An Examination of Physical Exercise as an Adjunct Treatment for Depressive Symptoms in Adults Aged 65 Years and Older

by

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Statement of Authorship and Originality

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Thesis Abstract

In light of impending demographic shifts and projected strain on healthcare systems, this thesis set out to progress our putative understanding of the benefits of physical exercise on mental health in older adults aged 65 years and over. Herein, four studies of divergent research design interrogated the current knowledge base relating to the potential benefits of exercise in older adults with depressive symptomology. Study 1 set out to establish preliminary experimental evidence that four years of unsupervised aerobic exercise can improve cardiorespiratory function (determined by VO_{2max}) and health-related quality of life (HRQL) in lifelong sedentary ageing men compared with lifelong exercising athletes. Results demonstrated preliminary proof of concept for exercise-induced benefits on cardiorespiratory function and HRQL in ageing men. Study 2 surveyed community-dwelling older adults (n = 586) to establish a hierarchy of exercise-associated factors to predict depressive symptomology. Contrary to expectation, exercise behaviour did not confer additional antidepressant effect, but was substantially predicted by exercise-induced mood, exercise self-efficacy, and social support (f^2 = 0.993). Study 3 pooled evidence from randomised controlled trials (RCTs) to quantitatively compare the treatment effectiveness from aerobic, resistance and mind-body exercise training in older adults with pre-existing clinical depression, whereas Study 4 followed the same methodology in apparently health older adults without pre-existing clinical depression. Using network meta-analytical techniques, both clinical depressed (g = -0.41 to -1.38) and apparently healthy (g = -0.27 to -0.51) older adults demonstrated equivalent effectiveness for aerobic, resistance, and mind-body exercise interventions, with encouraging levels of study compliance. Taken together, these findings encourage personal exercise preference when prescribing either aerobic, resistance, or mind-body exercise as a treatment adjunct for clinical depression and older adults with symptoms thereof. The sum of works herein provide new knowledge to guide exercise prescription for stakeholders in mental health and older adults over 65 years.

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List of Abbreviations

Abbreviation	**Description**
$1R_{max}$	One-repetition maximum
4DMS	Four-Dimension Mood Scale
AC	Attention-control
AER	Aerobic exercise
BDI	Beck Depression Inventory
CES-D	Center for Epidemiologic Studies Depression Scale
CHAMPS	Community Healthy Activities Model Program for Seniors
COPE	Committee on Publication Ethics
CSDD	Cornell Scale for Depression in Dementia
DSM	Diagnostic and Statistical Manual of Mental Disorders
EMI-II	Exercise Motivations Inventory-II
GDS	Geriatric Depression Scale
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HIIT	High-intensity interval training
HR_{max}	Heart rate maximum
HRQL	Health-related quality of life
HRSD	Hamilton Rating Scale for Depression
ICD	International Statistical Classification of Diseases and Related Health Problems
LEX	Lifelong exercisers
LEX-SED	Lifelong exercisers who had lapsed exercise training
MB	Mind-body exercise

Abbreviation	**Description**
MCS	Mental component summary
MDD	Major depressive disorder
MET	Metabolic equivalent of task
MOS SF-36	Medical Outcomes Survey Short Form-36
NMA	Network meta-analysis
PAR-Q	Physical activity readiness questionnaire
PCS	Physical component summary
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomised controlled trial
RES	Resistance exercise
RPE	Rating of perceived exertion
SED	Sedentary participants who did not continue exercise
SED-AER	Sedentary participants who continued regular aerobic exercise
SEE	Self-Efficacy for Exercise
SPS-10	Social Provisions Scale - Short Form
UC	Usual care
VO_{2max}	Maximal aerobic capacity
WL	Wait-list

Contributions to Thesis Chapters with Multiple Authors

Study 1 (Chapter III)

FG, PH & NS conceived the original clinical trial (2011), from which this study follows. FG and PH obtained ethical review board approval. PH re-recruited participants. KJM oversaw technical design in collaboration with FG, NS and PH. KJM performed data analysis, which was confirmed by FG. FG supervised KJM's manuscript drafting. All co-authors contributed to the intellectual content and approved the final manuscript.

Study 2 (Chapter IV)

KJM and RG planned the study. KJM, RG, and SM obtained ethical review board approval. KJM, MY, and FG recruited participants. KJM performed data analysis, which was confirmed by FG. FG and CM supervised KJM's manuscript drafting. RG, SM, and MY contributed to the final draft. All co-authors contributed to the intellectual content and approved the final manuscript.

Study 3 (Chapter V)

KJM, FG, and BM planned the study. KJM, DCGB, PA, and DH performed screening and data extraction. KJM and BM performed data analysis. FG, DCGB and CM supervised KJM's manuscript drafting. PA and DH contributed to the final draft. All co-authors contributed to the intellectual content and approved the final manuscript.

Study 4 (Chapter VI)

KJM, FG, and BM planned the study. KJM, PA, DH, and DCGB performed screening and data extraction. KJM and BM performed data analysis. FG and CM supervised KJM's manuscript drafting. PA, DH, and DCGB contributed to the final draft. All co-authors contributed to the intellectual content and approved the final manuscript.

****All published materials from this thesis complied with COPE guidelines on publication ethics, where each co-author met adequate contribution relating to intellectual content and approved the final manuscripts.*** (https://doi.org/10.24318/cope.2018.1.1)

CHAPTER I

Introduction

This thesis is presented with intention of formally publishing original research chapters (Chapters III, IV, V, and VI). Therefore, these chapters have been formatted to be consistent with the preferred formatting of individual journal outlets, each of which are currently published, in press, or navigating the peer-review process. To avoid repetition and remain true to the stepwise development of thesis rationale, this thesis follows a ‘sandwich’ format. Specifically, original research is bookended by a short introduction and summary discussion, with realisation of thesis objectives and the highlighting of future lines of inquiry.

1.1. Background to Geriatric Depression and the Putative Antidepressant Effects of Physical Exercise

Clinical depression is the most commonly reported mental health challenge in older adults aged over 65 years (World Health Organization, 2017). Consistent with available data across the world (Luppa et al., 2012; Seitz et al. 2010), approximately 10-15% of older Australians experience depression (National Ageing Research Institute, 2009; Pirkis et al., 2009), with up to 52% of permanent aged care residents reporting mild to severe depressive symptoms (Australian Institute of Health and Welfare, 2015). Symptoms of depression are typically characterised by a persistent sadness, irritable or anxious mood, low energy levels or fatigue, reduced concentration and attention, sleep or appetite problems, low self-esteem or self-confidence, feelings of hopelessness, loss of interest or pleasure in activities that were once enjoyable, and difficulty in carrying out usual work or social activities (American Psychiatric Association, 2013).

The prevalence of clinical depression amongst older adults is proportionally higher than any other age group (Kok & Reynolds, 2017; Volkert, Schulz, Härter, Wlodarczyk, & Andreas, 2013). Indeed, a longitudinal trajectory study (n = 2320; M_{age} = 58.1; range = 19-95) conducted by Sutin and colleagues (2013) first outlined a population-wide chronological trajectory of depressive symptoms, controlling for important covariates (i.e, comorbidity, functional limitation, impending death). Their work offered that an individual's chronological risk of developing depressive symptomology is a non-linear parabolic trajectory, whereby depression increases into early adulthood, decrease throughout middle adulthood, before rebounding into older adulthood. Notably, clinical diagnosis is further challenged by an inexorable decline in functional capacity and comorbid health conditions associated with advancing age (Knowles, Herbert, Easton, Sculthorpe, & Grace, 2015). More specifically, the presence of somatic symptoms of geriatric depression are open to misdiagnosis as psychiatric illnesses or concealed as typical signs of the ageing process (Gottfries, 1998; Patel, 2001). These inherent complexities in diagnosing (thus treating) geriatric depression, in coalition with impending 'silver tsunami' of population demographics, will place an unprecedented demand on healthcare systems. Therefore, there has never been a greater need of prevention strategies and treatment adjuncts to inform our ageing population and support primary care and allied health ecosystems.

The pleiotropic benefits of physical exercise on physical and mental health are well-recognised, yet older adults remain an underrepresented population in the primary prevention and therapeutic medicine literature. Physical exercise is an ubiquitous term for a more complicated and divergent interaction of repetitive concentric, eccentric, or isometric muscular activity performed to improve or maintain one or more aspects of physical or psychological health (American College of Sports Medicine, 2017; Caspersen et al., 1985; Ceria-Ulep et al., 2011; Winter & Fowler, 2009). Exercise training regimens have been successfully established as an effective intervention to reduce the risk of ageing-related diseases such as declines in muscle mass and aerobic capacity (Bouaziz et al., 2018; Chodzko-Zajko et al., 2009; Montero-Fernandez & Serra-Rexach, 2013), cardiovascular disease (Nocon et al., 2008), osteoporosis (Warburton, Nicol, & Bredin, 2006), and maintenance of psychological well-being and quality of life (Rhyner & Watts, 2016; Vagetti et al., 2014; Vasiliadis & Bélanger, 2018).

There is broad acceptance for physical exercise as a public health strategy to prevent or attenuate a wide range of health conditions. This perspective, however, presumes treatment equivalence for what are metabolically diverse physical regimens. It is well-recognised that exercise training regimens may be broadly (and conveniently) categorised according to their associated metabolic challenges and diverse treatment outcomes (American Psychiatric Association, 2010; National Health, Lung, and Blood Institute 2006; U.S. Department of Health and Human Services, 2018). Amongst other factors, the unique physiological idiosyncrasies between aerobic, resistance, and mind-body exercise training, make it difficult to accept that ‘all exercise is created equally’ in light of compelling evidence to the contrary. However, that is not to say that their relative capacity to induce secondary pathophysiological antidepressant effect is any different. Somewhat surprisingly, this seemingly basic question has not yet been considered by exercise physiologists nor their network of research colleagues and collaborators. Given that older adults, as an entity, are the least likely to be sufficiently convinced to partake in physical exercise, there appears to be distinct value in pursuing this line of research enquiry.

Aerobic exercise is a distinct form of physical activity that involves the integration of skeletal muscles (American College of Sports Medicine, 2017), which are coordinated in rhythmic propulsion of body mass with movements of different intensities (e.g., walking, jogging, or running) or activities of lower mechanical impact (e.g., swimming or cycling). Intensity of metabolic effort during aerobic exercise requires coordinated integration of breathing, heart rate, and blood flow to match the effort of intensity (Nelson et al., 2007). In general, aerobic exercise aims to attenuate the normal losses in neuromuscular connections, metabolism, cardiovascular endurance, and respiratory functioning that accompanies ageing, providing a greater independence throughout the lifespan (Wilmore & Knuttgen, 2003).

Resistance exercise is often directly contrasted with aerobic exercise. Resistance exercise is a specialised method of muscular conditioning that normally requires a variety of equipment (i.e., free weights, weight machines, elastic bands, and/or body weight exercises), which are designed to enhance health and fitness (Faigenbaum et al., 2009). Resistance exercise training is distinct from aerobic or mind-body exercise in that there is a focus on repeatedly overloading muscles during static, isometric, or dynamic contractions, which cause a closer and stronger connection between the musculature and nervous system. For older adults, resistance exercise is used to maintain strength and muscle mass, prevent muscular weakness associated with ageing, enhance energy expenditure and body composition, and reduce the difficulty of performing daily tasks (Hunter, McCarthy, & Bamman, 2004; Peterson, Rhea, Sen, & Gordon, 2010).

Lastly, mind-body exercise incorporates a range of activities integrating low impact muscular activity (e.g., flexibility, balance, stability) and an internally directed focus on breathing and proprioception (La Forge, 1997). Common mind-body exercises include yoga, tai chi, and qigong. In theory, the combination of mental and physical aspects of exercise may result in a stronger effect than physical exercise alone. Critical to these mental aspects is interoceptive sensations such as an internally directed focus on breathing and proprioception, which have been inversely linked to the experience of depression (Avery et al., 2014; Paulus & Stein, 2010).

Exercise can be used as an adjunct therapy, compounding the antidepressive effects of other traditional treatments such as antidepressant medication (Mura & Carta, 2013; Mura, Moro, Patten, & Carta, 2014). Indeed, international guidelines of public health management are in concert with the antidepressant effects of physical exercise as a prophylactic approach for mental health and well-being (American College of Sports Medicine, 2017; American Psychiatric Association, 2010; Stubbs et al., 2018; World Health Organization, 2010). These intervention programs can be incorporated into both community and clinical settings under the supervision of a health care or fitness professional, modifying the intensity and duration to ensure that the activities are suited to the targeted group. Different types of exercise can also provide variety to regular exercise and may facilitate synergistic benefits to overall physical and mental health.

1.2. A Theoretical Overview of the Mechanisms Responsible for Exercise as a Treatment for Geriatric Depression

During the past three decades, it has been an established association that physically fit older adults and those who participate in regular exercise regimens have a lower associated risk of clinical depression (Blumenthal et al., 1999; Chang et al., 2017; Mather et al., 2002). However, there is no convincing causal verification for any single mechanism or assemblage thereof to reliably explain the exercise-depression relationship in any age demographic (Paluska & Schwenk, 2000; Stubbs & Schuch, 2019). In the absence of direct mechanistic evidence, there is broad consensus that the antidepressant effect of exercise may be indirectly achieved via the coalition of psycho-physiological processes. Several key theories have been proposed to explain the antidepressant effects of exercise in terms of physiological (i.e., monoamine hypothesis, endorphin hypothesis) and psychosocial (i.e., distraction hypothesis, mastery hypothesis, self-efficacy theory, activity theory of ageing, social interaction hypothesis) mechanisms (see Paluska & Schwenk, 2000 for a theoretical review).

Critical to most of these theories is the underlying physiological response to incremental bouts of physical exercise. The monoamine hypothesis proposes that physical exercise stimulates the release of monoamine neurotransmitters such as dopamine, noradrenaline, and serotonin, which lead to effects like that of antidepressant medications (Hirschfeld, 2000). As clinical depression may be successfully managed by selective serotonin reuptake inhibitors (SSRI), there is also a widely purported endorphin hypothesis that is partially supported in the literature (Harber & Sutton, 1984) and in gerontology studies (Melancon Lorrain, & Dionne, 2014). The endorphin hypothesis supposes that physical exercise induces a secretion of endorphins, which in turn, effectively reduces the sensation of pain and produces a state of euphoria (Dinas, Koutedakis, & Flouris, 2011).

The earliest documented psychological theory for the potential antidepressive effect of exercise is the distraction hypothesis, founded on the concept that a simple diversion from a painful stimulus may lead to an improved mood state (Festinger & Maccoby, 1964). This hypothesis was initially demonstrated in an experimental study conducted by Bahrke and Morgan (1978), where 75 adult participants engaged in 20 minutes of treadmill exercise, general meditation, or reading in a sound-dampened chamber. Bahrke and Morgan theorised that participants reported a better post-treatment mood state in exercise than the other activities because exercise may be a good distraction from stress of daily life, leading to a decline in anxiety and depression.

Another theory for the connection between regular exercise and a reduction in depressive symptom is captured in the mastery hypothesis. According to the mastery hypothesis, the antidepressant effects of exercise derive from a sense of accomplishment or mastery that occurs once an activity is completed (Greist et al., 1979). This gives the individual a greater sense of self-worth, personal control over their environment, and ability to cope with stress in their everyday lives. Deep interrogation of the mastery hypothesis as an independent explanation for the relationship between exercise and depressive symptoms lacks empirical support (Lox et al., 2010; Paluska & Schwenk, 2000).

The mastery hypothesis has been connected with another theory known as self-efficacy theory, originally proposed by Bandura (1977). Like the mastery hypothesis, self-efficacy theory is based on the accomplishment or mastery of a task such as exercise. Whereas the mastery hypothesis proposes that depression is not reduced until the task is mastered, self-efficacy theory proposes that depression can be reduced when the individual believes that they are more capable of accomplishing the task. Thus, self-efficacy theory supposes that an individual’s depressive symptoms become less severe as their exercise self-efficacy increases, which may then be transferred to other general tasks (Bandura, 1997). Exercise self-efficacy is defined as one’s beliefs about the capability to successfully engage in incremental bouts of physical activity (Blacklock, Rhodes, Blanchard, & Gaul, 2010).

Whereas the theories discussed thus far have used a physiological and/or psychological approach, the activity theory of ageing includes elements of an individual's social environment. According to the activity theory of ageing, successful ageing occurs when older adults stay active and maintain social interactions (Havighurst, 1961). Thus, social interaction during regular engagement in exercise may assist older adults to maintain reasonable mental health because it offers an opportunity to engage in challenges, adjust to retirement, and maintain personal relationships and endeavors (Bengtson, Gans, Putney, & Silverstein, 2009).

An adapted version of the activity theory of ageing, known as the social interaction hypothesis (Ransford, 1982), has been rationalised to explain the exercise-depression relationship. The social interaction hypothesis includes aspects of social interaction and support in its theory for how regular exercise relieves depressive symptoms (Ransford, 1982). The social interaction hypothesis proposes that physical exercise may attenuate depressive symptoms by providing individuals with the opportunity to interact with others and build mutual support. Individuals gain a sense of social connectedness through training with other people, which results in an increased ability to cope with stress and depression. It goes without saying that the only way to achieve these benefits is through group, rather than individual, exercise training.

1.3. Thesis Aims and Objectives

Existing research advancements in exercise for optimal mental health in older adulthood is not without significant limitations. These limitations relate to a lack of robust longitudinal findings, inadequate interrogation of potential important indirect and interaction factors, and significant heterogeneity amongst those studies that do exist. Thus, the complexity of the relationship between exercise and mental health in older adults requires intricate research methods to investigate how, and to what extent, physical exercise acts as an antecedent for mental wellness in older adulthood.

Adults aged 65 years and older are, at best, equally vulnerable to the consequences associated with symptoms of depression as their younger counterparts. However, comparative studies are sparse, and until recent years, studies have predominantly enrolled young and middle-aged participants. For this reason, there is an assumption that what is effective in younger samples is equally effective in older demographics, despite the lack of scientific data to support this concept. Therefore, this thesis sets out to progress current theory that structured exercise improves mental health through physiological and psychological processes. The current scientific literature offers several key mechanistic factors to help explain the antidepressive effects of physical exercise, which are open to further scientific interrogation in order to establish relative and temporal sequence of causality.

Thus, to meet a collective need for better knowledge on how to ‘age successfully’, this thesis sets out to interrogate the value of physical exercise as an adjunct to the treatment and/or prevention of depressive symptoms in older adults aged 65 years and over. First, experimental proof of concept (Chapter III) will establish the relative existence of a value proposition on which to base this thesis (i.e., does it work?) and whether physical exercise may be used to establish the trajectory of change in mental health and quality of life between exercising and sedentary older adults over a longitudinal (4-year) period. Specifically, this study will test the physiological basis that regular exercise can influence psychological health in a small sample of sedentary older men compared with controls (*n* = 33).

Next, a cross-sectional survey (Chapters IV) will be employed to investigate underlying exercise-related psychosocial characteristics associated with developing depressive symptoms in a sample of community-dwelling older adults (*n* = 586). The focus of this study will be on exercise behaviour, exercise-induced mood, exercise self-efficacy, and social support, which will be used to establish a hierarchy based on the strength of their capacity to predict depressive symptoms.

