 and 75. While this was important to maintain consistency within the sample, it also means that the results may not be applicable to older adults outside this age range.

- Some of the confounding variables included in **Study III** were self-reported, such as the persistence of depression, economic comfort, pain interference and antidepressant medication, which raises the possibility of residual confounding. Although there is always bias associated with self-report measures, we tried to minimize this through the use of standardized procedures.

Strengths

- To our knowledge, **Study I** is the first systematic review providing a qualitative evaluation of all fitness components and depressive symptoms in healthy and depressed adults and older adults. Moreover, many papers and large samples were collected on physical fitness, allowing a global view of fitness in the current scientific evidence.
- Also, in **Study I**, validated and recognised tools such as PRISMA and NOS were used, and two major databases (PubMed and Web of Science) were searched.
- Another strength of **Study I** was the studies were assessed by two independent researchers for risk-of-bias, and the selection of studies, and data collection procedure were carefully analysed.
- Late-life depression begins at the age stage of **Study II**, and is underdiagnosed and under-treated (283).
- In **Study II**, analysing all fitness components in the same cohort allowed a better understanding of which fitness components are the most important. Moreover, the use of diverse and objective methods to measure physical fitness and body composition components is an added value providing accuracy to the current findings.
- In **Study III**, the sample of adults was previously diagnosed by psychiatrists, and in addition to this, information on their depressive symptoms was obtained. Moreover, to our knowledge, is the first study to examine fitness and depressive symptoms in a full sample of adults with depression.
- Lastly, both **Study II and Study III**, obtaining data on several fitness and body composition variables enables a more comprehensive understanding of the participants' physical health and can provide insight into specific factors that may influence the relationship between fitness and depressive symptoms.

CONCLUSIONS

CONCLUSIONS

The conclusions of this International Doctoral Thesis obtained from the three studies included, are outlined below.

- 1) CRF, strength, and gait speed were inversely related to depressive symptoms longitudinally, while all fitness components except flexibility and other gait parameters were inversely related to depressive symptoms cross-sectionally in healthy adults and older adults. However, there is no evidence regarding the specific population with diagnosed depression.
- 2) Higher levels of fitness, notably gait speed, and muscle strength and lower fatness seem to contribute to having fewer depressive symptoms in older adults. Higher performances in gait speed, agility, upper-limb muscular strength and CRF, as well as, more appropriate fat and muscle levels, appear to have a beneficial impact, individually, on these symptoms. Furthermore, older people identified as low-fit (considering flexibility, gait speed, upper limbs muscle strength and CRF) and high-fat might have increased odds of higher depressive symptoms compared to their high-fit and low-fat peers.
- 3) Better perceived fitness and higher balance performance may have a protective effect against depressive symptoms in adults with depression. Additionally, a larger hip circumference may be related to more depressive symptoms, while low-fit (considering balance and perceived fitness) combined with high-fat might further increase depressive symptoms compared to their high-fit and low-fat peers. Self-reported fitness is a simple and quick tool that can be used in clinical settings to assess an individual's perception of their fitness level, which may provide useful information for evaluating the relationship between physical fitness and depressive symptoms.

CONCLUSIONES

A continuación, se exponen las conclusiones de la presente Tesis Doctoral Internacional obtenidas a partir de los tres estudios incluidos.

- 1) CRF, la fuerza y la velocidad de la marcha se relacionaron inversamente con los síntomas depresivos de forma longitudinal, mientras que todos los componentes de la forma física, excepto la flexibilidad y otros parámetros de la marcha, se relacionaron inversamente con los síntomas depresivos de forma transversal en adultos sanos y adultos mayores. Sin embargo, no existen pruebas relativas a la población específica con depresión diagnosticada.
- 2) Los niveles más altos de forma física, en particular la velocidad de la marcha y la fuerza muscular, y el menor nivel de grasa corporal parecen contribuir a tener menos síntomas depresivos en los adultos mayores. Un mayor rendimiento en velocidad de la marcha, agilidad, fuerza muscular de las extremidades superiores y CRF, así como una mejor composición corporal de grasa y muscular, parecen tener un impacto beneficioso sobre estos síntomas individualmente. Además, las personas mayores identificadas como de baja forma física (teniendo en cuenta la flexibilidad, la velocidad de la marcha, la fuerza muscular de las extremidades superiores y la CRF) y con un alto nivel de grasa corporal podrían tener mayores probabilidades de presentar síntomas depresivos más elevados en comparación con sus compañeros de alta forma física y bajo nivel de grasa.
- 3) Una mejor forma física autopercebida y un mayor rendimiento en equilibrio pueden tener un efecto protector contra los síntomas depresivos en adultos con depresión. Además, un mayor perímetro de cadera puede estar relacionado con más síntomas depresivos, mientras que una baja forma física (teniendo en cuenta el equilibrio y la forma física autopercebida) combinada con una elevada grasa corporal podría aumentar aún más los síntomas depresivos en comparación con sus compañeros con una alta forma física y una baja grasa. La aptitud física autodeclarada es una herramienta sencilla y rápida que puede utilizarse en entornos clínicos para evaluar la percepción que tiene una persona de su nivel de aptitud física, lo que puede

proporcionar información útil para evaluar la relación entre la aptitud física y los síntomas depresivos.