Due to the largely unrecognized, yet potentially important, treatment characteristics of diverse exercise regimens, the latter half of the thesis will compare the effectiveness of three different exercise types (aerobic, resistance, and mind-body) as effective treatments for depressive symptoms in older adults. Notably, network meta-analytic techniques will scrutinise best evidence for the treatment of depressive symptoms, separating clinically depressed from apparently healthy aged counterparts (Chapters V and VI, respectively). The studies will independently examine the treatment effect of physical exercise for older adults diagnosed with clinical depression (*n* = 596), as well as the preventative antidepressive effect of exercise in apparently healthy older adults (*n* = 4,844).

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CHAPTER II

Thesis Hypotheses

Hypothesis 1a (Chapter III)

H_0: Aerobic capacity (VO_{2max}) will not change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong athletic control.

H_1: Aerobic capacity (VO_{2max}) will change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong athletic control.

Hypothesis 1b (Chapter III)

H_0: Aerobic capacity (VO_{2max}) will not change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong sedentary control.

H_1: Aerobic capacity (VO_{2max}) will change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong sedentary control.

Hypothesis 2a (Chapter III)

H_0: Self-perceived HRQL will not change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong athletic control.

H_1: Self-perceived HRQL will change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong athletic control.

Hypothesis 2b (Chapter III)

H_0: Self-perceived HRQL will not change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong sedentary control.

H_1: Self-perceived HRQL will change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong sedentary control.

Hypothesis 3a (Chapter IV)

H_0: Exercise behaviour will not predict depressive symptoms in community-dwelling older adults, when controlling for mood, self-efficacy, social support, health status, physical functioning, age, and gender.

H_1: Exercise behaviour will significantly predict depressive symptoms in community-dwelling older adults, when controlling for mood, self-efficacy, social support, health status, physical functioning, age, and gender.

Hypothesis 3b (Chapter IV)

H_0: Exercise-induced mood will not predict depressive symptoms in community-dwelling older adults, when controlling for exercise behaviour, self-efficacy, social support, health status, physical functioning, age, and gender.

H_1: Exercise-induced mood will significantly predict depressive symptoms in community-dwelling older adults, when controlling for exercise behaviour, self-efficacy, social support, health status, physical functioning, age, and gender.

Hypothesis 3c (Chapter IV)

H_0: Exercise self-efficacy will not predict depressive symptoms in community-dwelling older adults, when controlling for exercise behaviour, mood, social support, health status, physical functioning, age, and gender.

H_1: Exercise self-efficacy will significantly predict depressive symptoms in community-dwelling older adults, when controlling for exercise behaviour, mood, social support, health status, physical functioning, age, and gender.

Hypothesis 3d (Chapter IV)

H_0: Social support will not predict depressive symptoms in community-dwelling older adults, when controlling for exercise behaviour, mood, self-efficacy, health status, physical functioning, age, and gender.

H_1: Social support will significantly predict depressive symptoms in community-dwelling older adults, when controlling for exercise behaviour, mood, self-efficacy, health status, physical functioning, age, and gender.

Hypothesis 4a (Chapter V)

H_0: Collective RCT evidence will demonstrate that exercise training is equally as effective to treat depressive symptoms as control conditions in clinically depressed older adults.

H_1: Collective RCT evidence will demonstrate that exercise training is more effective to treat depressive symptoms compared with control conditions in clinically depressed older adults.

Hypothesis 4b (Chapter V)

H_0: Collective RCT evidence will demonstrate that mind-body exercise is equally as effective to treat depressive symptoms as aerobic or resistance exercise in clinically depressed older adults.

H_1: Collective RCT evidence will demonstrate that mind-body exercise is more effective to treat depressive symptoms compared with aerobic or resistance exercise in clinically depressed older adults.

Hypothesis 5a (Chapter VI)

H_0: Collective RCT evidence will demonstrate that exercise training is equally as effective to reduce depressive symptoms as control conditions in apparently healthy older adults.

H_1: Collective RCT evidence will demonstrate that exercise training is more effective to reduce depressive symptoms compared with control conditions in apparently healthy older adults.

Hypothesis 5b (Chapter VI)

H_0: Collective RCT evidence will demonstrate that mind-body exercise is equally as effective to reduce depressive symptoms as aerobic or resistance exercise in apparently healthy older adults.

H_1: Collective RCT evidence will demonstrate that mind-body exercise is more effective to reduce depressive symptoms compared with aerobic or resistance exercise in apparently healthy older adults.

Hypothesis 6 (Chapter VI)

H_0: Collective RCT evidence will demonstrate equal levels of attrition in exercise conditions compared with control conditions in apparently healthy older adults.

H_1: Collective RCT evidence will demonstrate higher levels of attrition in exercise conditions compared with control conditions in apparently healthy older adults.

CHAPTER III

Compliance with Self-Directed Exercise Training Maintains Aerobic Capacity and Health-Related Quality of Life in Previously Sedentary Ageing Men

In Preparation

"**Miller, K. J.**, Herbert, P., Sculthorpe, N., & Grace, F. (2020). Compliance with self-directed exercise training maintains aerobic capacity and health-related quality of life in previously sedentary ageing men. ***GeroScience***."

Ethics Approval: See *Appendix A*

Questionnaires: See *Appendix B*

Preface: This study is a 4-year follow-up of an experimental ageing cohort. To provide context, the reader is directed to the clinical trial by Knowles et al. (2015), where the original 2015 manuscript is available via open access at *GeroScience* (formally known as *AGE*). FG holds senior authorship of both studies.

"Knowles, A. M., Herbert, P., Easton, C., Sculthorpe, N., & Grace, F. (2015). Impact of low-volume, high-intensity interval training on maximal aerobic capacity, health-related quality of life and motivation to exercise in ageing men. *AGE*, *37*(2), 25."

doi: 10.1007/s11357-015-9763-3

3.1. Abstract

3.1.1. Background

Cardiorespiratory fitness is a key factor for successful ageing, but there are no long-term experimental follow-up studies. The purpose of this study was to examine the effects of exercise on maximal aerobic capacity and health-related quality of life (HRQL) in sedentary and exercising older men during a 4-year follow-up assessment of a prospective cohort study.

3.1.2. Methods

Thirty-three participants aged 65.2±5.4 years were followed up four years after completing a supervised exercise training program. Groups consisted of (i) sedentary participants who selected not to continue exercise (SED; *n* = 6), (ii) sedentary participants who commenced regular aerobic exercise (SED-AER; *n* = 11), (iii) lifelong exercisers (LEX; *n* = 12), and (iv) lifelong exercisers who had lapsed exercise training during the prior four years (LEX-SED; *n* = 4). Measurements of aerobic capacity (VO_{2max}), HRQL (Medical Outcomes Survey Short Form-36), and exercise motivations (Exercise Motivations Inventory-II) were compared between baseline, post-intervention, and 4-year follow-up.

3.1.3. Results

Long-term maintenance of aerobic capacity was achieved by the SED-AER and LEX groups, whereas deficits were found for the SED and LEX-SED groups after four years. HRQL was generally worse for SED and LEX-SED participants during 4-year follow-up, while their exercising counterparts remained relatively unchanged. A perceived deterioration in general physical health was mainly responsible for the worsening of HRQL. SED-AER participants exercise program tended to be more connected to their motivation to exercise, which reflected a range of motivational preferences.

3.1.4. Conclusions

These preliminary data provide the first evidence that regular aerobic exercise preserves aerobic capacity and self-reported HRQL, particularly within the general physical health domain, during older age. Regular engagement in exercise training can lessen the deficits associated with age-related decline, even when adopted in older age.

3.2. Introduction

Advancing age brings a gradual and inexorable decline in physical fitness that presents an overt challenge to one’s physical function. While the pleiotropic benefits of exercise are well established, the older populous remain one of the least physically active demographics (Grace et al., 2018; McPhee et al., 2016). When this is considered alongside the projected ageing demographics and its expected impact on age-associated healthcare resourcing, intervention strategies to mitigate the burden of a global ageing population are a key public health challenge.

Aerobic fitness is a critical determinant of successful ageing and is associated with a range of positive health outcomes (Bauman, Merom, Bull, Buchner, & Fiatarone Singh, 2016; Gremeaux et al., 2012; Fleg, 2012). Maintenance of aerobic fitness is particularly crucial during older adulthood because it is believed that aerobic capacity declines at a rate of 1-2% per year irrespective of physical activity levels (Fleg et al., 2005; Hawkins & Wiswell, 2003; Hollenberg, Yang, Haight, & Tager, 2006; Stathokostas, Jackson, Sui, Hébert, Church, & Blair, 2009; Jacob-Johnson, Petrella, & Paterson, 2004). However, long-term engagement with regular exercise is associated with higher baseline levels of aerobic capacity, and as such, provides greater functional reserve to offset some of the age-related decline. Pooled data from randomised controlled trials demonstrate that 26 weeks or less of aerobic training can lead to a 6.5-30% increase in aerobic capacity, with significant effects for both healthy and chronically unhealthy adults aged 70 and over (Bouaziz et al., 2018). Therefore, physical exercise can preserve aerobic capacity throughout life, or if not already performed, it can be adopted later in life to assist in the reversal of cardiorespiratory deficits from a lifelong sedentary lifestyle.

Epidemiological studies have established a relationship between aerobic capacity and preserving health-related quality of life (HRQL) during older adulthood (Olivares, Gusi, Prieto, & Hernandez-Mocholi, 2011; Wanderley et al., 2011), albeit using indirect measures of oxygen uptake. The assessment of HRQL is an important adjunct to any intervention strategy, as it can be used to evaluate the impact of illness and/or treatment. According to the World Health Organisation, HRQL offers a broad assessment of an individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns.

Regular physical activity during advanced age is reported to have significant positive effects on perceptions of HRQL (Vagetti et al., 2014). A recent single-arm trial found that as little as 10 weeks of exercise led to significantly higher ratings of total HRQL in 30 healthy adults aged over 65 years old (Haripriya, Kumar, Samuel, & Soman, 2018). Moreover, a 3-year longitudinal cohort study (Vasiliadis & Bélanger, 2018) found that older participants reporting lifelong sedentary behaviour, as well as those reporting a decrease in exercise behaviour, had lower HRQL at follow-up compared to their exercising counterparts. This indicated that exercise throughout the years is necessary for maintaining HRQL, and that past activity does not confer protection against future declines in HRQL (Vasiliadis & Bélanger, 2018). When the domains of HRQL are examined separately, the evidence is less clear. Whereas some studies have shown no change in any of the eight HRQL domains for older adults (Halbert, Silagy, Finucane, Withers, & Hamdorf, 2000; Kolt, Schofield, Kerse, Garrett, & Oliver, 2007), other studies have identified improvements in physical functioning, general health, and vitality (Kerse, Elley, Robinson, & Arroll, 2005; Knowles, Herbert, Easton, Sculthorpe, & Grace, 2015).

The mechanism linking HRQL and aerobic capacity is thought to be due to aerobic capacity providing older adults with greater physical functioning and independence, resulting in positive perceptions of quality of life (Fleg, 2012). Lavie and Milani (2000) initially tested the effect of an exercise rehabilitation program on 57 elderly coronary patients, observing large improvements on both aerobic capacity (+32%) and HRQL (+20%). Subsequently, our research group examined the effects of a 15-week conditioning and high-intensity interval training (HIIT) intervention in older men (Knowles et al., 2015). At baseline, lifelong exercisers had significantly better aerobic capacity (VO_{2max}) and higher ratings on two HRQL domains (physical functioning and general health) compared to sedentary counterparts. Immediately following the training intervention, aerobic capacity improved for both groups equally, however the improvement on physical functioning was significantly larger for the sedentary group. Thus, it is plausible that quality of life is predicated on aerobic capacity leading to greater physical functioning and independence.

The research described thus far highlights the scarcity of studies concurrently investigating the longitudinal impact of exercise on both aerobic capacity and HRQL in older adults. Indeed, to date, few experimental exercise studies and no long-term trials have investigated the impact of exercise during chronological ageing. Rather, most research has involved a follow-up of less than six months, which have overlooked the long-term health benefits of commencing exercise in older age. Existing studies generally show that exercise improves aerobic capacity, and that these improvements are associated with better general health and physical functioning, less pain, and improved vitality (Knowles et al., 2015; Sillanpää, Häkkinen, Holviala, & Häkkinen, 2012; Stewart et al., 2003), but less is known about whether these improvements are sustained beyond the lifetime of an intervention.

Thus, the purpose of this study was to examine the effects of exercise on maximal aerobic capacity and HRQL in ageing men during a 4-year follow-up assessment of a prospective cohort study originally conducted by Knowles et al. (2015). With these aspects in mind, we hypothesised that (i) VO_{2max} would be highest for lifelong exercisers (LEX), followed by SED-AER and lifelong exercises who ceased exercise training (LEX-SED), then lifelong sedentary (SED) counterparts, and (ii) lifelong exercisers (LEX) and sedentary participants who continued moderate-intensity exercise (SED-AER) would report higher 4-year follow-up HRQL compared to other subgroups.

3.3. Methods

3.3.1. Participants

Ethics was approved by the University of the West of Scotland research ethics committee. Participants completed a physical activity readiness questionnaire (PAR-Q) and provided written informed consent. Thirty-three male participants (*M* = 65.21, *SD* = 5.35) were followed up from our research group's prospective cohort intervention study (Knowles et al., 2015). Participants were initially identified as one of two groups: (i) sedentary participants did not participate in any formal exercise program and were inactive for a minimum of 30 years, or (ii) lifelong exercisers who were highly active exercisers and engaged in exercise for an average of 281±144 min per week, including twelve participants who were currently active Masters national competitors in sports (i.e., triathlon, athletics, sprint cycling, racquet sports).

During 4-year follow-up assessment, sedentary participants were subsequently categorised as either: (i) sedentary participants who continued a lifelong sedentary lifestyle (SED), or (ii) sedentary participants who began a regular aerobic exercise program (SED-AER). Similarly, lifelong exercisers were categorised as either: (i) lifelong exercisers who continuing their regular exercise habits (LEX), or (ii) lifelong exercisers that ceased exercise altogether (LEX-SED). *Figure 3.1* reports the allocation and attrition of participants included in the study.

3.3.2. Study design

The study design is depicted in *Figure 3.2* and procedures have been previously reported (Knowles et al., 2015). Briefly, the study employed a 12-week prospective cohort intervention design with the LEX group acting as a positive control. Baseline data were collected from all participants. Sedentary participants participated in a six weeks of progressive conditioning exercise, then all groups participated in six weeks of HIIT and a post-intervention assessment were performed. After the conclusion of the trial, all participants were provided with examples of training programs to encourage continued exercise participation in future years. Some sedentary participants used this information to facilitate engagement in aerobic exercise (MOD), whilst others ceased exercise altogether (SED). Four-year follow-up assessments of aerobic capacity and HRQL were performed on lifelong sedentary (SED), sedentary participants who continued aerobic exercise (MOD), lifelong exercisers (LEX), and lifelong exercises that ceased exercise training (LEX-SED).

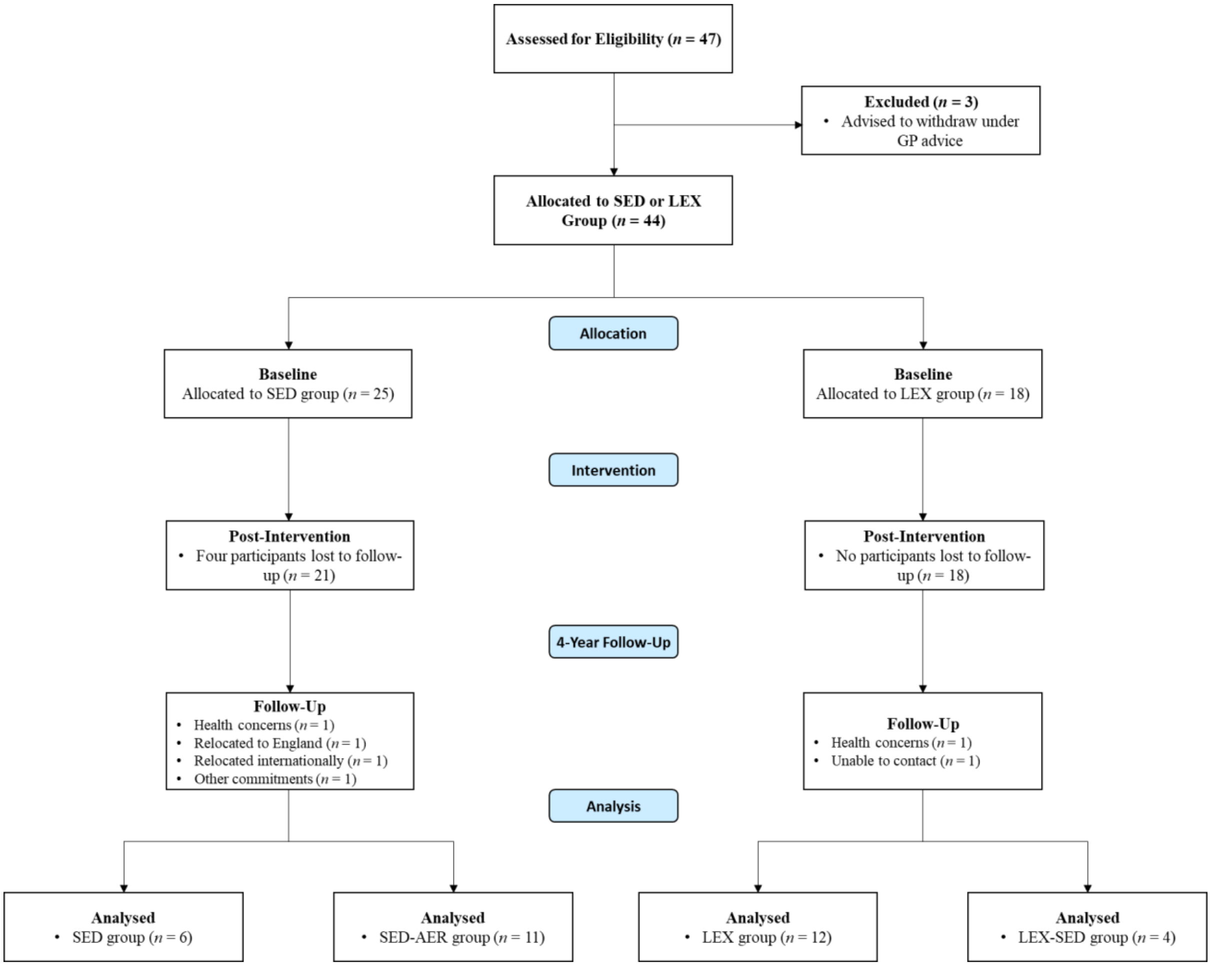

Figure 3.1. Flowchart of participants (*n* = 33). Sedentary participants were stratified into those who began an exercise program (SED-AER) or those who continued a sedentary lifestyle (SED). Lifelong exercisers were stratified into those who ceased exercise (LEX-SED) or those who continued exercise (LEX).

3.3.3. Measures

3.3.3.1. Aerobic capacity (VO_{2max}). Maximal aerobic capacity was determined by using open circuit spirometry using a Cortex II Metalyser 3B-R2 (Cortex, Biophysik, Leipzig, Germany), which can be found in extensive detail elsewhere (Grace et al. 2015, 2018; Knowles et al., 2015).

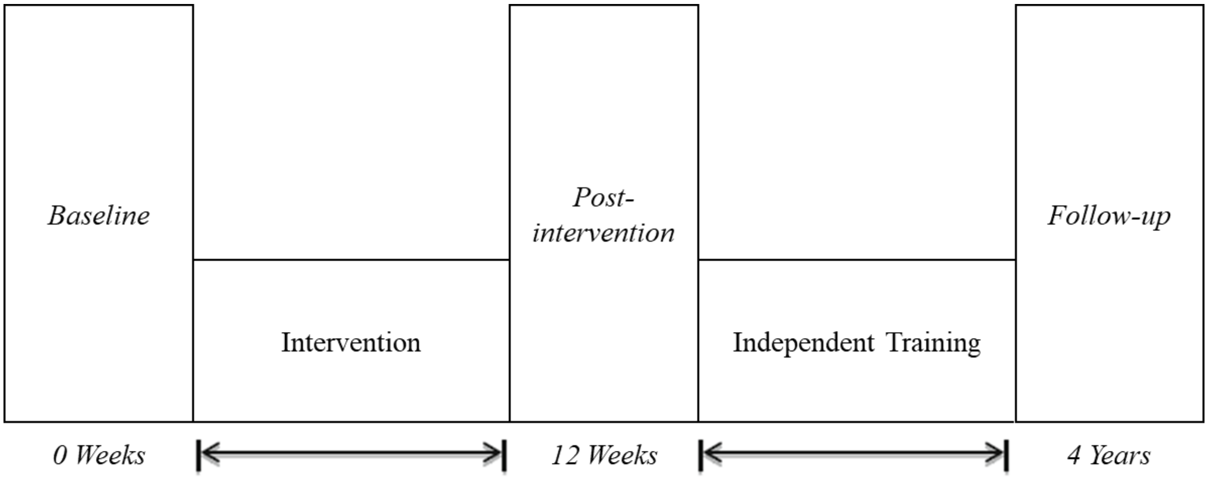

Figure 3.2. Schematic depicting study design incorporating three time-points, including baseline, post-intervention, and follow-up assessments.

3.3.3.2. Medical Outcomes Survey (MOS) Short Form-36 (SF-36). The SF-36 (Ware Jr. & Sherbourne, 1992) is a 36-item health questionnaire designed to assess eight basic domains of HRQL across two components: physical and mental component summary (PCS and MCS, respectively). Physical functioning, role limitations due to physical health (role-physical), pain, and general health form the PCS. Role limitations due to emotional problems (role-emotional), vitality (energy/fatigue), emotional well-being, and social functioning form the MCS. Participants are asked to rate the strength of their agreement to each statement on a series of Likert scales. Each domain was scored using a scale ranging between 0 and 100, with higher scores reflecting better perceived quality of life. The SF-36 has psychometrically sound properties in several countries (Gandek et al., 1998), with excellent internal consistency (Gandek, Sinclair, Kosinski, & Ware Jr., 2004) and test-retest reliability between

.65 and .87 over a 4-week period (Andresen, Bowley, Rothenberg, Panzer, & Katz, 1996) in older populations.

3.3.3.3. Exercise Motivations Inventory-II (EMI-II). The EMI-II (Markland & Ingledew, 1997) is a 51-item questionnaire designed to measure exercise motives across 14 domains: stress management, revitalisation, enjoyment, challenge, social recognition, affiliation, competition, health pressures, ill health avoidance, positive health, weight management, appearance, strength and endurance, and nimbleness. Each domain is constructed from three or four items, with higher scores reflecting greater motivation to engage in exercise from the specified domain. The EMI-II has demonstrated excellent internal consistency and discriminant validity in older adults (Dacey, Baltzell, & Zaichkowsky, 2008).

3.3.4. Statistical analysis

All statistical procedures were performed using STATA/SE 15.1 (StataCorp, 2017). Power calculation was performed using a single-tailed within group comparison with an effect size of 0.8 (Rywik et al., 1999), $\alpha = .05$, and $\beta = .8$, resulting in a minimum sample size of 17 participants per group. Data are reported as means (*M*) and standard deviations (*SD*). Differences in SF-36 and VO_{2max} scores were analysed using a two-factor (4×3) mixed-model repeated measures ANOVA to examine the effects of training status (SED, SED-AER, LEX, and LEX-SED) and time (baseline, post-intervention, and follow up), and the interaction. Post-hoc analyses were completed using Bonferroni multiple comparisons and the null hypothesis was rejected when $p < .05$. 95% Confidence intervals (95% *CI*), *p*-values, Hedges' *g*, and partial eta-squared (η^2) were used to examine significant effects. Cohen's (1988) conventions evaluated the strength of effect sizes for Hedges' *g* (0.2 = small, 0.5 = medium, and 0.8 = large) and partial η^2 (0.01 = small, 0.059 = medium, and 0.138 = large).

3.4. Results

3.4.1. Participant characteristics

Six participants were not available to provide data at the follow-up periods. Reasons for dropout included health concerns (*n* = 2), unable to contact (*n* = 1), relocated to England (*n* = 1), relocated internationally (*n* = 1), and other commitments (*n* = 1). Thus, data from a total of 33 participants were available for analysis.

3.4.2. Aerobic capacity (VO_{2max}) and health-related quality of life (SF-36)

The patterns of change for VO_{2max}, PCS, MCS, and general health are depicted in *Figure 3.3*. Two-factor mixed-model repeated measures ANOVAs were used to test direct comparisons and interaction effects between group membership (SED, SED-AER, LEX, and LEX-SED) and assessment time-points (baseline, post-intervention, and follow-up) on VO_{2max} (see *Table 3.1*). Main effects for both group, $F(3, 95) = 40.56$, $p < .001$, partial $\eta^2 = .583$, and time, $F(2, 96) = 6.22$, $p < .01$, partial $\eta^2 = .125$, were significant. The group × time interaction was not significant ($p = .502$). Post hoc analysis indicated significantly larger differences in VO_{2max} between LEX and SED groups during baseline (15.67±2.86 ml kg min^{-1}; 95% *CI* = 5.67, 25.66; $p < .001$; $g = 2.785$), post-intervention (16.50±2.86 ml kg min^{-1}; 95% *CI* = 6.50, 26.50; $p < .001$; $g = 2.283$), and 4-year follow-up (19.75±2.86 ml kg min^{-1}; 95% *CI* = 9.75, 29.75; $p < .001$; $g = 2.510$). Significantly larger differences in VO_{2max} were also found between LEX and SED-AER groups during baseline (10.14±2.39 ml kg min^{-1}; 95% *CI* = 1.79, 18.48; $p < .01$; $g = 2.177$), post-intervention (9.24±2.39 ml kg min^{-1}; 95% *CI* = 0.90, 17.59; $p < .05$; $g = 1.598$), and 4-year follow-up (11.10±2.39 ml kg min^{-1}; 95% *CI* = 2.75, 19.44; $p < .001$; $g = 1.732$). Finally, a significantly larger difference in

VO_{2max} was observed between LEX and LEX-SED groups during 4-year follow-up (13.17±3.31 ml kg min^{-1}; 95% *CI* = 1.62, 24.71; $p < .001$; $g = 1.703$).

Two-factor mixed-model repeated measures ANOVAs were performed for HRQL to test for direct comparisons and interaction effects. Overall HRQL had significant main effect for time, $F(2, 96) = 4.99$, $p < .01$, partial $\eta^2 = .103$, but not group membership ($p = .317$). PCS had significant main effects for both group, $F(3, 95) = 3.27$, $p < .05$, partial $\eta^2 = .101$, and time, $F(2, 96) = 4.68$, $p < .05$, partial $\eta^2 = .097$, but no group × time interaction was observed ($p = .198$). MCS had a significant main effect of time, $F(2, 96) = 4.15$, $p < .05$, partial $\eta^2 = .087$, but not group membership ($p = .488$).

When independently examining HRQL domains, there were significant main effects between measurement times for physical functioning, role-physical, pain, vitality, and emotional well-being. Similarly, there were significant main effects between groups for physical functioning and general health. General health had significant main effects for group membership, $F(3, 95) = 4.01$, $p < .01$, partial $\eta^2 = .122$, whereas time approached significance, $F(2, 96) = 2.92$, $p = .059$, partial $\eta^2 = .063$. A significant group × time interaction also persisted, $F(5, 93) = 2.42$, $p < .05$, partial $\eta^2 = .143$. Post hoc analysis showed that LEX participants reported significantly higher follow-up perceptions of general health than SED participants (31.25±6.82; 95% *CI* = 7.42, 55.08; $p < .001$; $g = 1.674$), representing a large difference in effect. Moreover, the SED group reported a significant decline in perceptions of general health between post-intervention and 4-year follow-up (-27.5±7.88; 95% *CI* = -55.01, 0.01; $p < .05$; $g = 1.380$). No significant group differences or interaction effects were identified for physical functioning, role-physical, pain, role-emotional, vitality, emotional well-being, or social functioning.

Table 3.1

Descriptive statistics for aerobic capacity (VO_{2max}) and the SF-36 questionnaire at each phase of the study

	SED ($n = 6$)			SED-AER ($n = 11$)			LEX ($n = 12$)			LEX-SED ($n = 4$)		
	Baseline	Post-Intervention	Follow-Up	Baseline	Post-Intervention	Follow-Up	Baseline	Post-Intervention	Follow-Up	Baseline	Post-Intervention	Follow-Up
VO_{2max}	**23.8 ± 6.7^{e}**	**27.8 ± 6.9^{e}**	**22.1 ± 6.9^{e}**	**29.4 ± 4.3^{e}**	**35.1 ± 3.7^{e}**	**30.8 ± 3.8^{e}**	**39.5 ± 4.6^{cd}**	**44.3 ± 6.9^{cd}**	**41.9 ± 7.7^{cdf}**	36.3 ± 5.5	37.5 ± 5.5	**28.8 ± 5.5^{e}**
HRQL	75.5 ± 11.5	89.8 ± 7.7	73.6 ± 18.9	79.3 ± 10.2	91.1 ± 2.3	87.3 ± 6.1	86.8 ± 8.5	90.3 ± 2.8	85.2 ± 20.7	89.4 ± 3.6	90.2 ± 2.9	82.3 ± 4.9
PCS	73.9 ± 13.0	89.8 ± 6.9	72.0 ± 21.4	77.7 ± 11.9	91.8 ± 3.3	87.9 ± 7.7	87.9 ± 8.5	90.7 ± 4.5	86.2 ± 19.7	89.9 ± 3.5	90.5 ± 2.3	85.1 ± 8.5
MCS	77.8 ± 9.7	89.8 ± 9.2	76.2 ± 15.8	81.5 ± 12.5	89.9 ± 4.8	86.5 ± 6.7	85.1 ± 10.9	89.6 ± 2.8	83.6 ± 22.9	88.6 ± 4.2	89.9 ± 4.2	78.1 ± 3.1
Physical functioning	70.8 ± 22.0	90.0 ± 11.0	79.2 ± 16.6	78.6 ± 12.5	95.5 ± 4.7	95.0 ± 6.7	91.7 ± 10.5	94.6 ± 8.9	89.6 ± 23.8	95.0 ± 4.1	95.5 ± 1.00	93.8 ± 6.3
Role-physical	91.7 ± 20.4	100 ± 0	78.1 ± 27.9	88.6 ± 20.5	100 ± 0	89.8 ± 15.9	97.9 ± 7.2	97.9 ± 7.2	85.4 ± 26.0	100 ± 0	93.3 ± 12.2	93.8 ± 8.8
Pain	78.3 ± 27.0	90.8 ± 11.0	70.8 ± 36.8	75.2 ± 19.5	91.4 ± 8.3	76.1 ± 21.3	78.5 ± 19.9	89.2 ± 12.3	75.0 ± 26.1	84.4 ± 11.3	94.7 ± 5.4	68.8 ± 16.1
General health	64.2 ± 8.6	80.8 ± 10.7	**53.3 ± 25.0^{be}**	68.2 ± 14.2	78.2 ± 6.0	76.8 ± 12.9	76.3 ± 14.0	77.9 ± 11.6	**84.6 ± 13.2^{c}**	73.8 ± 12.5	76.4 ± 17.8	67.5 ± 19.4
Role-emotional	100 ± 0	100 ± 0	90.3 ± 17.0	93.9 ± 13.5	97.0 ± 10.1	97.0 ± 10.0	94.4 ± 19.3	97.2 ± 9.6	89.6 ± 23.9	100 ± 0	100 ± 0	91.7 ± 16.7
Vitality	61.7 ± 16.3	80.8 ± 13.2	59.4 ± 20.4	70.0 ± 17.8	81.4 ± 6.7	74.4 ± 12.0	76.3 ± 14.2	80.4 ± 9.4	75.5 ± 24.2	75.0 ± 13.5	77.6 ± 12.6	64.1 ± 12.9
Emotional well-being	72.7 ± 17.8	89.3 ± 10.3	77.5 ± 15.4	80.0 ± 12.9	89.5 ± 6.5	86.4 ± 11.9	83.0 ± 12.8	88.7 ± 5.4	84.6 ± 22.7	88.0 ± 3.3	89.5 ± 3.0	75.0 ± 10.8
Social functioning	89.6 ± 14.6	93.8 ± 15.3	85.4 ± 20.0	89.8 ± 13.5	97.7 ± 5.1	95. 5 ± 8.4	93.8 ± 15.5	99.0 ± 3.6	88.5 ± 25.8	100 ± 0	100 ±0	93.8 ± 7.2

Note. Values are means ± standard deviations; higher HRQL values indicate better quality of life; significant *p*-values are indicated in bold; HRQL = health-related quality of life; PCS = physical component summary; MCS = mental component summary.

^{a}Significantly different from baseline

^{b}Significantly different from post-intervention

^{c}Significantly different from SED group

^{d}Significantly different from SED-AER group

^{e}Significantly different from LEX group

^{f}Significantly different from LEX-SED group

3.4.3. Exercise motivations (EMI-II)

Comparisons of EMI-II scores between SED and SED-AER groups at baseline and post-intervention can be found in *Table 3.2*. Briefly, both groups reported significant within-groups differences for enjoyment, appearance, and strength and endurance as motivations to exercise. The SED-AER group reported significant increases in stress management, revitalisation, challenge, ill health avoidance, and weight management. Only one significant between-groups difference was observed during post-intervention, in which the SED-AER group reported competition as significantly greater motivation to exercise.

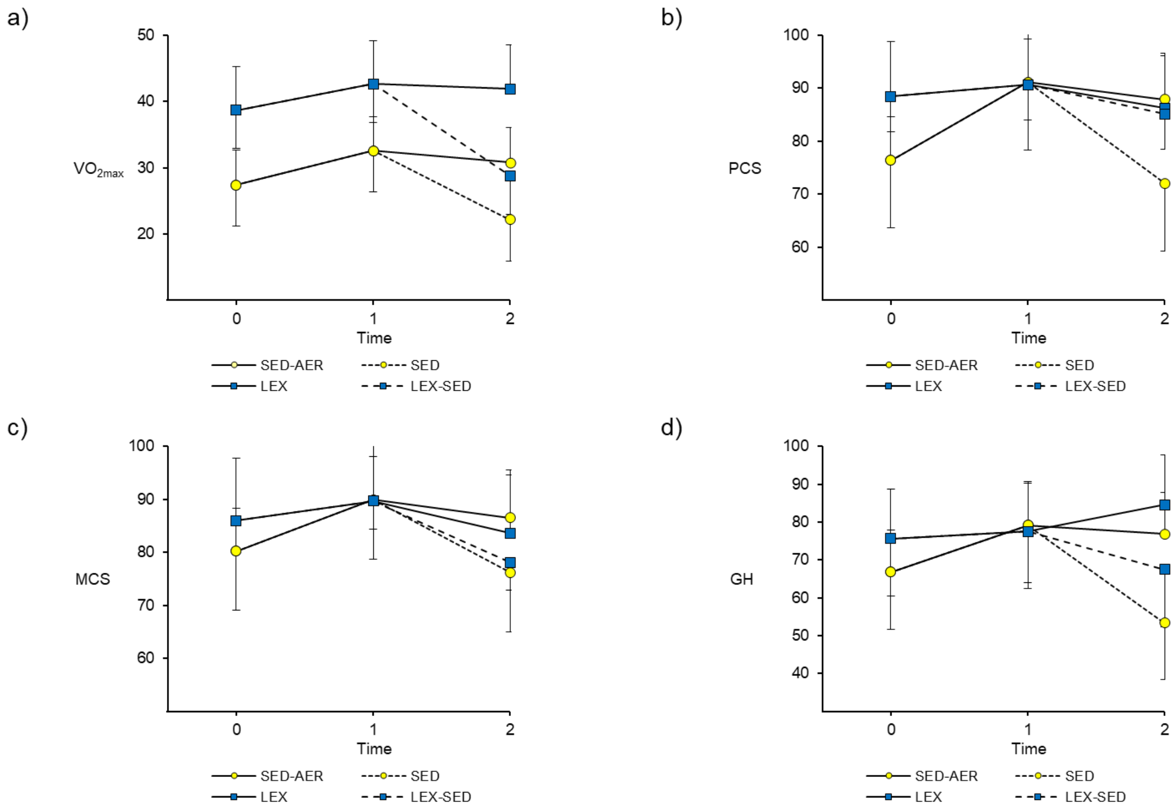

Figure 3.3. Line plots depicting mean scores for (a) VO_{2max}, (b) physical component summary, (c) mental component summary, and (d) general health at three time-points: (0) baseline, (1) post-intervention, and (2) follow-up assessments.

3.5. Discussion

3.5.1. Summary of findings

The main findings from this 4-year experimental follow-up show that sedentary ageing men who comply with regular aerobic exercise have better aerobic fitness and more positive perceptions of general health than their relative counterparts. Aerobic capacity was maintained for the those who continued to exercise, whereas substantial decreases were observed for the sedentary groups after four years. Likewise, HRQL was generally worse for sedentary participants during 4-year follow-up, while their exercising counterparts remained relatively unchanged. The main HRQL component responsible for this change was a perceived deterioration in general physical health. Taken together with the participants' self-reported motivations to exercise, these preliminary findings have novel implications for older adults.

3.5.2. Implications of the current findings

The findings of this study show that aerobic capacity was consistently better for those who engaged in lifelong exercise, highlighting the importance for individuals to engage in regular aerobic exercise throughout life to preserve higher aerobic capacity in older age. Indeed, many randomised controlled trials have shown that short exercise programs have profound benefits on aerobic capacity during older age (Bouaziz et al., 2018), and long-term adherence to exercise is associated with a range of cardiorespiratory health outcomes (Bauman, 2016; Gremeaux et al., 2012). Therefore, it is conceivable that older adults who begin exercising early in life are likely to have better aerobic capacity, particularly at a higher intensity (Huang et al., 2016).