FUTURE RESEARCH DIRECTIONS

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During the course of this International Doctoral Thesis, as well as the process of research and reflection carried out for the best interpretation of our data, we have found relevant unknowns in the understanding of fitness, body composition and depressive symptoms. Therefore, in this section we suggest future lines of research as well as methodological improvements in the field of fitness, body composition and depressive symptoms in healthy and depressive adults and older adults:

1. To analyse all available scientific evidence synthesised in the systematic review, by means of a meta-analysis. Hence, statistically analyse and combine the results of the individual studies into a single estimate of effect.
2. To examine the effect of a long-term supervised exercise intervention for healthy older adults on physical fitness, body composition and depressive symptoms. This data available from the INTERMAE study will allow us to establish causal relationships.
3. To study the effect of a long-term online exercise intervention for adults with depression on physical fitness, body composition and depressive symptoms. This will be based on data available from the SONRIE study, allowing us to determine causal relationships.
4. To examine specifically by sex and age group the relationships between fitness, body composition and depressive symptoms across larger samples.
5. To develop future studies focusing on people suffering from depression, in order to further explore this field and achieve a broader knowledge as it is currently scarce.

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ANNEXES

ANNEX I: Supplementary Tables

Table S1. PRISMA Checklist for Systematic Review of Study I.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	45
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	11
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	19
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	37
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	48
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	47
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	47
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	47 and 221
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	47
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	48
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	48

Section and Topic	Item #	Checklist item	Location where item is reported
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	48
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	49
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	48
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	48
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	48
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	48
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	49
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	49
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	48
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	49
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	77 and 78
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	77
Study characteristics	17	Cite each included study and present its characteristics.	94
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	79

Section and Topic	Item #	Checklist item	Location where item is reported
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	91
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	77
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	121
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	94
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	77
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	77
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	128
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	130
	23b	Discuss any limitations of the evidence included in the review.	169
	23c	Discuss any limitations of the review processes used.	169
	23d	Discuss implications of the results for practice, policy, and future research.	132
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	47
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	47
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	47
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	

Section and Topic	Item #	Checklist item	Location where item is reported
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

Table S2. Search terms and search strategies to each database.

PUBMED
((("cardiorespiratory fitness"[Title/Abstract] OR cardiorespiratory fitness [MeSH] OR "aerobic capacity"[Title/Abstract] OR "aerobic fitness" [Title/Abstract] OR Muscle strength [MeSH] OR "Muscle strength"[Title/Abstract] OR "Muscular strength" [Title/Abstract] OR "Muscular fitness" [Title/Abstract] OR Range of Motion, Articular [Majr] OR "Range of motion" [Title/Abstract] OR Flexibility [Title/Abstract] OR "physical fitness"[Title/Abstract] OR "functional capacity" [Title/Abstract] OR "physical characteristic*" [Title/Abstract] OR "oxygen consumption" [Title/Abstract] OR "vo2max" [Title/Abstract] OR "vo2peak" [Title/Abstract] OR "oxygen capacity" [Title/Abstract] OR fitness[Title/Abstract] OR speed-agility [Title/Abstract] OR "motor fitness" [Title/Abstract] OR balance [Title/Abstract]) AND (Depression [Title/Abstract] OR Depression [MeSH] OR Depressive disorder [MeSH] OR Depressive [Title/Abstract]) AND (Adult [MeSH] OR Adult [Title/Abstract] OR Middle Aged [MeSH] OR "Middle Age*" [Title/Abstract] OR Aged [MeSH] OR Aged [Title/Abstract] OR Ageing [Title/Abstract] OR Aging [Title/Abstract] OR Elderly [Title/Abstract] OR older* [Title/Abstract]))
WEB OF SCIENCE
((("cardiorespiratory fitness" OR "aerobic capacity" OR "aerobic fitness" OR "Muscle strength" OR "Strength" OR "Muscular strength" OR "Muscular fitness" OR "Range of Motion" OR Flexibility OR "physical fitness" OR "functional capacity" OR "physical characteristic*" OR "oxygen consumption" OR "vo2max" OR "vo2peak" OR "oxygen capacity" OR fitness OR speed-agility OR "motor fitness" OR "balance") AND (Depression OR "depressive symptom" OR "depressive symptoms" OR "emotional depression" OR "emotional depressions" OR "depressive disorder" OR "depressive disorders") AND (Adult OR "Middle Age" OR "Middle aged" OR Aged OR Ageing OR Aging OR Elderly OR "older people" OR "older adults"))

MeSH, Medical Subject Heading ; **Majr**, MeSH Major Topic.