Table 3.2

Descriptive statistics for the EMI-II questionnaire for SED and SED-AER groups

	SED (*n* = 6)		SED-AER (*n* = 11)	
	Baseline	Post-Intervention	Baseline	Post-Intervention
Stress management	1.92 ± 1.59	3.63 ± 1.15	1.75 ± 0.97	**3.70 ± 0.70**[a]
Revitalisation	2.94 ± 1.60	4.33 ± 0.89	2.85 ± 0.86	**4.45 ± 0.45**[a]
Enjoyment	2.50 ± 1.76	**4.21 ± 0.58**[a]	2.43 ± 0.64	**4.25 ± 0.43**[a]
Challenge	2.04 ± 0.83	3.04 ± 1.04	1.95 ± 0.88	**3.41 ± 0.59**[a]
Social recognition	0.92 ± 0.65	1.25 ± 0.84	0.89 ± 0.85	1.50 ± 0.77
Affiliation	1.58 ± 1.03	1.13 ± 1.09	1.18 ± 0.85	1.77 ± 0.89
Competition	1.04 ± 0.83	1.42 ± 0.90	1.75 ± 1.01	**2.48 ± 1.01**[b]
Health pressures	1.33 ± 1.05	1.72 ± 1.99	0.81 ± 0.96	1.36 ± 1.08
Ill health avoidance	4.39 ± 0.57	4.67 ± 0.42	3.94 ± 0.57	**4.52 ± 0.50**[a]
Positive health	4.39 ± 0.53	4.67 ± 0.30	4.06 ± 0.94	4.58 ± 0.30
Weight management	3.25 ± 1.26	4.33 ± 0.38	3.39 ± 0.44	**4.30 ± 0.40**[a]
Appearance	1.58 ± 1.07	**3.80 ± 0.62**[a]	1.93 ± 1.01	**3.73 ± 0.61**[a]
Strength and endurance	2.96 ± 0.78	**4.17 ± 0.56**[a]	3.43 ± 0.64	**4.18 ± 0.42**[a]
Nimbleness	4.00 ± 0.97	4.39 ± 0.44	4.24 ± 0.63	4.42 ± 0.47

Note. Values are means ± standard deviations; higher EMI-II values indicate higher motivation in specified domain; significant *p*-values are indicated in bold.

[a] Significant increase from baseline

[b] Significant difference between groups

Low levels of aerobic capacity are associated with increased risk for cardiovascular and all-cause mortality in people of all ages, and initiation of a regular exercise regime lessens risk across the lifespan (Thompson et al. 2003). Moreover, given that small improvements in cardiorespiratory fitness can have a major impact on health and survival (Kodama et al. 2009; Kaminsky et al. 2013) then it stands to reason that lifelong sedentary individuals who take-up exercise later in life stand to achieve the greatest relative health benefit (Grace et al. 2014). Preservation of aerobic capacity is important for successful ageing, as it provides older adults with physical independence. Lifelong sedentary participants (SED) had a slight decline in VO_{2max} during 4-year follow-up compared to baseline (M = 23.83 vs. 22.17 ml kg min^{-1}), representing a 7.5% decrease in aerobic capacity from enrolment to the study. This decline resembles the 1-2% natural decline in aerobic capacity per year associated with ageing (Fleg et al., 2005; Hawkins & Wiswell, 2003; Hollenberg et al., 2006; Stathokostas et al., 2004). Conversely, those who commenced moderate-intensity exercise over the 4-year period (SED-AER) improved in VO_{2max} (M = 29.36 vs. 30.82 ml kg min^{-1}). This 5.9% improvement reflects a true change in aerobic capacity, as changes in VO_{2max} contributed from body mass were trivial (-0.2%). Therefore, it is likely that sedentary people experience a natural decline in aerobic capacity, whilst their physically active counterparts may preserve aerobic capacity with regular moderate-to-high intensity exercise, and even when exercise is adopted later in life, exercise can reverse the cardiorespiratory deficits associated with a lifelong sedentary lifestyle.

There were also novel findings for the active participants. Those who maintained lifelong exercise throughout the 4-year period (LEX) had better VO_{2max} (M = 39.50 vs. 41.92 ml kg min^{-1}), representing a 5.4% improvement in aerobic capacity. Interestingly, lifelong exercisers that discontinued their training regimens exhibited substantially lower 4-year follow-up VO_{2max} (M = 36.25 vs. 28.75 ml kg min^{-1}), reflecting a 20.9% decrease in aerobic capacity. Considering the expected age-related decline (-8%) and changes in body mass (-5.7%), a substantive loss of aerobic capacity for LEX-SED participants was due to cessation of exercise (-7.2%). This is likely due to detraining, as older exercisers who reduce their training workload can experience a decline in functional fitness (Ratel et al., 2012). These findings indicate that physical exercise needs to be sustained in order to maintain the benefits associated aerobic fitness.

Since these changes in cardiorespiratory fitness are due to changes in maximal oxygen uptake, differences in MET values (calculated as a ratio of work metabolic rate to a standard resting metabolic rate) may reflect real-world discrepancies in the functional ability to engage in everyday activities. For instance, the LEX-SED group had a decrease of 2.1 METs (from 10.4 to 8.2) within their 4-year sedentary period, which may correspond to the inability to engage in vigorous-intensity dancing, moderate-intensity swimming, or carrying heavy loads/objects (Ainsworth et al., 2000, 2011). Similarly, there was a 2.5 MET difference between the SED and SED-AER groups (6.3 vs. 8.8 METs, respectively), which may reflect practical difficulties in the ability to jog, play tennis, or even carry groceries upstairs. Nevertheless, having low aerobic function does not preclude older adults from engaging in physical exercise, and rather, metabolic capacities should dictate exercise prescription based on aerobic capacity.

Sedentary participants tended to show worse self-reported HRQL during 4-year follow-up, while exercising participants remained relatively unchanged. When physical and psychosocial HRQL were examined separately, further incongruencies emerged. Most notably, sedentary participants that commenced an exercise program were the only group to report improvements in both physical and psychosocial HRQL compared to baseline (M_{diff} = 10.15 and 5.00, respectively).

Inconsistency remains between exercise and specific domains of HRQL (Halbert et al., 2000; Kerse et al., 2005; Knowles et al., 2015; Kolt et al., 2007). By looking at 10-point changes on the domains of HRQL (equating to a 10% change), it is possible to identify patterns of exercise activity that accentuate improvements in HRQL, or at the very least, enable older adults to maintain their quality of life. For instance, lifelong exercisers that discontinued their training regimens (LEX-SED) reported deficits in all domains of HRQL during the 4-year follow-up, including large decreases in pain tolerance, vitality, and emotional well-being. This is likely an artifact of detraining, which has recently been shown to influence HRQL in older adults who regularly exercise (Esain, Gil, Bidaurrazaga-Letona, & Rodriguez-Larrad, 2019). On the other hand, those who took up moderate-intensity exercise over the 4-year period (SED-AER) were the only group to report improvements in all HRQL domains, including a remarkable increase in perceived physical functioning. This suggests that commencing exercise later in life may still be beneficial for quality of life and functional independence, even when preceded by a lifetime of sedentary behaviour.

General health was the only HRQL domain to show statistically significant differences between groups. In particular, a large difference (Hedges' *g* = 1.674) was reported between LEX and SED participants (*M* = 84.58 vs. 53.33, respectively), indicating that lifelong exercise is associated with significantly better ratings of general health than a sedentary lifestyle. This was further supported by the significant decline in general health between post-intervention and follow-up for the SED group, reflecting a large mean change (Hedges' *g* = 1.380). Overall, as speculated by Vasiliadis & Bélanger (2018), it is plausible that the maintenance of exercise throughout the years is necessary to maintain HRQL, but that past activity does not confer protection against future decline.

3.5.3. Practical implications

Differences in motivations to exercise were also explored between the two groups of participants who were sedentary at baseline. In general, these findings can provide some rudimentary theories as to why older males choose to continue with exercise training once they are no longer supervised. In response to the original 12-week exercise program, all sedentary participants reported increases in feelings to exercising for enjoyment, appearance, and strength/endurance. It is important to note, however, that not all sedentary participants were the same. Sedentary participants who began an exercise program after the 12 weeks (SED-AER) reported competition as a significantly higher motivation to exercise than those who continued a sedentary lifestyle (SED). It is plausible that some participants came into the study with higher competition, which might reflect higher VO_{2max} and subsequent motivation to continue exercise.

There were also several noteworthy changes reported solely by the SED-AER group (i.e., stress management, revitalisation, challenge, ill health avoidance, weight management). Firstly, it is possible that those who self-selected to engage in exercise after the 12-week program are more likely to engage in exercise because they believe the changes in appearance may also result in benefits to weight composition. There also seems to be a psychological component to these motivations. In particular, those who ceased exercise were reported a lack of revitalisation and stress management despite their increase motivation for enjoyment. It might be that the SED group perceived exercise as difficult, whereas the SED-AER group were willing to accept this difficulty and enjoy a positively perceived challenge, resulting in a perception of exercise as a means for revitalisation and stress management. Lastly, there were no significant changes for health pressures for either group, but the SED-AER group reported higher ill health avoidance. This may reflect a need to exercise for ‘internally’ perceived pressures, such as health conditions, rather than ‘external’ pressures placed on the individual by family, friends, or healthcare professionals. Taken together, sedentary participants who engage in an exercise program tend to be more connected to their motivation to exercise, and alternatively, those that choose to discontinue exercise are likely to be unconnected with their motivations.

Although causality between outcomes is beyond the capabilities of the current study, our findings indicate that moderate-to-high intensity exercise may concurrently preserve and/or improve both aerobic capacity and HRQL, supporting past scientific evidence (Lavie & Milani, 2000; Sillanpää et al., 2012; Stewart et al., 2003). It is unknown to what extent aerobic capacity directly impacts perceptions of quality of life, however the present findings suggest that improvements in aerobic capacity, and subsequent increases in cardiorespiratory fitness and functional independence, are more important for HRQL than simply maintaining aerobic fitness. That is, it is not the physiological improvements in aerobic fitness per se, but rather, it is the increased perception in one’s physiological and functional abilities.

Treating health conditions during older adulthood is often more problematic because they can be easily masked by other comorbidities. Thus, it is imperative that healthcare professionals use safe and effective interventions for public policy and health promotion. Exercise is often used as an effective adjunct to standard care, which allows older adults to maintain control over their health and potentially reverse health conditions associated with ageing. Our findings highlight the importance of exercise prescription in older populations to improve self-perceived aerobic capacity and HRQL. It is therefore recommended that healthy exercise habits are continued throughout older adulthood, or if not already performed, they are adopted to promote successful ageing and lessen the natural decline of aerobic capacity typically associated with older age.

3.5.4. Limitations and future directions

The current study had several limitations. Most notably, sample sizes for the subgroups were relatively small. This may have reduced the likelihood that an estimated result reflects a true effect (Button et al., 2013), and therefore, line graphs were used to depict the potential longitudinal trends in key variables. Nevertheless, this should be used as preliminary evidence to encourage future experimental trials to conduct long-term experimental follow-ups within larger samples to strengthen statistical power.

It is also important to acknowledge that exercise characteristics (i.e., type, intensity, frequency, duration) were not directly monitored during the 4-year period, which could have had an impact on the findings. For instance, intensity is known to moderate the effects of exercise on cardiorespiratory fitness (Huang et al., 2016), and therefore, it is likely that lifelong exercisers and moderate-intensity groups reflect two different modalities of exercise. In the current study, potential variation from different levels of exercise were mitigated by scores on aerobic capacity. Therefore, it is recommended that future cohort studies collect data on exercise characteristics so that these potential confounding effects can be controlled during analysis of the data.

3.5.5. Conclusions

This preliminary evidence approaches the gap in long-term experimental follow-up designs of exercise-based interventions within older adult cohorts. Preliminary findings indicate that commencing aerobic exercise later in life is associated with better aerobic capacity during older adulthood than a sedentary lifestyle, although aerobic benefits can still be achieved later in life. Regular aerobic exercise can also result in higher self-reported HRQL, particularly better perceptions of general physical health. Thus, healthy exercise habits, even when adopted in older age, can promote successful ageing and lessen the natural decline typically associated with ageing.

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CHAPTER IV

Exercise, Mood, Self-Efficacy, and Social Support as Predictors of Depressive Symptoms in Older Adults: Direct and Interaction Effects

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Supplementary Material: See *Appendix E*

Preface

Preliminary evidence from the Study (Chapter III) highlights the physiological benefits of regular aerobic exercise, which might precede (or coalesce with) perceived change in quality of life, or components thereof. The findings within the present 4-year observational study of ageing men provides novel prospective evidence for exercise-induced improvement in cardiorespiratory fitness to be consistent with concurrent improvements to HRQL. This is important because HRQL has been shown to be highly sensitive to symptoms of depression in older adults (Bell, DaCosta DiBonaventura, Witt, Ben-Joseph, & Reeve, 2017; Matcham, Norton, Steer, & Hotopf, 2016; Silveira et al., 2005).

The next step is to establish how regular exercise can protect individuals against depression in older age by investigating the dynamic relationships between exercise and depressive symptoms. Three key underlying psychosocial mechanisms are used to explain the antidepressive effects of physical exercise (Paluska & Schwenk, 2000). First, exercise improves mood states through distraction and alleviate depressive symptoms by increasing levels of endorphins, serotonin, and norepinephrine (Gupta & Mittal, 2015; Thorén, Floras, Hoffmann, & Seals, 1990). Second, exercise may enhance beliefs of mastery and self-efficacy, which lead to a sense of accomplishment and greater control over daily tasks (Bandura, 1997; Greist et al., 1979). Lastly, exercise provides an opportunity to adjust to retirement through gaining a sense of social connectedness and maintaining personal relationships, which may result in an increased ability to cope with stress and depression (Bengtson, Gans, Putney, & Silverstein, 2009; Ransford, 1982).

The number of studies investigating these dynamic relationships in older adults is small compared to similar studies among other age-based groups (e.g., children, adolescents, adults), and therefore, many underlying mechanisms have been investigated in isolation using a single theoretical model. For a better understanding of the influence that these factors have on the relationship between exercise and depressive symptoms, studies that integrate the indirect and interaction effects of moderating variables in the same model are needed. Thus, in the following study, a cross-sectional design was used to examine a regression model integrating potential key predictor variables (i.e., general health, physical functioning, physical exercise, mood, self-efficacy, social support), both as unique effects and interactions, to investigate their relative impact on depressive symptoms specifically in older adults.

4.1. Abstract

4.1.1. Background

Depression is a chronic condition that affects up to 15% of older adults. The healthogenic effects of regular exercise are well established, but it is still unclear which exercise-related variables characterise the antidepressant effects of exercise. Thus, the purpose of this study was to examine the extent to which exercise-related variables (exercise behaviour, exercise-induced mood, exercise self-efficacy, and social support) can predict depressive symptoms in a cohort of community-dwelling older adults.

4.1.2. Methods

This study employed a cross-sectional analysis of questionnaire data from a sample of 586 community-dwelling older Australians aged 65 to 96 years old. Participants completed the Center for Epidemiologic Studies Depression Scale, modified CHAMPS Physical Activity Questionnaire for Older Adults, Four-Dimension Mood Scale, Self-Efficacy for Exercise Scale, and Social Provisions Scale - Short Form. Bivariate correlations were performed, and hierarchical multiple regression was subsequently used to test the regression model.

4.1.3. Results

Exercise behaviour, exercise-induced mood, exercise self-efficacy, and social support were all negatively associated with depressive symptoms (r = -.20 to -.56). When the variables were entered as predictors into the hierarchical multiple regression model, social support was the strongest predictor of depressive symptoms (β = -.42), followed by exercise-induced mood (β = -.23), and exercise self-efficacy (β = -.07). Exercise behaviour did not

explain any additional variance in depressive symptoms. A modest interaction effect was also observed between exercise-induced mood and social support.

4.1.4. Conclusions

These findings indicate that social support is the strongest predictor of depressive symptomology in community-dwelling older adults, particularly when combined with positive exercise-induced mood states. When addressing the needs of older adults at risk of depression, healthcare professionals should consider the implementation of exercise programs that are likely to benefit older adults by improving mood, enhancing self-efficacy, and building social support.

4.2. Introduction

The proportion of older adults aged 65 years and over in the Australian population is gradually rising, leading to an ageing population (Australian Bureau of Statistics, 2016). Ageing is associated with a greater prevalence of long-term health problems, including significantly higher rates of comorbid mental health problems within the older demographic (Barnett et al., 2012; Volkert, Schulz, Härter, Wlodarczyk, & Andreas, 2013). Depression is one of the most prevalent mental health problems in older adulthood (Argyropoulos et al., 2012), with estimates of 10-15% of community-dwelling older adults aged 65 years and over experiencing depressive symptoms at any given time (Laborde et al., 2015; Luppa et al., 2012; Pirkis et al., 2009). Depressive symptoms can include a persistent sadness, irritable or anxious mood, reduced concentration and attention, low energy levels or fatigue, low self-esteem or self-confidence, feelings of hopelessness, sleep or appetite problems, loss of interest or pleasure in activities that used to be enjoyable, or difficulty in carrying out usual work or social activities (American Psychiatric Association, 2013).

To date, researchers have largely focused on interventions that can delay the ageing process, and in doing so, encourage a healthspan consistent with prolonged positive mental health in later life. Physical exercise is commonly integrated into daily living to build social support and enhance quality of life, resulting in a significant increase to longevity (Gremeaux et al., 2012; Vagetti et al., 2014). Exercise refers to structured and repetitive concentric, eccentric, or isometric muscular activity performed to improve or maintain one or more aspects of physical or psychological health (Caspersen et al., 1985; Ceria-Ulep et al., 2011; Winter & Fowler, 2009). Exercise has been identified as a key protective factor against depression during older adulthood (see Rhyner & Watts, 2016 for a review), and may be used in addition to traditional treatments, such as antidepressant drug therapy, to further reduce depressive symptoms (Belvederi Murri et al., 2019; Mura et al., 2014).

Clarity in geriatric depression research has been widely discussed during the past two decades (Blazer, 1997), but there remains a pervasive inconsistency of research outcomes, and many common misconceptions (Haigh, Bogucki, Sigmon, & Blazer, 2018). In part, this is likely due to the weight of scientific inquiry being heavily directed towards younger and middle-aged adults, relative to older populations (evidenced by brief literature search; see *Appendix E*). Moreover, the geriatric literature remains focused on single isolated factors which forgoes the complexity of important interactions. Three key underlying psychosocial mechanisms predominate in understanding the relationship between exercise and depression, including a distraction from negative mood states, enhanced self-efficacy, and increased social support (see Paluska & Schwenk, 2000 for a theoretical review).

The earliest explanation for the depression-reducing effects of exercise is the distraction hypothesis, which is based on the theory that a simple diversion from a painful stimulus can lead to an improved mood state following physical exercise (Festinger & Maccoby, 1964). This was initially demonstrated in an intervention study (Bahrke & Morgan, 1978) whereby 75 adult participants engaged in 20 minutes of treadmill exercise, general meditation, or reading in a sound-dampened chamber. Bahrke and Morgan reported that participants had a better post-intervention affect in all forms of activity, concluding that exercise, as well as other activities, provide a valuable distraction from the stress of daily living, anxiety, and depression. Evidence from a meta-analysis conducted by Arent and colleagues (2000) has further supported the mood-inducing effect of exercise in older adults. A quantitative analysis of 32 studies found that chronic exercise leads to significantly more positive affect (Hedges' g = .33) and less negative affect (Hedges' g = .35) compared to control conditions, indicating that exercise has acute effects on negative dispositions (Arent et al., 2000).

According to self-efficacy theory, an individual's depressive symptoms may also become less severe should their self-efficacy become increased (Bandura, 1977; 1997). Exercise self-efficacy is defined as one's beliefs about the capability to successfully engage in incremental bouts of physical activity (Blacklock et al., 2010). When older adults engage in regular exercise, it provides them with a greater sense of mastery and personal control over their environment, which they can then transfer onto other everyday tasks to cope with stress and depression. Preliminary evidence has identified self-efficacy as an independent mechanism for the antidepressant effects of exercise in adult samples (Annesi, 2012; Craft, 2005; Ryan, 2008). Moreover, a recent cross-sectional study of 42 older adults revealed that depressive symptoms were independently and negatively associated with exercise self-efficacy (Byrne & Horgan, 2018). Since the size of this sample was underpowered, however, further investigation is necessary to ascertain the extent to which exercise self-efficacy independently predicts depressive symptoms.

Affective responses and efficacy beliefs have been proposed to form two distinct, yet interrelated, influences on mental health (Bandura, 1997). A randomised controlled trial on a small cohort of 12 clinically depressed adults (M_{age} = 36.6 years) initially reported that acute exercise aimed at enhancing self-efficacy had significant improvements on self-reported mood (Bodin & Martinsen, 2004). Subsequently, Pickett and colleagues (2012) employed a cross sectional study of 164 moderately depressed adults (M_{age} = 30 years), theorising that self-efficacy mediates the exercise-depression relationship through positive affect. A single longitudinal study has supported this tenet, whereby exercise-induced mood interacts with self-efficacy in depressed adults (White et al., 2009). To date, few studies have examined the independent and interactive effects of exercise-induced mood and self-efficacy on depressive symptoms in older cohorts, and therefore, further research is needed to establish these patterns in older age.

The capacity for exercise to build social support networks and concomitant positive effects on mood and depression during older adulthood is widely accepted (Makino et al., 2015; McAuley et al., 2000). Social support refers to the helpful resources an individual perceives available to them in the context of both formal and informal relationships (Gottlieb & Bergen, 2010). For older adults, physical exercise allows opportunities to engage in challenges, adjust to retirement, and maintain personal relationships and endeavours (Bengtson et al., 2009). Consequently, older individuals gain a sense of social connectedness by developing new and diverse shared experiences (Lindsay-Smith et al., 2018), resulting in an improved ability to cope with stress and depression (Cornwell & Waite, 2009; Glass et al., 2006). Indeed, a cross-sectional study involving 583 community-dwelling older adults revealed that both exercise behaviour and social support independently predicted depressive symptoms (McHugh & Lawlor, 2012).

Despite the wealth of evidence for the benefits of social interaction and support on depressive symptoms in older cohorts (Gariépy et al., 2016), few studies have investigated whether social support interacts with exercise self-efficacy and/or mood to further predict depressive symptoms. Preliminary longitudinal research has shown that self-efficacy reduces depression directly as well as interacting indirectly through social support (Holahan & Holahan, 1987). McAuley and colleagues (2000) found that a social, group-based exercise predicted stronger changes in affective states (i.e., positive well-being, lower psychological distress, fewer feelings of fatigue) than individual exercise in a group of older adults (*n* = 80). When self-efficacy was included in the model, more positive and less negative mood states occurred, but these mood states were dependent on the intensity and social conditions of exercise (McAuley et al., 2000). Interestingly, these findings outline potential interaction effects between social support and exercise-induced mood and/or self-efficacy on depressive symptoms, which are worthy of examination in a larger participant sample.

Because researchers have examined depressive symptoms and their associated predictors in isolation (i.e., exercise behaviour, exercise-induced mood, exercise self-efficacy, social support), there is currently limited benchmarking of predictors within the same analysis, accounting for overlapping variance and potential interaction effects between two predictor variables. Moreover, existing studies have predominately tested these associations in younger adult cohorts without consideration of age-related changes, such as deficits in health status and/or physical functioning (Barry et al., 2011; Nyunt et al., 2012).

This study extends previous scientific enquiry in several advantageous ways: (1) exercise behaviour, exercise-induced mood, exercise self-efficacy, and social support are tested in the same regression model, allowing effects to be quantified according to how much unique variance can be explained by a specific predictor variable while controlling for all other variables, (2) interaction effects are tested between predictor variables, which can assist in identifying potential underlying synergistic effects between two seemingly independent predictors, and (3) this study employs an adequately powered sample ($n > 300$), thus reducing the opportunity for Type II errors.

The purpose of this study was to investigate the extent to which exercise-related variables (exercise behaviour, exercise-induced mood, exercise self-efficacy, and social support) predict depressive symptoms in a sample of community-dwelling older adults (> 65 years) by employing hierarchical multiple regression techniques. A regression model was hypothesised whereby exercise behaviour, exercise-induced mood, exercise self-efficacy, and social support were used to predict depressive symptoms in older adults. This model was used to compare the strength of prediction estimates, controlling for health status, physical functioning, age, gender, and other known predictor variables. Two-way interaction effects between exercise-induced mood, exercise self-efficacy, and social support in the model were further explored.

4.3. Methods

4.3.1. Participants

Ethical approval was obtained from the Australia Human Research Ethics Committee prior to data collection. The study included a sample of 586 community-dwelling older Australians aged over 65 years, recruited from retirement villages, senior citizen centres, community groups, bowling clubs, and fitness centres. The sample consisted of 172 males and 414 females, with ages ranging from 65 to 96 years (*M* = 72.47, *SD* = 6.22). Full participant demographics can be found in *Table 4.1*. In general, participants had a secondary school qualification or higher, lived with a partner or alone, were married, and currently retired. Most participants reported good health or better, with no physical limitations or only minor limitations.

4.3.2. Measures

Data were collected using a battery of questionnaires, including a demographics questionnaire, Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977), modified CHAMPS Physical Activity Questionnaire for Older Adults (Stewart et al., 2001), Four-Dimension Mood Scale (4DMS; Huelsman et al., 1998), Self-Efficacy for Exercise (SEE) Scale (Resnick & Jenkins, 2000), and Social Provisions Scale - Short Form (SPS-10; Cutrona & Russell, 1987).

Table 4.1

Participant descriptive data

Variable	**Total** (***n*** **= 586)**	**Electronic** (***n*** **= 435)**	**Paper** (***n*** **= 151)**	**Between-Groups**
Age (years)	72.47 ± 6.22	71.43 ± 5.38	75.47 ± 7.41	-7.16^{***}
Body weight (kg)	72.58 ± 15.52	72.11 ± 15.22	73.93 ± 16.33	-1.23
Exercise behaviour (calories/week)	1307 ± 1315	1306 ± 1245	1314 ± 1527	-0.03
Females, *n* (%)	414 (70.65)	309 (71.03)	105 (69.54)	0.12
CES-D ≥ 16, *n* (%)	129 (22.01)	91 (20.92)	38 (25.17)	1.18
Pet owner, *n* (%)	196 (33.45)	152 (34.94)	44 (29.33)	1.58
Health status, *n* (%)				
Excellent	89 (15.19)	72 (16.55)	17 (11.26)	9.20
Very good	240 (40.96)	184 (42.23)	56 (39.07)	
Good	181 (30.89)	132 (30.35)	49 (32.45)	
Fair	67 (11.43)	41 (9.43)	26 (17.22)	
Poor	9 (1.54)	6 (1.38)	3 (1.99)	
Physical functioning, *n* (%)				
Not limited	264 (45.05)	207 (47.59)	57 (37.75)	4.66
A little limited	269 (45.90)	192 (44.14)	77 (50.99)	
Very limited	53 (9.04)	36 (8.28)	17 (11.26)	
Living arrangements, *n* (%)				
Partner	344 (58.70)	267 (61.38)	77 (50.99)	5.50
Family members	34 (5.80)	22 (5.06)	12 (7.95)	
Friends	4 (0.68)	3 (0.69)	1 (0.66)	
Alone	204 (34.81)	143 (32.87)	61 (40.40)	
Relationship status, *n* (%)				
Partner	43 (7.34)	34 (7.82)	9 (6.00)	18.82^{**}
Single	37 (6.31)	30 (6.90)	7 (4.67)	
Married	313 (53.41)	242 (55.63)	71 (47.33)	
Separated/divorced	85 (14.51)	67 (15.40)	18 (12.00)	
Widowed	107 (18.26)	62 (14.25)	45 (30.00)	
Education, *n* (%)				
Primary	17 (2.90)	3 (0.69)	14 (9.33)	87.34^{***}
Secondary	174 (29.69)	100 (22.99)	74 (49.33)	
TAFE/trade cert.	119 (20.31)	90 (20.69)	29 (19.33)	
Undergraduate	105 (17.92)	84 (19.31)	21 (14.00)	
Postgraduate	170 (29.01)	158 (36.32)	12 (8.00)	
Employment status, *n* (%)				
Full-time	5 (0.85)	4 (0.92)	1 (0.66)	21.26^{***}
Part-time/casual	51 (8.70)	46 (10.57)	5 (3.31)	
Homemaker	13 (2.22)	4 (0.92)	9 (6.00)	
Retired	513 (87.54)	377 (86.67)	136 (90.07)	
Unemployed	4 (0.68)	4 (0.92)	0 (0.00)	

Note. Descriptive data are reported as means and standard deviations unless otherwise stated. Between-groups test statistic was *t* for continuous values and χ^2 for categorical values. Missing data for body weight (*n* = 3), pet owner (*n* = 1), relationship status (*n* = 1), and education (*n* = 1).

*p < .05. **p < .01. ***p < .001.

4.3.2.1. Demographics questionnaire. Participants were asked to complete a brief demographic questionnaire requesting background information on age, gender, weight, living arrangement, education, ethnicity, employment status, relationship status, and ownership of pets. Two items from the 36-item Short-Form Health Survey (SF-36; Ware Jr. & Sherbourne, 1992) were also adapted and included on the demographic questionnaire to assess health status (i.e., *in general, how would you rate your health?*) and physical functioning (i.e., *does your health limit you in exercise-related activities?*).

4.3.2.2. Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D is a 20-item self-report measure of depressive symptom severity (Radloff, 1977), which is suitable for use within older adult samples (Górkiewicz & Chmiel, 2015). The CES-D reflects four distinct factors: depressive affect, somatic symptoms, interpersonal distress, and positive affect. Participants were instructed to report how often they experience particular depressive symptoms (e.g., *I felt lonely*) over the preceding 4 weeks on a 4-point Likert scale from 0 (*rarely or none of the time - less than 1 day*) to 3 (*most or all of the time - 5 to 7 days*), with the four positive affect items reverse scored.

Past studies have found high internal consistency for the total CES-D in older adults, with alpha coefficients above .80 (Górkiewicz & Chmiel, 2015; Ros et al., 2011). A Cronbach’s alpha of .86 was calculated for the current sample. The CES-D has been successfully used to identify clinical depression (Ros et al., 2011), as well as being concurrently validated with subscales of depression (r = .58) and suicide ideation (r = .47) on the General Health Questionnaire in older adults (Gomez & McLaren, 2015).

4.3.2.3. Modified CHAMPS Physical Activity Questionnaire for Older Adults. The CHAMPS is a 28-item questionnaire designed to measure the caloric expenditure of physical activity during older adulthood, which takes into account the intensity, frequency, and duration of activity, as well as correcting for differences in body weight (Stewart et al., 2001). For the current study, a modified CHAMPS comprising of 20 items was used to measure exercise behaviour (Resnicow et al., 2003). Exercise behaviour was operationally defined as weekly caloric expenditure in intentional sport and recreational activities that are not part of daily functioning. Participants were instructed to report how many times per week and total hours in a typical week they have engaged in each exercise-related activity (e.g., *do water exercises*) over the preceding 4 weeks.

The CHAMPS correlated highly with two commonly used physical activity measures, including the Physical Activity Questionnaire Physical Activity Survey for the Elderly (*r* = .64) and Yale Physical Activity Survey (*r* = .68), and test-retest reliability was .76 over a 2-week period (see Harada et al., 2001 for measure comparisons and rationale). The CHAMPS also has extensive construct validity with measures of lower body functioning and endurance (.15 to .28; Stewart et al., 2001), physical health (*r* =.14 to .32; Cyarto et al., 2006), and pedometer step count (*r* =.21 to .57; Giles & Marshall, 2009).

4.3.2.4. Four-Dimension Mood Scale (4DMS). The 4DMS is a 20-item questionnaire designed to measure four dimensions of dispositional mood: positive energy, negative arousal, tiredness, relaxation (Huelsman et al., 1998). Participants were instructed to indicate to what extent each adjective item reflects the way they generally feel after exercise (e.g., *energetic*) on a 5-point Likert scale from 1 (*very slightly or not at all*) to 5 (*extremely*).

The 4DMS was selected because it was conceptualised with a theoretical understanding of affect and mood, uses exercise-relevant mood adjectives, has less floor and ceiling effects, avoids dimension loading problems by not using reverse worded items, and involved sufficient confirmatory factor analysis procedures during item selection and questionnaire validation (Boyle et al., 2015; see Ekkekakis, 2013 for measure comparisons and rationale). Moreover, the 4DMS is more sensitive to the effects of physical exercise than other similar mood measures (Gregg & Shepherd, 2009). Cronbach's alpha values ranged between .87 and .93 in a sample of adults (M_{age} = 42.6; Huelsman et al., 1998). The current study reported a Cronbach coefficient of .87. Concurrent validity was found between the 4DMS and similar mood measures, including the Activation-Deactivation Adjective Check List (*r* = .65 and .45), Job Affect Scale (*r* = .82 and .75), and Positive and Negative Affect Schedule (*r* = .62 and .68; Huelsman et al., 2003).

4.3.2.5. Self-Efficacy for Exercise (SEE) Scale. The 9-item Self-Efficacy for Exercise (SEE) Scale (Resnick & Jenkins, 2000) assesses one's self-efficacy expectations in their ability to continue exercising in the face of perceived barriers, which has been developed for use in older populations (see McAuley et al., 2013 for measure comparisons and rationale). Participants were instructed to report their confidence in engaging in exercise 3 times a week for 20 minutes if faced with a barrier (e.g., *if you were bored by the program or activity*) from 0 (*not confident*) to 10 (*very confident*).

Resnick et al. (2004) reported excellent internal consistency in older adults (α = .89 and .90). Likewise, a Cronbach's alpha value of .90 was calculated in the current sample. The SEE reflects good construct validity, correlating with outcome expectations (*r* = .39), physical functioning (*r* = .31), general health perceptions (*r* = .23), mental health (*r* = .24) regular exercise (*r* = .29), and recreational activity (*r* = .17; Resnick et al., 2006).

4.3.2.6. Social Provisions Scale - Short Form (SPS-10). The SPS-10 is a shortened, 10-item version of the original 24-item questionnaire (Cutrona & Russell, 1987), which was designed to measure the degree to which an individual's social relationships provide six dimensions of social support: attachment, social integration, reassurance of worth, reliable alliance, guidance, and opportunity for nurturance (Russell et al., 1984). Confirmatory factor analysis indicated that the six subscales reflect six first-order factors and a single second-order factor structure (Cutrona & Russell, 1987). The opportunity for nurturance subscale was excluded in the shortened measure because it reflects a dimension of social support that is provided to others rather than received. Participants were instructed to rate the strength of their agreement for each statement (e.g., *there are people who enjoy the same social activities as I do*) on a 4-point Likert scale from 1 (*strongly disagree*) to 4 (*strongly agree*). Each of the five subscales comprised of two items, with one positively worded and one negatively worded (reverse scored) item, for a total of 10 items.

The SPS-10 was selected over the original SPS because it is more manageable for older adults while maintaining strong psychometrical properties (see Gottlieb & Bergen, 2010 for measure comparisons and rationale). Internal consistency for the SPS-10 was .75 in a sample of older adults (Randall et al., 2010). The Cronbach's alpha value was .83 in the current sample. Total scores on the SPS correlated with life dissatisfaction, loneliness, and depression (r = -.28 to -.31), indicating good construct validity (Cutrona et al., 1984). Moreover, the social integration (r = .14) and reliable alliance (r = -.25) subscales were predictive of follow-up depression (Russell & Cutrona, 1991).

4.3.3. Procedures

Interested participants received a questionnaire package, which included a plain language statement and the battery of questionnaires. For participants who elected to complete the package in their own time, a reply-paid envelope was also supplied. An electronic version of the questionnaire using the SurveyMonkey online software was available for those who were recruited indirectly via social media or community advertisements. The questionnaire package took approximately 20 minutes to complete and measures were arranged in a randomised order to prevent any order effects.

4.3.4. Power analysis and sample size

A-priori sample size calculation was used to determine the approximate lower bound sample size needed to detect the specified effects (Soper, 2019). The calculation was made based on a conservative effect size (Cohen's $f^2 = .05$) and the number of predictor variables in the model ($m = 13$), desired statistical power level ($\pi = .8$), and significance level ($p = .05$). The required sample size for the regression model was calculated to be a minimum of 368 participants to detect a small effect size.

4.3.5. Statistical analysis

All statistical procedures were performed using STATA/SE 15.1 (StataCorp, 2017). Missing data were imputed using multiple imputation (using the MI IMPUTE command in Stata) with a recommended 20 imputed datasets (Sterne et al., 2009). Sensitivity analyses using independent *t*-tests were performed to compare variables between complete and imputed cases. No significant differences were found for any imputed variable, and therefore, missing participant data were assumed to be missing at random. Normality of the data was confirmed, then parametric statistics were used. Notably, social support was negatively skewed (see *Figure E1* in *Appendix E* for a histogram), however subsequent transformations resulted in greater skewness than the untransformed data. Independent t-tests and χ^2 tests were also used to compare demographic and outcome statistics between paper and electronic questionnaires.

Descriptive statistics are reported as means (*M*), standard deviations (*SD*), and Pearson product-moment correlation coefficients (*r*). Hierarchical multiple regression was used to test the regression model and interaction effects. Predictor variables were standardised by centering the scores at the mean. Control variables for health status, physical functioning, age, and gender were entered in Step 1 of the regression model, then the hypothesised predictor variables (i.e., exercise behaviour, exercise-induced mood, exercise self-efficacy, social support) were entered in Step 2. Interaction terms (predictor × predictor) were entered in Step 3 of the model to test the interactions between two predictor variables. Beta coefficients (β) provided standardised comparisons between predictor variables and squared semi-partial correlation coefficients (sr^2) indicated the proportion of unique effect contributed by each predictor variable. Confidence intervals (95% *CI*), Cohen's *f*-squared (f^2), and *p*-values were used to examine significant effects in the regression model. Cohen's (1988) guidelines were used to evaluate the strength of the f^2 effect size, whereby .02 is considered "small", .15 is considered "moderate" and .35 is considered "large". Statistical significance was achieved with criterion $p < .05$.

4.4. Results

4.4.1. Descriptive statistics

Data from a total of 586 participants were included in the analysis. A total of 230 paper questionnaire packages were distributed, with 151 usable packages being returned (65.65% compliance rate). An additional 489 electronic questionnaire packages were completed online, with 435 usable packages providing an 88.96% compliance rate. In total, 586 out of 719 questionnaires were completed with a compliance rate of 81.50%.

Demographic and outcome statistics between paper and electronic questionnaires were statistically compared using independent t-tests and χ^2 tests, which can be found in *Table 4.1*. Those who completed the electronic questionnaire package were generally younger (M_{diff} = 4.04 years; t = -7.16; p < .001) and had a higher level of education (χ^2 = 87.34; p < .001). Significant differences were also observed for relationship status (χ^2 = 18.82; p < .01) and employment status (χ^2 = 21.26; p < .001). These differences were unremarkable, and therefore, data were collapsed into a single dataset.

Full descriptive statistics and bivariate correlations (Pearson product-moment correlation coefficients) are characterised in *Table 4.2*. Briefly, depressive symptoms were significantly and negatively associated with all hypothesised predictor variables, including (1) exercise behaviour, (2) exercise-induced mood, (3) exercise self-efficacy, and (4) social support. Both health status and physical functioning demonstrated significant relationships with exercise behaviour, exercise-induced mood, exercise self-efficacy, and social support, and were subsequently included in the subsequent regression model.