Table S3. List of tests by fitness component and the number of studies applying it.

CRF	• Maximal exercise cycle ergometer testing (n= 4) • Submaximal exercise cycle ergometer testing (n= 5) • Maximal exercise treadmill testing (n=4) • Submaximal exercise treadmill testing (n= 2) • 3-min walking test (n=1) • 6-min walking test- Senior Fitness Test (n= 4) • 2-min step test (n=1) • 4-min step test (n=1) • 5-min step test (n=1) • 20-m shuttle run test (n=1)
Upper-limbs muscle strength	• Hand-held dynamometer (n= 59) • 30-sec arm curl- Senior Fitness Test (n=3) • Lifting 8 kg and reaching above the head (n=1) • 1 RM chest press (n=1) • Sit up (n=1) • Isometric trunk extension (n=1)
Lower-limbs muscle strength	• 1-rep chair stand (n= 1) • 3-rep chair stand (n= 1) • 5-rep chair stand- Functional capacity index 1 and 2 and SPPB (n=12) • 30-sec chair stand- Senior Fitness Test (n= 4) • Isometric quadriceps strength in chair (n=1) • Jumping mechanigraphy (n=1) • 1RM leg press (n=1) • Knee extensor and hip flexor by dynamometer (n=1)
Upper-limbs flexibility	• Back scratch- Senior Fitness Test (n= 4)
Lower-limbs flexibility	• Chair sit and reach- Senior Fitness Test (n= 6)
Gait performance	Gait speed: • Not specified m walking at normal pace (n=2) • 2.4-m walking at normal pace- Functional capacity index 2 (n= 2) • 3-m walking at normal pace (n= 3) • 4-m walking at normal pace- Functional capacity index 1 and SPPB (n=14) • 4.6-m walking at normal pace (n= 2) • 5-m walking at normal pace (n= 3) • 6-m walking at normal pace (n= 2) • 10-m walking at normal pace (n= 2) • 12.20-m walking at normal pace (n= 1) • 10-m walking at fast pace (n= 1) • 15-m walking at fast pace (n= 1) • 30-sec walking in treadmill (n= 1) Other gait parameters • Gait plasticity (stride speed and stride variability walking at normal, fast, and slow pace) (n= 1) • Gait stability (dynamic stability of the foot) and variability (stride length and time) in single task condition (walk 4-min in normal pace) and dual-task condition (adding reciting serial three subtractions) (n= 1)

	Gait variability (stride time variations in 2-min walking at normal pace in 25-m long) (n= 1)
Agility-coordination	8-ft up and go- Senior Fitness Test (n= 3) - Timed up and go- Functional capacity index 1 (n= 9) - Putting on and taking off a cardigan- Functional capacity index 2 (n=1) 10-m shuttle run test (n=1) - time in 10-foot tapping (n=1)
Balance	- Not specified sec unipedal leg stance (n= 1) 60-sec unipedal stance- Functional capacity index 1 (n=2) 10-sec side by side, semi tandem and tandem- SPPB (n= 9) 10- sec tandem- Functional capacity index 2 (n= 1) 30-sec tandem and 8-rep alternate step (n= 1) - Tinetti scale (n= 1) - Berg balance scale (n= 3) - Sway in standing position with open eyes (n= 1) - Stair climb and descend (n= 1) - Biomechanical parameters using the single-step protocol of Dietrich and Brenière (n= 1) 3- m timed tandem walk (n= 1) 10-sec in different positions and functional reach test: maximal distance beyond arm's length in standing position (n= 1) - Stair climb and 0.90-kg lift from the floor to a plane (n= 1)
Functional capacity (Total score)	- Functional capacity index 1 (5-rep chair stand, 4-m walking at normal pace, timed up and go, and 60-sec unipedal stance) (n= 1) and index 2 (5-rep chair stand, 2.4-m walking at normal pace, Putting on and taking off a cardigan, and 10-sec tandem) (n= 1) - SPPB (n= 8) - Nagi physical disability scale (n=1) - Senior Fitness Test Battery (n=1) - Upper-limbs muscle strength (hand-held dynamometer) and gait speed (4-m walking at normal pace) index (n= 2)

CRF, cardiorespiratory fitness; **RM**, repetition maximum; **SPPB**, Short Physical Performance Battery.

Supplementary Table S4. Associations of physical fitness and fatness groups with the odds of increasing depressive symptoms in older adults (Study II).