Table 4.2

Means, standard deviations, and intercorrelations among study variables

Variable	***M* ± *SD***	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
1. Age	72.47 ± 6.22	1							
2. Health status	3.57 ± 0.93	-.06	1						
3. Physical functioning	2.36 ± 0.64	-.11**	.52***	1					
4. Depressive symptoms	10.73 ± 8.38	-.07	-.43***	-.34***	1				
5. Exercise (calories/week)	1307 ± 1315	-.17***	.32***	.28***	-.20***	1			
6. Exercise-induced mood	76.78 ± 9.84	-.08	.42***	.40***	-.50***	.33***	1		
7. Exercise self-efficacy	51.14 ± 21.87	-.10*	.30***	.24***	-.28***	.44***	.43***	1	
8. Social support	33.79 ± 4.61	.02	.26***	.16***	-.56***	.09*	.33***	.11*	1

Note. Higher mean values reflect a high level on the given variable.

**p* < .05. ***p* < .01. ****p* < .001.

4.4.2. The regression model

The regression model was tested using hierarchical multiple regression to compare the strength of prediction estimates from exercise-related variables (exercise behaviour, exercise-induced mood, exercise self-efficacy, social support) on depressive symptoms, after controlling for health status, physical functioning, age, and gender (see *Table 4.3*). The four control variables were entered at Step 1 of the analysis, accounting for a significant 23.80% of the variance in depressive symptoms. At Step 2, the four predictor variables were entered in the regression analysis, which accounted for a total of 49.83% of the variance in the model as a whole. The addition of the predictor variables account for an additional 26.03% variance in depressive symptoms, $\Delta R^2 = 26.03$, $F(4, 573) = 74.33$, $p < .001$. In the final model, social support ($sr^2 = .154$), exercise-induced mood ($sr^2 = .032$), and exercise self-efficacy ($sr^2 = .004$) were significant and unique predictors in the combined effect ($f^2 = 0.993$). According to Cohen’s (1988) conventions, this demonstrates of a large effect size.

Two-way interaction terms between exercise-induced mood, exercise self-efficacy, and social support were entered independently into Step 3 of the model using an interaction variable (predictor × predictor). There were no interaction effects between exercise-induced mood × exercise self-efficacy ($\beta = .19$, $t = -0.77$, $SE = 0.00$, $p = .44$) nor exercise self-efficacy × social support ($\beta = .34$, $t = 1.57$, $SE = 0.00$, $p = .12$). When exercise-induced mood × social support was entered into the model, a modest interaction effect persisted ($\beta = .98$, $t = 3.17$, $SE = 0.00$, $p < .01$). Exercise-induced mood was significantly related to depressive symptoms which was moderated by social support (see *Figure 4.1*).

Table 4.3

Hierarchical multiple regression analysis on depressive symptoms

Variable	**β**	***SE***	***t***	R^2	ΔR^2	***F(df)***	**VIF**
Step 1 Constant		4.54	5.93***	.24	.24	22.53*** (8, 577)	
Health status							
Fair	.10	2.66	1.02				7.80
Good	-.10	2.65	-0.71				16.29
Very good	-.35	2.67	-2.22*				18.94
Excellent	-.29	2.77	-2.43*				10.96
Physical functioning							
Limited a little	-.21	1.22	-2.83**				4.18
Not limited at all	-.31	1.30	-4.00***				4.85
Age	-.10	0.05	-2.61**				1.08
Gender	.07	0.68	1.89				1.06
Step 2 Constant		4.39	14.69***	.50	. 26	47.43*** (12, 573)	
Exercise (calories/week)	.01	0.02	0.37				1.38
Exercise-induced mood	-.23	0.03	-6.03***				1.62
Exercise self-efficacy	-.07	0.01	-2.09*				1.42
Social support	-.42	0.06	-13.26***				1.17
Step 3 Constant		12.46	8.15***	.51	.01	45.25*** (13, 572)	
Mood × social support	.98	0.00	3.17**				

Note. VIF = Variance inflation factor.

$^{*}p < .05$. $^{**}p < .01$. $^{***}p < .001$.

4.5. Discussion

The main findings from the study demonstrated that social support is the strongest criterion predictor of depressive symptoms, and that exercise self-efficacy and exercise-induced mood also accounted for moderate independent variance within the model. In contrast, exercise behaviour (calories per week) does not provide any additional value to the prediction of depressive symptoms in community-dwelling adults aged 65 years or older.

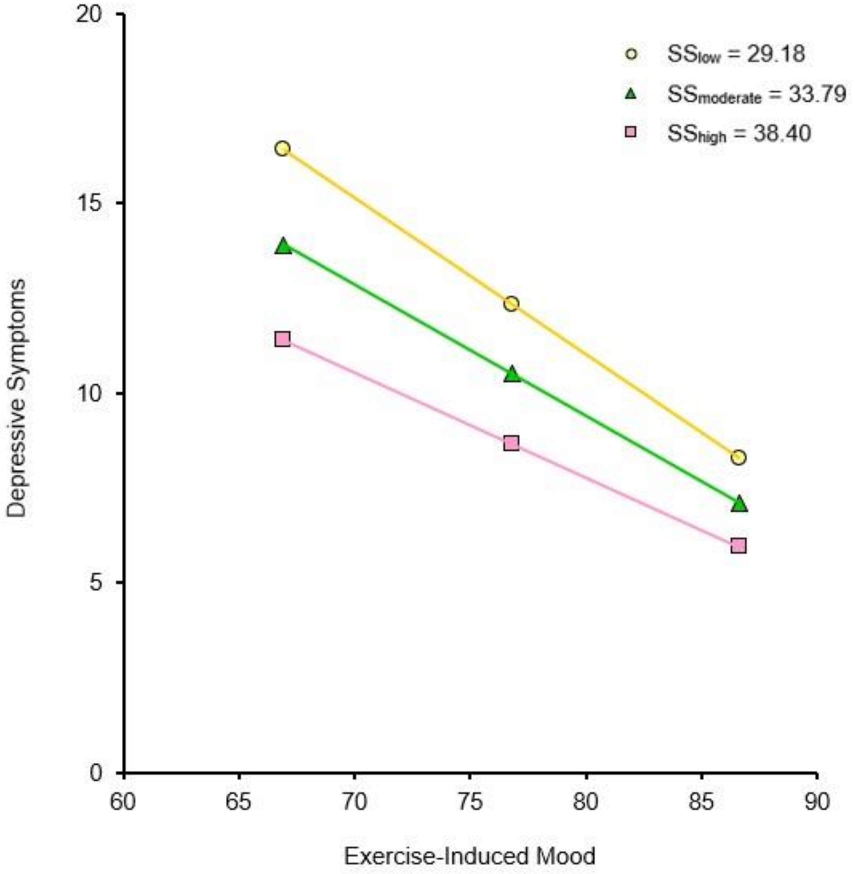

Figure 4.1. Simple slopes of the relationship between depressive symptoms and exercise-induced mood for low (*M* – 1*SD*), moderate (*M*), and high (*M* + 1*SD*) levels of social support in community-dwelling older adults aged 65-96 years (*n* = 586).

4.5.1. Theoretical implications of the current findings

Exercise is known to enhance mood, leading to more positive mood states and a reduction in depression (Pickett et al., 2012; Rhyner & Watts, 2016; White et al., 2009). The current study supports this evidence, indicating that exercise-induced mood can predict lower depressive symptoms in older adults with moderate accuracy. Current theoretical substantiation for this phenomenon is that exercise participation provides a distraction from stress and depression by inducing a positive mood effect (Festinger & Maccoby, 1964). Since affective states are usually short-lived, it is likely that exercise-induced mood reflects acute changes in depressive symptoms. This theory is predicated on the assumption that exercise only promotes positive mood states. If this model holds true, an increased emphasis on the positive experiences of exercise is more likely to achieve the desired effect of reducing depressive symptoms. As with most interventions, however, there are also a proportion of non-respondents to the treatment effect. For those who do not respond to physical exercise (i.e., those who experience negative mood states during exercise such as negative arousal and/or tiredness), emphasis should be placed on other activities that cause a distraction from negative dispositions instead.

The present findings also identify self-efficacy to be an independent predictor of depressive symptoms, albeit at a smaller margin than previously estimated (Annesi, 2012; Byrne & Horgan, 2018; Craft, 2005; Ryan, 2008). We rationalise this to be a consequence of the current regression model because it was able to control for the other predictors and potential confounding variables, estimating an effect size closer to the true effect. Despite a weaker association than exercise-induced mood and social support, these findings indicate that self-efficacy beliefs deriving from regular exercise can predict changes in depressive symptomology. It is therefore conceivable that encouraging older adults to engage in more challenging types of exercise may build the confidence in their ability to accomplish everyday tasks and cope with depression.

In agreement with previous research (Gariépy et al., 2016; McHugh & Lawlor, 2012), these data identify social support to be the strongest predictor of depressive symptoms, and to further interact with mood in strengthening this regression model. Since exercise can be used to maintain personal relationships and increase feelings of social connectedness (Bengtson et al., 2009; Lindsay-Smith et al., 2018), it is likely that group-based exercise can effectively increase the ability to cope with stress and depression (Cornwell & Waite, 2009; Glass et al., 2006). Therefore, interventions that focus on building social support through exercise may be implemented in older at-risk cohorts to strengthen resilience against depressive symptoms.

Lastly, an interaction effect was observed between exercise-induced mood and social support on depressive symptoms, reflecting a monotonic interaction. This indicates that when social support is low, positive mood states from exercise have a stronger association with depressive symptoms, and vice versa. Thus, this interaction can be interpreted in one of two ways: (1) those with lower social support respond better to positive mood states, or (2) those with more negative mood states respond better to social support. Although this interaction was modest, social support together with the mood-enhancing benefits of exercise are associated with less depressive symptomology than participating in rudimentary exercise alone. This highlights the importance of a multifaceted approach when trying to predict, and subsequently treat, depression in older populations.

Exercise behaviour (measured as calories per week) was tested as a predictor of depressive symptoms in the current analysis. Despite strong evidence of the antidepressive effects of exercise (Annesi, 2012; McHugh & Lawlor; 2012; Rhyner & Watts, 2016), exercise behaviour did not predict any additional variance in depressive symptoms. Latent growth modeling has demonstrated that exercise behaviour has direct and indirect pathways through mood, self-efficacy, and social support (McAuley et al., 2003). It is speculated that the indirect influences of these three psychosocial factors were able to account for all the variation in depressive symptoms. Thus, the physical characteristics of exercise, such as calorie expenditure and time spent in activities, do not appear to be important if exercise-induced mood is positive, and exercise self-efficacy and social support are maintained.

Although numerous investigations have attempted to quantify the proportion of variance that specific factors contribute to depressive symptoms, this is the first study to use an adequately powered sample to reliably examine the combination of these factors. The model that has been generated in the present study accounts for the collective strength of social support, exercise-induced mood, exercise self-efficacy, and exercise behaviour. This opens avenues for exploration to further expand the understanding of the key exercise-based components responsible for changes in depressive symptomology. Moreover, this provides insight into the multifaceted interactions between seemingly independent factors associated with depression and advances the foundations of previously established geriatric research.

4.5.2. Practical implications

Participants in the current study reported similar levels of caloric expenditure in moderate-to-high exercise (Stewart et al., 2001; Giles & Marshall; 2009), exercise self-efficacy (Resnick et al., 2004; Resnick & Jenkins, 2000), and social support (Randall et al., 2010) compared to previous studies. On the contrary, participants reported lower depressive symptoms (Gomez & McLaren, 2015; Ros et al., 2011) and more positive mood states (Huelsman et al., 1998; Huelsman et al., 2003), reflecting a tendency to report fewer negative dispositions. Nevertheless, our findings have important real-world implications for community-dwelling older adults, both as an approach to identify those susceptible to depression and/or as a precautionary intervention to manage depressive symptoms.

Depression is more difficult to treat in later life because it is often masked by other comorbid medical and psychiatric morbidities. This may include, for instance, depressed moods being confused with anxiety and other psychiatric illnesses, somatic symptoms being confused with medical illnesses, and reduction in activities and cognitive impairments being confused with aging (Gottfries, 1998; Patel, 2001). According to the current findings, deficits in mood, self-efficacy, and social support are useful indicators for identifying those who are susceptible to depressive symptoms in older age. Thus, clinicians and researchers may be able to use these factors to identify those most at risk of depression, particularly those with comorbid psychiatric disorders or those with lower rates of treatment-seeking behaviours (Manetti et al., 2014).

Exercise programs are a cost-effective alternative to traditional cognitive-behavioural approaches used to treat depression and have additional benefits to antidepressant medications (Mura et al., 2014). Our findings highlight the possible benefits of exercise as a behavioural intervention to target those most susceptible to depressive symptoms. Exercise can also be modified to meet the physical needs, abilities, and personal interests of aged populations, allowing exercise programs to be personalised for the specific individuals or groups. By taking advantage of different exercise types and modalities, older adults may be able to discover specific ways to promote positive mood states, build self-efficacy beliefs, and enlist social support, therefore reducing their susceptibility to depressive symptoms.

The implementation of exercise-based intervention policies and programs have merit to facilitate resilience to depressive symptoms during older adulthood. In particular, healthcare professionals can identify older adults at risk of negative mood states and depression, then implement group programs that build self-efficacy and social support through regular exercise habits. Self-efficacy training has been incorporated into exercise intervention programs to treat depressive symptoms in older adults (Resnick et al., 2008).

Moreover, exercise programs in a community and/or group setting can provide a cost-effective form of social engagement, promoting positive affective states and further enhancing self-efficacy beliefs (McAuley et al., 2000).

4.5.3. Limitations and future directions

The current study has several limitations worthy of mention. Questionnaires in cross-sectional designs share common-method variance. For the current study, self-selection bias was observed whereby females and those with a higher level of education tended to be more likely to participate in the research and complete electronic questionnaire packages. To minimise potential bias, we used both paper and electronic questionnaires to target specific subgroups, including men's organisations, low-income senior citizen centres, multicultural centres, and other at-risk groups.

During independent t-tests and χ^2 tests, differences between paper and electronic questionnaire formats emerged for age, education, relationship status, and employment status. No significant patterns were apparent for relationship or employment status, however younger age and higher level of education were evident. Since differences in these two demographic variables were expected (Ebert et al., 2018), we perceived this as being low risk of bias and subsequently collapsed the data into a single dataset.

It is important to note that the SPS-10, with scores ranging from 10 to 40, was used in the current study to assess participants' social support. The histogram (see *Figure E1* in *Appendix E*) reflected a significantly high proportion of scores falling in the upper limit of the distribution, indicating the presence of a ceiling effect. This reduced the variability in the gathered data for social support, which may falsely indicate that the factor had a smaller effect (i.e., Type II error). This is important to note when interpreting the results, as this may have underestimated the relationship between social support and other variables (Cramer & Howitt, 2004).

Although causal links have been theorised in the current study, it is important to note that this is an extension of correlational analysis, and therefore, caution should be taken when assuming any causal relationship. Instead, these findings can be used to guide the existing theories and provide a foundation for future experimental research. It is possible, for example, that (1) regular exercise induces a positive mood, which then leads to more opportunities for older adults to socialise and build support, (2) those with high social support are more likely to engage in exercise and regulate their negative mood and feelings of depression, or (3) depression levels dictate the engagement in, or avoidance of, regular exercise and social interaction during older adulthood. Randomised controlled trials and longitudinal designs in which depression and moderator/mediator variables are assessed prior to commencing an exercise-based intervention program, then retested over one or more follow-up periods, would assist in identifying causal relationships in the regression model.

4.5.4. Conclusions

Social support presents the strongest predictor of depressive symptomology, although exercise-induced mood and exercise self-efficacy have additional merit. These findings have significant implications for public health and can be used to guide exercise prescription in community-dwelling older adults. In particular, healthcare professionals may target older adults most at risk of depression and implement exercise programs that are likely to improve mood, enhance self-efficacy, and build social support. Further investigation, however, is required to demonstrate a treatment effect.

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CHAPTER V

Comparative Effectiveness of Three Exercise Types to Treat Clinical Depression in Older Adults: A Systematic Review and Network Meta-Analysis of Randomised Controlled Trials

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Supplementary Material: See *Appendix F* and *Appendix G*

Preface

Evidence from Study 2 (Chapter IV) demonstrates the influence of exercise-related factors (mood, self-efficacy, and social support) as key mechanisms for the antidepressive effects of physical exercise, and therefore, the next step is to ascertain the extent to which structured exercise can positively impact geriatric depression. To achieve this aim, many researchers have performed RCTs to investigate the antidepressive effects of exercise in samples of older adults. Since systematically reviewing existing research is an imperative step in the evaluation of scientific research (Glass, 1978), it is rational to collectively interrogate this evidence through quantitative analysis.

Meta-analysis is a systematic methodology used for quantitatively combining the results of independent studies on a standardised scale of measurement, offering many important advantages (Fagard, Staessen, & Thijs, 1996; Greenland & O'Rourke, 2008). First, meta-analysis can identify the nature and magnitude of modifying variables between exercise and depressive symptoms, which are normally difficult to identify when inspecting studies independently. Second, rather than examining studies individually, studies are pooled together and categorised so that more precise conclusions can be made about the relationship and the findings can be generalised to wider populations. Finally, heterogeneity, research gaps, and study limitations can be taken into account so that findings can be more comprehensively understood, methodologies can be improved, and new theories can be developed and tested.

Since an underlying assumption of meta-analysis is that the comparison group estimates are derived from pooling studies with homogenous between-study effect modifiers (Jansen & Naci, 2013), it is likely that this heterogeneity is due to different types of exercise programs having different treatment effects. Indeed, evidence from multi-arm RCTs (Bonura & Tenenbaum, 2014; Ettinger et al., 1997; Oken et al., 2006; Penninx et al., 2002; Prakhinkit, Suppapitiporn, Tanaka, & Suksom, 2014) have demonstrated that older adults respond distinctively to different volumes of aerobic, resistance, and/or mind-body exercise.

Given that there are currently insufficient multi-arm RCTs to confidently compared the efficacy of aerobic, resistance and/or mind-body exercise interventions using direct comparisons, it is practical to indirectly compare these exercise interventions using meta-analytic procedures. The existing meta-analyses have used subgroup analysis to test indirect pairwise comparisons of one parameter across a pool of studies, which may have systematically overestimated the effectiveness of the effect size estimates (Bucher, Guyatt, Griffith, & Walter, 1997). Network meta-analysis, however, allows several related parameters to be estimated in the one model, going beyond simple pairwise comparisons (Salanti, Higgins, Ades, & Ioannidis, 2008). In the context of the following network meta-analyses, exercise conditions (i.e., aerobic, resistance, mind-body) and control conditions (i.e., wait-list, usual care, attention-control) are separated to account for the between-study variation of these effect modifiers.

By accounting for the modifying effects of exercise type, we can accurately ascertain the true treatment effect of exercise-based interventions on depressive symptoms in older adults. Thus, the purpose of the following study was to perform a systematic review and network meta-analysis of RCTs to establish and rank the comparative effectiveness of three exercise types (resistance, aerobic, and mind-body exercise) for the treatment of depressive symptoms in clinically depressed older adults.

5.1. Abstract

5.1.1. Background

Few studies have directly compared the effects of different exercise therapies on clinical depression in older adults. Thus, we conducted a systematic review and network meta-analysis of current evidence from randomised controlled trials (RCTs) to compare the effectiveness of three major exercise types (aerobic, resistance, and mind-body exercise) in clinically depressed older adults.