Variable		BMI			Fat mass percentage			Waist circumference		
	Fitness and fatness group	N	OR	CI 95%	N	OR	CI 95%	N	OR	CI 95%
Back scratch	Fit and not fat (reference)	12	1		29	1		51	1	
	Fit and fat	53	4.09	(1.16 - 14.46)	36	1.62	(0.65 - 4.02)	14	1.39	(0.49 - 4.00)
	Unfit and not fat	5	9.25	(1.32 - 64.66)	9	4.58	(1.08 - 19.52)	13	2.02	(0.65 - 6.26)
	Unfit and fat	21	4.29	(1.07 - 17.18)	18	1.57	(0.55 - 4.52)	13	1.42	(0.50 - 4.07)
Usual gait speed at 6-m (m/s)	Fit and not fat (reference)	13	1		23	1		45	1	
	Fit and fat	51	2.89	(0.81 - 10.32)	41	2.79	(0.98 - 7.98)	19	1.59	(0.61 - 4.18)
	Unfit and not fat	4	7.66	(1.09 - 53.74)	15	10.17	(2.74 - 37.79)	19	4.68	(1.70 - 12.87)
	Unfit and fat	23	9.17	(2.23 - 37.69)	13	5.77	(1.51 - 22.11)	8	3.49	(0.92 - 13.24)
8-ft up-and-go test	Fit and not fat (reference)	13	1		28	1		52	1	
	Fit and fat	52	2.05	(0.66 - 6.40)	37	1.57	(0.62 - 3.99)	13	1.55	(0.51 - 4.71)
	Unfit and not fat	4	2.04	(0.24 - 17.61)	10	3.72	(1.00 - 13.90)	12	2.79	(0.90 - 8.65)
	Unfit and fat	22	3.32	(0.95 - 11.58)	17	1.90	(0.64 - 5.68)	14	1.47	(0.54 - 4.06)
Handgrip test	Fit and not fat (reference)	12	1		28	1		46	1	
	Fit and fat	51	2.74	(0.82 - 9.16)	36	1.46	(0.59 - 3.64)	17	1.53	(0.56 - 4.19)
	Unfit and not fat	5	2.32	(0.34 - 15.93)	9	1.45	(0.37 - 5.76)	17	1.15	(0.40 - 3.32)
	Unfit and fat	22	2.28	(0.60 - 8.69)	18	1.15	(0.38 - 3.47)	10	1.10	(0.35 - 3.44)

Arm curl test	Fit and not fat (reference)	9	1		29	1		46	1	
	Fit and fat	56	2.94	(0.69 - 12.52)	37	1.28	(0.50 - 3.32)	19	1.19	(0.45 - 3.17)
	Unfit and not fat	8	3.33	(0.47 - 18.16)	9	1.93	(0.54 - 6.87)	16	1.75	(0.63 - 4.88)
	Unfit and fat	15	8.00	(1.15 - 29.91)	17	2.41	(0.72 - 8.06)	7	2.18	(0.59 - 7.99)
Chair stand test	Fit and not fat (reference)	16	1		33	1		59	1	
	Fit and fat	61	2.03	(0.73 - 5.64)	44	1.25	(0.54 - 2.87)	18	1.4	(0.59 - 3.69)
	Unfit and not fat	1	1.90	(0 -)	3	0.90	(0.12 - 6.56)	3	0.38	(0.03 - 4.16)
	Unfit and fat	11	1.22	(0.30 - 4.98)	10	0.76	(0.20 - 2.86)	9	0.78	(0.22 - 2.75)
6 min walking test	Fit and not fat (reference)	14	1		29	1		54	1	
	Fit and fat	52	2.28	(0.74 - 7.00)	37	1.65	(0.66 - 4.14)	12	1.52	(0.50 - 4.56)
	Unfit and not fat	3	4.45	(0.47 - 42.17)	9	6.25	(1.47 - 26.52)	10	4.11	(1.17 - 14.41)
	Unfit and fat	22	3.89	(1.12 - 13.55)	17	2.05	(0.69 - 6.04)	15	1.57	(0.57 - 4.30)
VO _{2peak} relative†	Fit and not fat (reference)	9	1		21	1		37	1	
	Fit and fat	39	1.53	(0.39 - 6.09)	27	1.08	(0.37 - 3.15)	11	1.46	(0.44 - 4.81)
	Unfit and not fat	2	1.46	(0.09 - 24.97)	6	3.89	(0.70 - 21.75)	9	5.68	(1.41 - 22.97)
	Unfit and fat	17	4.76	(1.03 - 21.98)	13	2.81	(0.79 - 9.98)	10	2.13	(0.62 - 7.40)

Data are presented as odd ratio (OR), confidence interval (CI). Odds ratios were unadjusted. Statistically significant associations are in bold. †Only data from participants who met the maximality criteria of the CPET. Fit was defined as the 70% top of the overall study sample and unfit as the bottom 30%, showed in several physical fitness variables. Fat was defined depending on BMI, fat mass percentage or waist circumference criteria.

Supplementary Table S5. Associations of physical fitness and fatness groups with the odds of increasing depressive symptoms in adults with depression.

Variable		BMI			Fat mass percentage			Waist circumference		
	Fitness and fatness level	N	OR	IC 95%	N	OR	IC 95%	N	OR	IC 95%
Balance										
Unipedal stance test	Fit and not fat (reference)	14	1		17	1		30	1	
	Fit and fat	23	0.63	(0.18-2.17)	20	1.04	(0.31-3.48)	8	0.56	(0.13-2.40)
	Unfit and not fat	4	1.32	(0.18-9.78)	8	2.23	(0.44-11.32)	28	3.85	(1.24-11.93)*
	Unfit and fat	35	4.57	(1.23-16.99)*	31	6.78	(1.86-24.70)**	11	5.02	(0.95-26.61)
Subjectively measured fitness										
Self-reported fitness	Fit and not fat (reference)	11	1		17	1		21	1	
	Fit and fat	25	0.89	(0.24-3.28)	19	1.64	(0.49-5.53)	15	1.08	(0.29-4.00)
	Unfit and not fat	8	2.39	(0.42-13.64)	9	6.27	(1.06-37.18)*	21	5.05	(1.65-15.42)**
	Unfit and fat	35	5.61	(1.37-22.91)*	34	6.28	(1.88-21.05)**	23	5.50	(0.99-30.47)

Data are presented as odd ratio (OR), and confidence interval (CI). Odds ratios were unadjusted. Statistically significant associations are in bold and marked as * <0.05 ** <0.005 . Fit was defined as the 50% top of the age group (divided by tertiles) and sex, and unfit as the bottom 50%, shown in all physical fitness variables. Fat was defined depending on BMI, fat mass percentage (113) or waist circumference (112) criteria.