5.1.2. Methods

We followed PRISMA-NMA guidelines and searched databases for eligible RCTs (inception – September 12th, 2019). RCTs were eligible if they included clinically depressed adults aged >65 years, implemented one or more exercise therapy arms using aerobic, resistance, or mind-body exercise, and assessed depressive symptoms at baseline and follow-up using a validated clinical questionnaire.

5.1.3. Results

A network meta-analysis was performed on 15 eligible RCTs comprising 596 participants (321 treatment and 275 controls), including aerobic (n = 6), resistance (n = 5), and mind-body (n = 4) exercise trials. Compared with controls, mind-body exercise showed the largest improvement on depressive symptoms (g = -0.87 to -1.38), followed by aerobic exercise (g = -0.51 to -1.02), and resistance exercise (g = -0.41 to -0.92). Notably, there were no statistically significant differences between exercise types: aerobic versus resistance (g = -0.10, PrI = -2.23, 2.03), mind-body versus aerobic (g = -0.36, PrI = -2.69, 1.97), or mind-body versus resistance (g = -0.46, PrI = -2.75, 1.83).

5.1.4. Conclusions

These findings should be used to advise allied health professionals and stakeholders in clinical geriatrics that clinically depressed older adults can self-select their preferred exercise type in order to achieve therapeutic benefit on symptoms of depression. In coalition with high levels of compliance, these data provide encouraging evidence for the antidepressant effect of either aerobic, resistance, or mind-body exercise as an adjunct to prescribed therapy for clinical depression in older populations.

5.2. Introduction

Population studies consistently indicate that older adults aged 65 years and over have an elevated risk of acute and chronic depression than their younger counterparts, estimated to exceed 15-20% in some cohorts (Luppa et al., 2012; Seitz et al. 2010; Volkert, Schulz, Härter, Wlodarczyk, & Andreas, 2013). Clinical depression during older age is linked to higher rates of physical illness and disease (Sinnige et al., 2013), disability and cognitive impairment (Scuteri et al., 2011), and comorbid psychiatric disorders (Laborde et al., 2014). Therefore, it is unsurprising that an estimated 20-50% of depressed older adults have a poor prognosis or are prone to relapse (Comijs et al., 2015; Licht-Strunk et al., 2007). In light of the projections in ageing demographics and impending demand on healthcare systems, there is shared interest to optimise clinically meaningful, non-pharmacological adjunctive therapies that are allied to the medical treatment of age-related challenges to mental well-being.

Older adults are more reluctant to discuss their mental health and seek necessary treatment for clinical depression than their younger counterparts (Garrido et al., 2011; Wang et al., 2005). To compound this issue, there are unique obstacles to successful treatment, such as the notable phenomenon whereby a significant proportion (~30%) of older adults have problematic compliance with their antidepressant medication (Rossom et al., 2016; Stein-Shvachman et al., 2013), as well as non-compliance often leading to worsening of symptoms and other age-related comorbidities (Ho et al., 2016). Pharmacological and psychotherapeutic antidepressant treatments, either alone or in combination, are the *sine qua non* for standard medical treatment of clinical depression in older adults. However, this does not forego the requirement for a broad appreciation of the adjunctive non-pharmacological treatments for clinical depression in optimising mental health-span and supporting the treatment of clinical depression during older age.

There is broad cross-disciplinary acknowledgement across medical and allied health professions that physical exercise has the potential for clinically meaningful antidepressant effects. We can generalise exercise into three major exercise types: aerobic, resistance, and mind-body exercise (American Psychiatric Association, 2010; National Health, Lung, and Blood Institute 2006; U.S. Department of Health and Human Services, 2018). Patrons of accumulated research knowledge declare that routine engagement in physical activity and/or exercise has the potential to impact symptoms of clinical depression (American College of Sports Medicine, 2017; American Psychiatric Association, 2010; World Health Organization, 2010). It may, therefore, seem surprising that there has been little attempt to compare the effectiveness of different exercise modes to gain a deeper understanding of exercise as a *bona fide* adjunctive therapy. Indeed, ongoing public health branding strategies, such as ‘Exercise is Medicine’, are promulgated to connect a broad message towards the pleiotropic benefits of physical activity to improve characteristics such as mobility, cardio-respiratory fitness, muscular strength, and body-mindfulness. However, there are profound physiological, mechanical, and metabolic differences between the three broad exercise modes (aerobic, resistance, and mind-body) and few data on the comparative effectiveness to treat symptoms of clinical depression in older adults.

Aerobic exercise is a distinct form of activity that involves the integration of large muscle groups, such as in the rhythmic propulsion of body mass during movements of different intensities (e.g., walking, jogging, or running) or activities of lower mechanical impact (e.g., swimming or cycling). Aerobic exercise is matched by increasing metabolic effort, which necessitates effort of breathing, heart rate, and blood flow to match the effort of intensity (American College of Sports Medicine, 2017; Nelson et al., 2007). In contrast, resistance exercise refers to a specialised method of muscular conditioning which normally requires a variety of equipment, such as free weights, weight machines, elastic bands, and/or body weight exercises (Faigenbaum et al., 2009). Resistance exercise is distinct from aerobic or mind-body exercise in that there is a focus on repeatedly overloading muscles during static, isometric, or dynamic contractions, which cause a closer and stronger connection between the musculature and nervous system. Remarkably, only one randomised controlled trial (RCT) has directly compared the effectiveness of aerobic versus resistance exercise in clinically depressed older adults (Penninx et al., 2002). A subsequent analysis of this 18-month Fitness, Arthritis and Seniors Trial (Ettinger et al., 1997) revealed that aerobic exercise induced a more favourable antidepressant effect than resistance exercise, highlighting that there may be distinguishable differences between aerobic and resistance exercise types (Penninx et al., 2002).

Mind-body exercise incorporates a range of low impact and deliberately slow movements in addition to breathing, meditation, and/or progressive relaxation. This exercise mode integrates low-intensity muscular activity, such as flexibility or balance training, with an internally directed focus that encourages a self-contemplative mental state (La Forge, 1997). Many forms of mind-body exercise are available for older populations (e.g., yoga, tai chi, qigong), yet a single RCT has directly compared the effectiveness of mind-body exercise with other exercise treatments. Prakhinkit et al. (2014) compared the effects of a traditional aerobic walking program with a Buddhism-based walking meditation program in a sample of 45 depressed elderly. The walking meditation program resulted in a significantly larger decrease in depression than aerobic walking alone, suggesting that exercise incorporating both mind and body components are most effective for elderly with mild and moderate depressive symptoms (Prakhinkit et al., 2014).

Perhaps the foremost obstacle to exercise prescription for mental health during ageing is that there are few adequately controlled trials that compare different exercise types within the same investigation. To approach this important research problem, recent meta-analytical reviews have been published to indirectly compare the antidepressive effects of different exercise types by employing subgroup analysis of pooled literature (Bridle, Spanjers, Patel, Atherton, & Lamb, 2012; Heinzel, Lawrence, Kallies, Rapp, & Heissel, 2015; Schuch et al., 2016), resulting in some interesting findings. For instance, interventions using a combination of aerobic and resistance exercises appear to be most effective for the treatment of depressive symptoms in clinically depressed older adults (Bridle et al., 2012; Schuch et al., 2016). There is, however, some discordance in these efforts to compare exercise modalities, as Heinzel and colleagues (2015) concluded that mind-body exercise is most effective out of the three types of exercise.

There is coalition between the known reluctance of older adults to participate in formal exercise regimens, as well as confusion of specific knowledge amongst clinicians, that restricts clinical guidance on exercise prescription. Clarity on the comparative effectiveness of the antidepressive effects of different exercise modalities might inform clinician-patient discussion, as well as encourage patients to have more control over their selection of the best evidence-based therapeutic exercise that is allied to ongoing treatment for clinical depression. Meta-analysis, however, has an inherent lack of precision to accurately examine the comparative effectiveness of related exercise therapies, which is required to better understand the antidepressive effects of separate exercise types. Network meta-analysis offers a solution to this problem by statistically comparing treatment effects by simultaneously assessing both the direct and indirect evidence of independent treatments. This goes beyond simple pairwise comparisons and provides a more accurate calculation of true effect size estimates than would otherwise be achievable with meta-analysis using subgroups (Caldwell et al., 2005; Salanti et al., 2008).

Thus, the primary purpose of this review was to perform a systematic review and network meta-analysis of current evidence from RCTs to compare the effectiveness of three major exercise therapies (aerobic, resistance, or mind-body exercise) in clinically depressed older adults. We hypothesised that (1) aerobic, resistance, and mind-body exercise would have larger pooled effects on depressive symptoms than wait-list, usual care, and attention-control comparisons, and (2) mind-body exercise would have a larger pooled effect on depressive symptoms than either aerobic or resistance exercise. Secondary outcomes including adverse events, adherence, and attrition were used to evaluate compliance.

5.3. Methods

We prospectively registered the current review in the PROSPERO database (registration number: CRD42018094667). The network meta-analysis extension for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-NMA) guidelines (Hutton et al., 2015) and the Cochrane Intervention Review that Compares Multiple Interventions (Cochrane Methods, 2014) were used as a guide for this review. Specific geriatric guidelines for meta-analyses (Shenkin et al., 2017) were also consulted to identify inclusion/exclusion criteria, effect modifiers, and potential risks of bias.

5.3.1. Eligibility criteria

We included studies if (1) participants were diagnosed with clinical depression at baseline according to a structured diagnostic interview based on Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Statistical Classification of Diseases and Related Health Problems (ICD) criteria, or a clinical threshold on a questionnaire validated against a structured diagnostic interview, (2) an RCT protocol was used to assess the effectiveness of one or more exercise therapy arms, (3) depressive symptoms were assessed at baseline and follow-up using a questionnaire that had been psychometrically validated against DSM or ICD criteria, and (4) a minimum mean sample age of 65 years was included. We excluded studies if (1) participants were not clinically depressed at baseline, (2) the intervention condition used a multicomponent treatment with non-exercise components, (3) the intervention condition could not be exclusively categorised as one of three types of exercise (aerobic, resistance, or mind-body), (4) depressive symptoms were not assessed as an outcome, based on change scores between baseline and follow-up, or (5) the sample had a mean age below 65 years.

Clinical cut-off scores on questionnaires validated against a structured diagnostic interview based on DSM or ICD criteria were used to determine if participants were diagnosed with depression at baseline. These included scores of 10 or higher on the Beck Depression Inventory (BDI; Beck et al., 1988, 1996), 16 or higher on the Center for Epidemiological Studies Depression Scale (CESD; Lewinsohn et al., 1997; Radloff, 1977), six or higher on the Cornell Scale for Depression in Dementia (CSDD; Kørner et al., 2006), nine or higher on the Geriatric Depression Scale-30 (GDS-30; Kørner et al., 2006; Wancata et al., 2006), five or higher on the Geriatric Depression Scale-15 (GDS-15; Almeida & Almeida, 1999; Kørner et al., 2006; Wancata et al., 2006), and 12 or higher on the Hamilton Rating Scale for Depression (HRSD; Baghy et al., 2004).

5.3.2. Literature search

PubMed, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Health Source: Nursing/Academic Edition, PsycARTICLES, PsycINFO, and SPORTDiscus were searched from the date of their inception up to September 12th, 2019. Text mining procedures were used to identify key search terms related to population, intervention, and study design. Full search terms and an example of the search strategy can be found in *Appendix F*. References lists from included studies, systematic reviews, and meta-analyses (i.e., Blake et al., 2009; Bridle et al., 2012; Heinzel et al., 2015; Mura & Carta, 2013; Rhyner & Watts, 2016; Schuch et al., 2016; Sjösten & Kivelä, 2006) were screened for additional articles.

5.3.3. Data extraction and coding

Study characteristics and outcome statistics were extracted independently by two researchers (KJM, PA, and/or DH) using a data extraction form (see *Appendix F*) and discrepancies were resolved by consensus with a fourth researcher (CM). Authors of particular studies were contacted if a sufficiently detailed report of the data was not available. Type of control group was categorised as wait-list, usual control, or attention-control. Wait-list conditions were assigned to a waiting list and received the exercise intervention once the trial had concluded. Usual care conditions had no mention of a waiting list or any additional activities during the trial. Attention-control conditions (also known as attention placebo control or active control) included the engagement in a non-physical activity during the trial (e.g., social activities, educational programs, etc.).

Study characteristics were used to evaluate the plausibility of the transitivity assumption and evaluate the quality of included studies (see *Table 5.1*). Methodological characteristics were coded according to the intention-to-treat principle, use of a cluster design, and the depression measure(s) used. Participant characteristics were coded according to sample size, age (mean and standard deviation), percentage of females, depression diagnosis, and primary place of residence (community-dwelling or residential care). Relevant inclusion criteria (e.g., sedentary, dementia, etc.) were also used to judge the risk of bias from equity considerations (O'Neill et al., 2014).

Table 5.1

Participant, intervention, and methodological characteristics of studies included in the systematic review

Author (year)	Treatment M_{age} (SD), females (%)	Control M_{age} (SD), females (%)	Source of participants	Inclusion criteria	Depression diagnosis	Intention -to-treat	Cluster design	Treatment group	Control group	Length of intervention	Adherence (%)	Outcome measure(s)
Cheng (2012)	81.0 (7.7) 50	82.5 (7.1) 75	Residential	Dementia	≥ 6 GDS-15 score	N/R	Yes (9)	*n* = 12 Mind-body (Tai Chi), supervised, group, N/R, 3 times/week, 60 mins/session	*n* = 12 Attention-control (handcrafts)	12 weeks	N/R	GDS-15
Chou (2004)	72.6 (4.2) 50		Community	Sedentary	≥ 16 CESD score; DSM-IV MDD or dysthymia diagnosis	N/R	No	*n* = 7 Mind-body (Tai Chi), supervised, group, N/R, 3 times/week, 45 mins/session	*n* = 7 Wait-list	12 weeks	95	CESD-20
Favilla (1992)	73 (4.0) 57.1	73 (4.0) 86.4	Community	Sedentary	≥ 7 GDS-30 score	N/R	No	*n* = 21 Resistance (progressive weight training), supervised, group, high intensity (80% $1R_{max}$), 3 times/week, 60 mins/session	*n* = 22 Wait-list	6 weeks	95	GDS-30
	73 (4.0) 66.7							*n* = 21 Resistance (modified weight training), supervised, group, moderate intensity (50% $1R_{max}$), 3 times/week, 60 mins/session			95	
Haboush (2006)	69.4 (5.4) 67		Community	N/R	≥ 10 HRSD score	N/R	No	*n* = 10 Aerobic (ballroom dance), supervised, individual, N/R, 1 time/week, 45 mins/session	*n* = 12 Wait-list	8 weeks	96	GDS-30; HRSD*
Lok (2017)	65+ 42.5	65+ 47.5	Residential	N/R	≥ 10 BDI score	N/R	No	*n* = 40 Aerobic (walking and rhythmic exercises), supervised, group, N/R, 4 times/week, 70 mins/session	*n* = 40 Usual care	10 weeks	N/R	BDI

McNeil (1991)	72.5 (6.9) N/R		Community	N/R	12-24 BDI score	N/R	No	*n* = 10 Aerobic (walking), supervised, individual, N/R, 3 times/week, 20-40 mins/session	*n* = 10 Wait-list *n* = 10 Attention-control (social contact)	6 weeks	N/R	BDI
Patel (2004)	72.2 (N/R) 61.5	73.4 (N/R) 53.8	Residential	N/R	≥ 5 GDS-15 score	N/R	No	*n* = 13 Aerobic (walking), supervised, group, N/R, 3 times/week, 20 mins/session	*n* = 13 Usual care	4 weeks	N/R	GDS-15
Prakhinkit (2014)	74.8 (1.7) 100	81.0 (1.7) 100	Community	N/R	13-24 GDS-30 score	N/R	No	*n* = 13 Aerobic (walking), supervised, group, low intensity (20-50% HR_{max}), 3 times/week, 20-30 mins/session	*n* = 13 Usual care	12 weeks	80+	GDS-30
Shahidi (2011)	65.7 (4.2) 100	68.4 (6.3) 100	Community	N/R	≥ 10 GDS-30 score	N/R	No	*n* = 20 Aerobic (jogging), supervised, group, N/R, N/R, 30 mins/session	*n* = 20 N/R	10 sessions	N/R	GDS-30
Sims (2006)	75.3 (5.8) 85.7	74.3 (5.7) 50	Community	N/R	≥ 11 GDS-30 score	Yes	No	*n* = 13 Resistance (progressive resistance training), supervised, individual, high intensity (80% $1R_{max}$), 3 times/week, 40 mins/session	*n* = 17 Attention-control (brief advice)	10 weeks	N/R	CESD-20*; GDS-30
Sims (2009)	68.0 (14.8) 39.1	66.3 (16.0) 40.9	Community	History of stroke	≥ 5 PHQ-D score; psychiatrist depression confirmation	Yes	No	*n* = 23 Resistance (progressive resistance training), supervised, group, high intensity (80% $1R_{max}$), 2 times/week, N/R	*n* = 22 Wait-list	10 weeks	75	CESD-20
Singh (1997)	70 (1.5) 70.6	72 (2.0) 53.3	Community	Low activity (exercise no more than twice a week)	≥ 13 BDI score; DSM-IV MDD, minor depression, or dysthymia diagnosis	N/R	No	*n* = 17 Resistance (progressive resistance training), supervised, group, high intensity (80% $1R_{max}$), 3 times/week, 50 mins/session	*n* = 15 Attention-control (health education)	10 weeks	93	BDI*; GDS-30; HRSD

Singh (2005)	70 (7) 60	69 (7) 50	Community	Low activity (exercise no more than twice a week)	≥ 14 GDS-30 score; DSM-IV MDD, minor depression, or dysthymia diagnosis	N/R	No	*n* = 17 Resistance (progressive resistance training), supervised, group, low intensity (20% $1R_{max}$), 3 times/week, 65 mins/session	*n* = 19 Usual care	8 weeks	100	GDS-30; HRSD*
	69 (5) 55							*n* = 18 Resistance (progressive resistance training), supervised, group, high intensity (15-18/20 RPE; 80% $1R_{max}$), 3 times/week, 65 mins/session			100	
Tsang (2006)	82.1 (7.2) 79.2	82.7 (6.8) 82.4	Residential	N/R	≥ 9 GDS-15 score	N/R	No	*n* = 48 Mind-body (Baduanjin qigong), supervised, group, N/R, 3 times/week, 30-45 mins/session	*n* = 34 Attention-control (newspaper reading)	16 weeks	N/R	GDS-15
Tsang (2013)	79.7 (6.6) 76.2	80.7 (4.4) 58.8	Residential	Chronic medical illness	≥ 8 GDS-15 score; DSM-IV MDD diagnosis	Yes	No	*n* = 21 Mind-body (eight-section brocades qigong), supervised, group, N/R, 3 times/week, 45 mins/session	*n* = 17 Attention-control (newspaper reading)	12 weeks	N/R	GDS-15; HRSD*
Williams (2008)	87.9 (6.0) 88.9		Residential	Low activity (walked unaided for 30 minutes or more); Dementia	≥ 7 CSDD score	Yes	No	*n* = 17 Aerobic (walking), supervised, individual, N/R, 5 times/week, 30 mins/session	*n* = 12 Attention-control (social conversation)	16 weeks	N/R	CSDD

Note. N/R = not reported; *n* = Total participants included in intention-to-treat or post-treatment data analysis; MDD = Major depressive disorder; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders (4th Edition); PHQ-D = Patient Health Questionnaire (depression subscale); HR_{max} = Heart rate maximum; $1R_{max}$ = One-repetition maximum; RPE = Rating of perceived exertion; BDI = Beck Depression Inventory; CESD = Center for Epidemiological Studies Depression Scale; CSDD = Cornell Scale for Depression in Dementia; GDS = Geriatric Depression Scale; HRSD = Hamilton Rating Scale for Depression.