ANNEX II: Supplementary figures

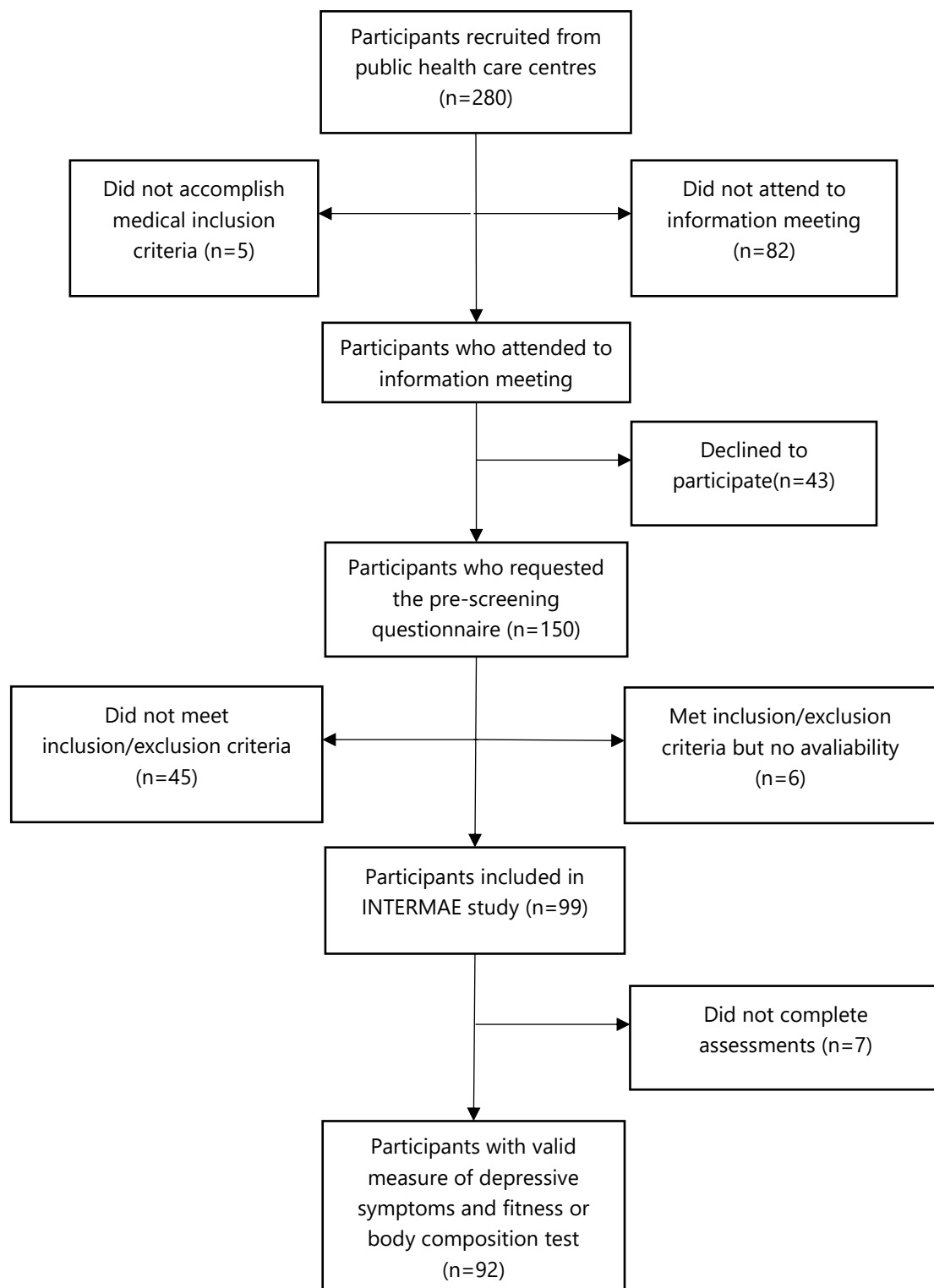


Figure S1. Baseline flow chart of the INTERMAE study.

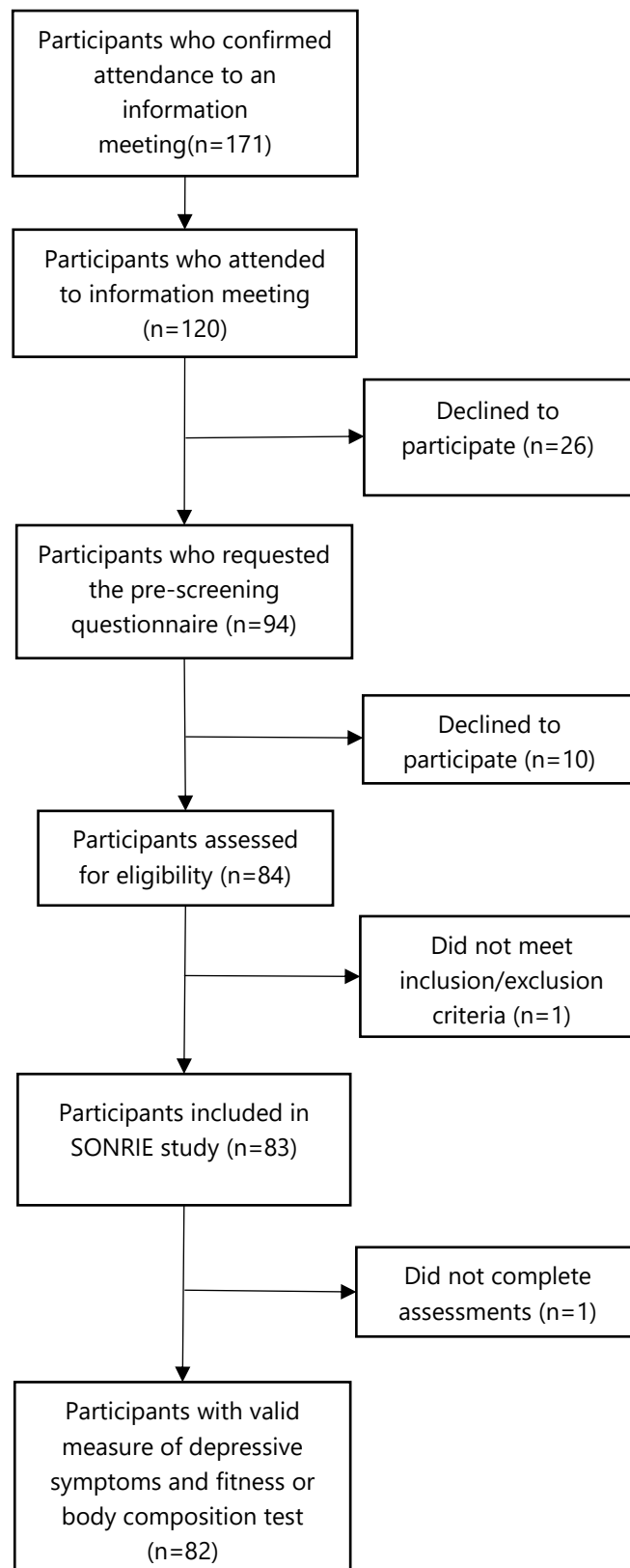


Figure S2. Baseline flow chart of the SONRIE study.

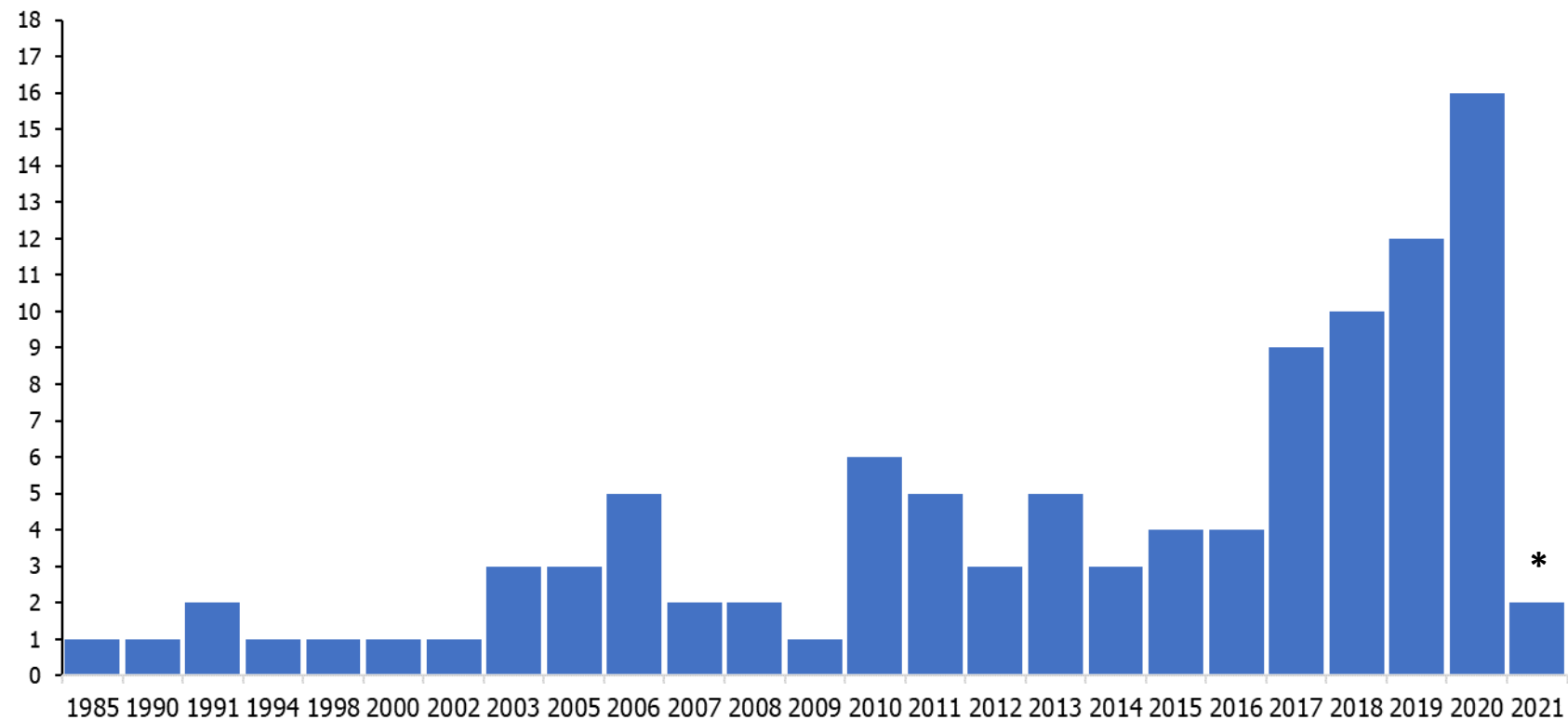


Figure S3. Number of studies published per year included in the Systematic Review of Study I.

*Considered the year 2021 until February.

SHORT CURRICULUM VITAE

Personal information

Sonia Ortega Gómez

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Born: June the 5th of 1995. Chiclana de la Frontera, Cádiz, Spain.

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Education

- 2013-2017 Bachelor's degree in Sport Sciences. University of Cadiz, Spain.
- 2017-2018 Master's degree in Physical Activity and Health. University of Cádiz, Spain.
- 2018-2019 Master's degree in Compulsory Secondary Education and High School Teaching, Vocational Training, and Language Teaching (Physical education). University of Cádiz, Spain.
- 2019-2023 PhD Student in Health Sciences. University of Cadiz, Spain.

Previous and current positions

- 2017-2018 Sport instructor. SIDEKU S.A. Supera Sport Center, Chiclana de la Frontera, Cádiz, Spain.
- 2019-2022 Predoctoral FPI fellow. Department of Physical Education, Faculty of Education Sciences, University of Cádiz, Spain.

Research stay

- 2019-2021 Center for Healthy Aging, Xlab, Department of Biomedical Sciences. University of Copenhagen, Denmark.
Prof. Steen Larsen
Duration: 3 months

Research Experience

- Papel de una estrategia educativa nutricional y de ejercicio físico en la regulación del apetito y composición corporal en función del perfil de exosomas en diabéticos tipo 2. Proyecto APETEX. i+D+I Project within the framework of the 'RETOS' Ministry of Science and Innovation of the Government of Spain (PID2020-120034RA-I00). 2021-2024. 49,852 €.
- Eficacia de una estrategia de educación nutricional y el rol del ejercicio físico en la modulación del metabolismo muscular a través de la microbiota intestinal en diabético. Estudio EDUGUTION. i+D+I Project within the framework of the 'RETOS' Ministry of Science and Innovation of the Government of Spain (PID2019-110063RA-I00). 2020-2023. 36,300 €.
- Influence of lifestyle behaviors and cellular hallmarks of aging on age-related health problems associated with dementia and fragility. InLIFEAGING. i + D + I project within the framework of the 'FEDER' Andalusia 2014-2020 (FEDER UCA18-107040). 2020-2021. 67,704 €.
- Estudio multidisciplinar sobre los mecanismos reguladores de la capacidad de oxidar grasas, sensibilidad a la insulina y el apetito en diabéticos tipo 2 tras 12 semanas de entrenamiento: FatMax vs HIIT. Estudio LIPIDOX. Funded by Biomedical Research and Innovation Institute of Cádiz (INiBICA) Research Unit. (LI19/21IN-CO09). 2020-2021. 20,000 €.
- Actividades físicas en el medio natural en personas con depresión. Efectos sobre el bienestar psíquico y social. Estudio SONRÍE. Program for the financing of biomedical and health sciences i+D+I in health sciences in Andalusia. (PI0068-2018). 2019-2021. 60,174 €.
- Influence of a physical exercise intervention on markers associated with aging, proteomic profile and fragility. INTERMAE study. Program for the financing of biomedical i+D+I and of health sciences in the province of Cadiz, Spain (PI-0002-2017). 2018-2021. 492,107.54 €.
- Promoting the shift sedentary Lifestyle towards active Ageing. LifeAge Study. Competitiveness ERASMUS+ SPORT 2018 (603121-EPP-1-2018-1-ES-SPO-SCP). 2019-2020. 389,830 €.

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- Prototipo: Sistema portátil para la evaluación y entrenamiento de la fuerza isométrica mediante guía. Funded by the University of Cádiz. (AT2016-038). 2016-2017. 3000 €.
- Aspectos Fisiológicos y Psicológicos en Escalada: Proyecto C-HIPPER. Vanesa España Romero. Funded by the University of Cádiz. (PR2016-056). 2016-2017. 1,800 €.

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Losa-Reyna, J.; **Ortega-Gómez, S.**; Sagarra, L. 2022. Evaluación global del adulto mayor. Recomendaciones para un Envejecimiento Activo y Saludable: Guía de la Red de Investigación Healthy-Age. Wanceulen Editorial. 1, pp.245-259.

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Book

Jiménez-García, J.D.; **Ortega-Gómez, S.**; Velázquez-Díaz, D.; Cadenas-Sanchez, C.; Carbonell-Baeza, A.; Jiménez-Pavón, D. 2020. Guía de actuación durante el confinamiento y actividad física recomendada para personas mayores. Covid-19. Edited by José Daniel Jiménez García. Especial edition, pp.1-18. ISBN 978-8-4092-0131-0.

Awards

- 2019 Award for the second best oral communication. **Sonia Ortega-Gómez**, Mireia Adelantado-Renau, Diego Moliner-Urdiales y David Jiménez-Pavón. Role of physical fitness on self-confidence and interpersonal relationships in adolescents: DADOS STUDY. Jornadas Nacionales de Medicina y Ciencias del Deporte SAMEDE, Almería, Spain.
- 2020 Award for the best oral communication. Manuel Ruiz-Muñoz, Inmaculada Garrido-Palomino, Juan Manuel Escudier-Vázquez, **Sonia Ortega Gómez**, Natalia Sánchez-Alarcón y Vanesa España-Romero. Efectividad de tratamiento de actividad física presencial y online en pacientes con depresión. Estudio SONRIE. II Congreso Internacional de Salud Mental FEAFES, Huelva, Spain.

Other merits

- Lecturer in the degree of Sport Sciences. Faculty of Education Sciences, University of Cádiz. A total of 168 hours (2020-2022).
- Lecturer in other university training courses, congresses, or others. A total of 12 hours.
- Speaker in an international congress.
- Participation in 2 teaching innovation projects.
- Author and co-author of 20 congress oral communications and 4 congress poster communications (both national and international).
- Organizing committee in 1 international congress and 1 national congress.
- External reviewer for the scientific journals "Movimiento Humano y Salud" and "Retos: Nuevas Tendencias en Educación Física, Deporte y Recreación".
- Participation in 7 research transfer activities.

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