*Outcome measure used in network meta-analysis.

Type of exercise was categorised as aerobic, resistance, or mind-body exercise therapy. Length of the program was coded as total number of weeks. Intensity was evaluated based on ratings of perceived exertion (Borg, 1982), heart rate maximum (HR_{max}; low = <50%, moderate = 50-70%, high = >70%), maximal oxygen uptake (VO_{2max}; low = <40%, moderate = 40-60%, high = >60%) or one-repetition maximum ($1R_{max}$; low = <50%, moderate = 50-74%, high = >74%; Sigal et al., 2004). Frequency was coded as total sessions per week. Duration was coded as the average number of minutes per session. Format of program was dichotomously coded as group or individual training. Format of supervision was dichotomously coded as supervised or unsupervised training. Agreement between the three researchers was 91.3%.

5.3.4. Risk of bias and quality assessment

We assessed the risk of bias in the included studies using the Cochrane Collaboration’s Tool for Assessing Risk of Bias (Higgins et al., 2011). Judgements for ‘other sources of bias’ were based on small sample size ($n < 15$), low adherence (less than 80%), cluster randomisation, and inequity in the selection of the participants. Appraisal was performed by two researchers (KJM, PA, and/or DH), and consensus was reached with a fourth researcher (CM).

5.3.5. Summary of outcomes

Primary outcome statistics including means (*M*), standard deviations (*SD*), and sample sizes (*n*) were used to calculate the mean changes in depressive symptoms. If a study reported more than one post-treatment depression score (e.g., midway, follow-up), only the assessment time-point immediately following the conclusion of the intervention phase was used. If a study reported depression scores on multiple outcome measures, only the most clinically relevant depression measure was used (Costa et al., 2016; Smarr & Keefer, 2011). Pairwise relative treatment effects for depressive symptoms were estimated using Hedges' *g* (Hedges, 1981) and the 95% confidence interval (95% *CI*). Hedges' *g* coefficients were interpreted according to Cohen (1988) conversions, whereby effects were considered small (0.2), medium (0.5), and large (0.8). Secondary outcome data were also extracted for adverse events, adherence, and attrition. Adverse events were qualitatively reported according to the descriptive information available in the transcript. Attrition and adherence were reported as the percentage of total attendance/attrition during the exercise intervention.

5.3.6. Data synthesis

An underlying assumption of network meta-analysis is that estimates are derived from a pool of studies with homogenous between-study effect modifiers (Jansen & Naci, 2013). If the distribution of an effect modifier is heterogeneous across studies, the assumption of transitivity may be violated. For instance, if no distinction is made between different control conditions, exercise conditions weighted heavily on a single control comparison may artificially inflate or deflate effect size estimates (Pagoto et al., 2013). Within the context of the current network meta-analysis, exercise conditions (i.e., aerobic, resistance, mind-body) and control conditions (i.e., wait-list, usual care, attention-control) were separated into separate network estimates to account for the between-study variation of these effect modifiers.

Data were analysed and figures were generated using STATA/SE 15.1 (StataCorp, 2017). We evaluated publication bias and small-study effects using a comparison-adjusted funnel plot. The assumption of transitivity was assessed with exploratory meta-regression sensitivity analyses comparing the distribution of participant and exercise modifiers across treatment comparisons. Participant, intervention, and methodological characteristics were assessed, which have been identified as potential risks to transitivity in geriatric meta-analyses (Netz, Wu, Becker, & Tenenbaum, 2005; Rhyner & Watts, 2016; Schuch et al., 2016).

A multivariate random-effects meta-analysis was performed using the ‘mvmeta’ command (White, 2009). A random-effects model assumes variance both within and between studies, explaining the heterogeneity of treatment effects (Borenstein et al., 2010). A common heterogeneity parameter was assumed across comparisons. Heterogeneity was evaluated using tau-squared (τ^2), which estimates the deviation in effect sizes across the population of studies (Borenstein et al., 2009). The 95% prediction interval (*PrI*) was used to estimate the true dispersion of effect within two standard deviations of the mean effect size (Borenstein et al., 2009). The certainty of evidence contributing to network estimates was assessed with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Salanti et al., 2014). The significance level was $p < .05$ for all analyses.

5.4. Results

5.4.1. Study selection

The literature search yielded a total of 2,309 eligible records after duplicate studies were removed ($n = 1,395$). Titles and abstracts were screened by two independent researchers (KJM and DCGB) with an agreement of 91.9%. We assessed 356 full-text articles for eligibility, of which 340 were excluded from the systematic review (see *Figure 5.1*). Notably, one study (Shahidi et al., 2011) fulfilled all criteria but was excluded from the quantitative analysis because the control condition was not clearly defined, and the authors were unobtainable. The remaining 15 studies formed the data used in the final analyses. Full-text screening was performed independently by two researchers (KJM and PA) with an agreement of 81.8% and discrepancies were resolved by consensus from a third researcher (CM).

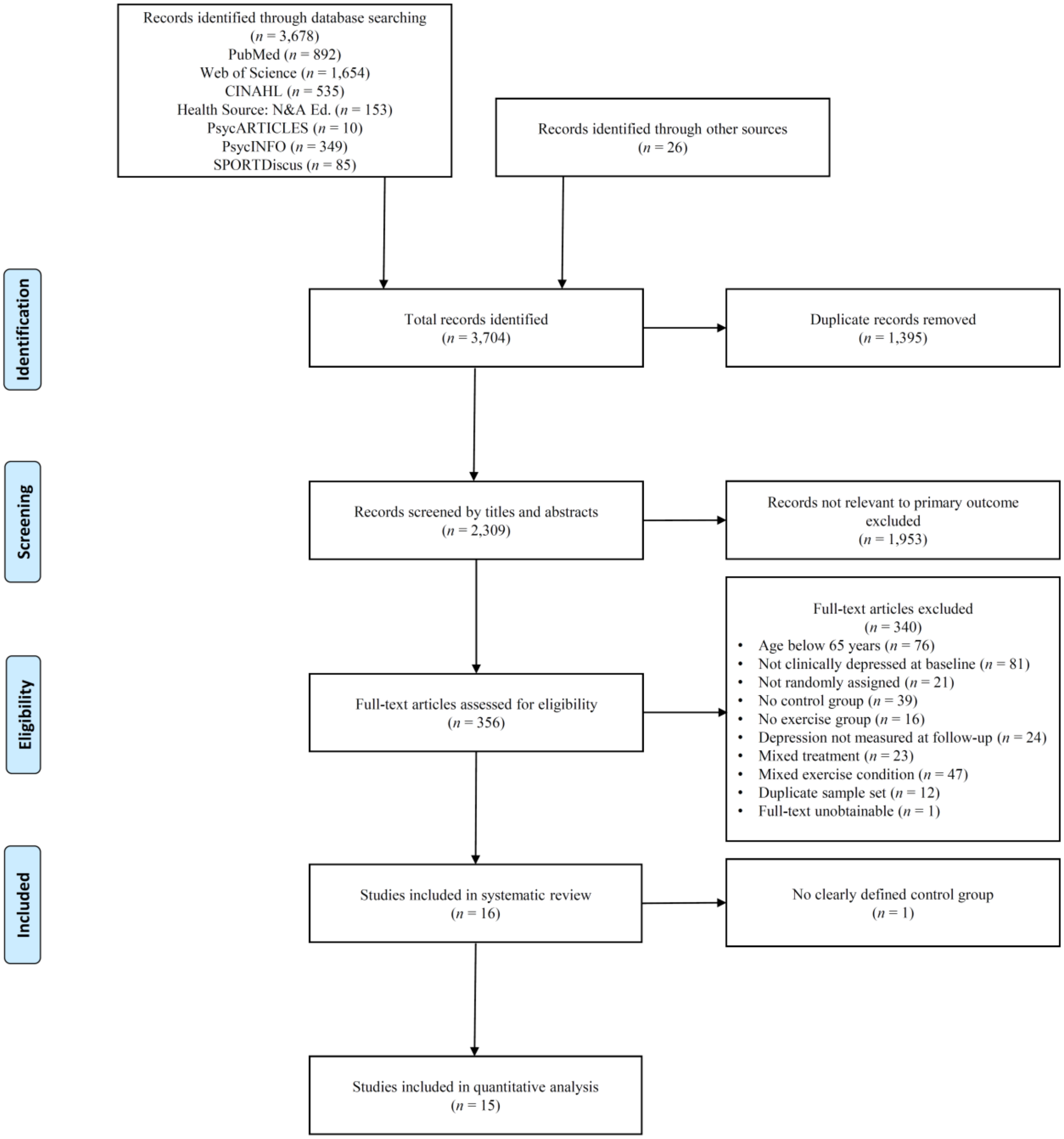

Figure 5.1. Flowchart of screening process.

5.4.2. Characteristics of the studies

Data from a total of 596 participants (321 treatment and 275 controls) across 15 studies (aerobic = 6, resistance = 5, mind-body = 4) were included in the network meta-analysis (see *Figure 5.2* for a network plot of pairwise comparisons across all studies). In general, 10 samples included participants who were young-old (65-75 years) and five included participants who were old-old (>75 years), with one sample uncategorised (>65 years). Participants were identified as either community-dwelling (*n* = 9) or living in residential care (*n* = 6). Samples were typically healthy, except for one sample including participants with a history of stroke (Sims et al., 2009) and another including participants with chronic medical illnesses (Tsang et al., 2013). An additional two RCTs included participants with dementia (Cheng et al., 2012; Williams & Tappen, 2008). Only five trials included participants with sedentary or low activity lifestyles (Chou et al., 2004; Favilla, 1992; Singh et al., 2005). Antidepressant medication was not adequately reported and/or controlled in most studies. Five studies excluded participants if they were currently using antidepressants (Sims et al., 2006; Singh et al., 1997, 2005), or unless the medication was stabilised for at least 2-3 months (Favilla, 1992; Haboush et al., 2006). Only three studies reported the use of antidepressants, comprising of 11% (Favilla, 1992), 17% (Cheng et al., 2012), and 36% (Williams & Tappen, 2008) of the total samples.

Five out of six aerobic RCTs included walking interventions (Lok et al., 2017; McNeil et al., 1991; Patel, 2004; Prakhinkit et al., 2014; Williams & Tappen, 2008), while the sixth trial included ballroom dancing (Haboush et al., 2006). All five resistance RCTs used progressive weight training (Favilla, 1992; Sims et al., 2006, 2009; Singh et al., 1997, 2005). Two mind-body RCTs were tai chi interventions (Cheng et al., 2012; Chou et al., 2004), whereas the other two were qigong interventions (Tsang et al., 2006; Tsang et al., 2013).

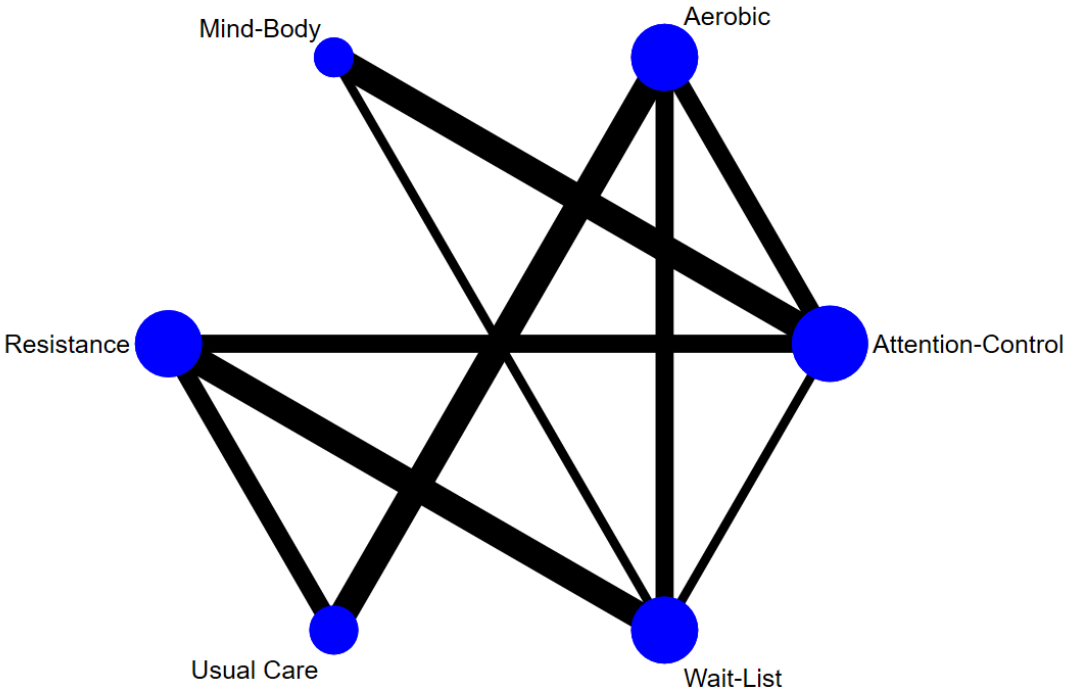

Figure 5.2. Network plot of comparisons for all studies included in the network meta-analysis. Line width is proportional to the number of pairwise effect size estimates and node size is proportional to the number of participants.

The average length (weeks) for exercise programs was longer for mind-body (*M* = 13.00, *SD* = 2.00), than aerobic (*M* = 9.33, *SD* = 4.32) or resistance (*M* = 8.29, *SD* = 1.80). The average minutes per week (calculated as frequency multiplied by duration) varied between exercise therapies, with the most time spent in resistance (*M* = 170.00, *SD* = 29.50), followed by mind-body (*M* = 140.63, *SD* = 28.31) and aerobic (*M* = 116.67, *SD* = 87.84).

5.4.3. Risk of bias and quality assessment

Risk of bias within each study was generally low, with only three studies reporting substantial risk of bias across three of the seven criteria (Cheng et al., 2012; Chou et al., 2004; Lok et al., 2017). Full details on risk of bias for each study can be found in *Appendix G* (see *Figure G1*). Notably, blinding of participants and personnel was not possible in exercise-based interventions, which resulted in a high risk of performance bias for all studies. The remaining six risk of bias criteria were generally low-to-moderate across all studies (see *Figure 5.3*). Blinding of outcome assessment (detection bias) was not performed in three RCTs (Cheng et al., 2012; Chou et al., 2004; Lok et al., 2017), and incomplete outcome data (attrition bias) was identified in four trials (Favilla, 1992; Prakhinkit et al., 2014; Singh et al., 2005; Tsang et al., 2006). High ‘other sources of bias’ was generally due to small sample sizes (Cheng et al., 2012; Chou et al., 200; McNeil et al., 1991; Patel, 2004; Sims et al., 2006), with one study reporting low adherence (Sims et al., 2009).

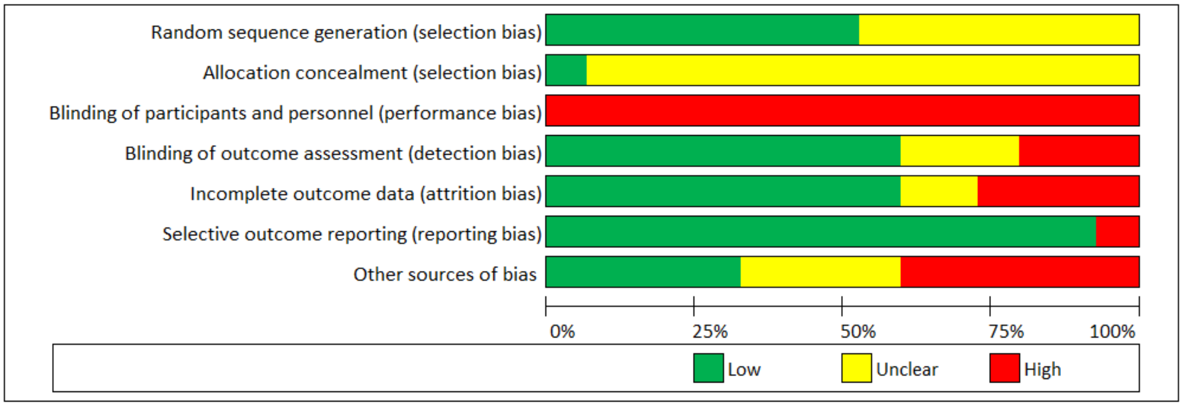

Figure 5.3. Risk of bias chart of studies included in the quantitative analysis.

5.4.4. Secondary outcomes

Secondary outcomes included adverse events, adherence, and attrition. No adverse events were reported in any of the included studies. Aerobic exercise had an adherence rate of 96%, which was based on statistics from a single study (Haboush et al., 2006). Six studies reported adherence rates for resistance exercise (*M* = 93.0%, *SD* = 9.27, 95% *CI* = 83.27, 102.73). Mind-body exercise had an adherence rate of 95%, which was based on statistics from a single study (Chou et al., 2004). Attrition was higher for mind-body exercise (11.8%), followed by resistance exercise (10.5%), and aerobic exercise (7.6%).

5.4.5. Assessment of inconsistency

Inconsistency network models were used to test the global consistency of direct and indirect effects for pairwise and multi-arm comparisons simultaneously. The assumption of consistency was satisfied for the overall level of each treatment ($p > .05$). Inconsistency tests between direct and indirect estimates in the resistance versus attention-control comparison revealed that direct evidence was significantly different to indirect estimates (difference = -2.01; $p < .05$). The remaining tests of inconsistency between direct and indirect estimates were non-significant ($p > .05$), indicating that indirect estimates were not different to direct evidence.

Loop-specific heterogeneity was explored with an inconsistency plot. Inconsistency factors (*IF*) did not indicate high inconsistency (*IF* = 0.25 to 2.05), however loop-specific heterogeneity was detected in the AC-RES-WL loop ($\tau^2 = 1.16$). No other loops reported heterogeneity or departed from the minimum lower-bound *CI*, and therefore, assumption of consistency was upheld. Full results from the inconsistency tests and plots can be found in the *Appendix G* (see *Table G1* and *Figure G6*).

5.4.6. Publication bias and sensitivity analyses

Publication bias and small-study effects were evaluated using a comparison-adjusted funnel plot (see *Figure 5.4*). The funnel plot was roughly symmetrical for the depression network, indicating no publication bias from small-study effects. Transitivity was explored using meta-regression sensitivity analyses. No significant modifying effects were found for year of study, risk of bias, publication status, intention-to-treat analysis, cluster design, age, gender, source of participants, length of intervention, format of program, exercise intensity, frequency, duration, or adherence, indicating that the assumption of transitivity was upheld. All meta-regression analyses can be found in the *Appendix G* (see *Table G3*).

5.4.7. Results of the network meta-analysis

Data was pooled from the 15 studies and provided a total of 19 effect sizes. Network estimates were calculated to measure the relative effectiveness between pairs of comparisons within the network (see *Figure 5.5* for full results of network meta-analysis). In brief, a greater decrease in depressive symptoms was observed for all exercise conditions when compared to control conditions. Indirect comparisons between the three exercise conditions demonstrated the strongest effect sizes for mind-body exercise, followed by aerobic exercise, and resistance exercise. Notably, the confidence intervals indicated that there is a large proportion of overlapping variance across these three indirect comparisons.

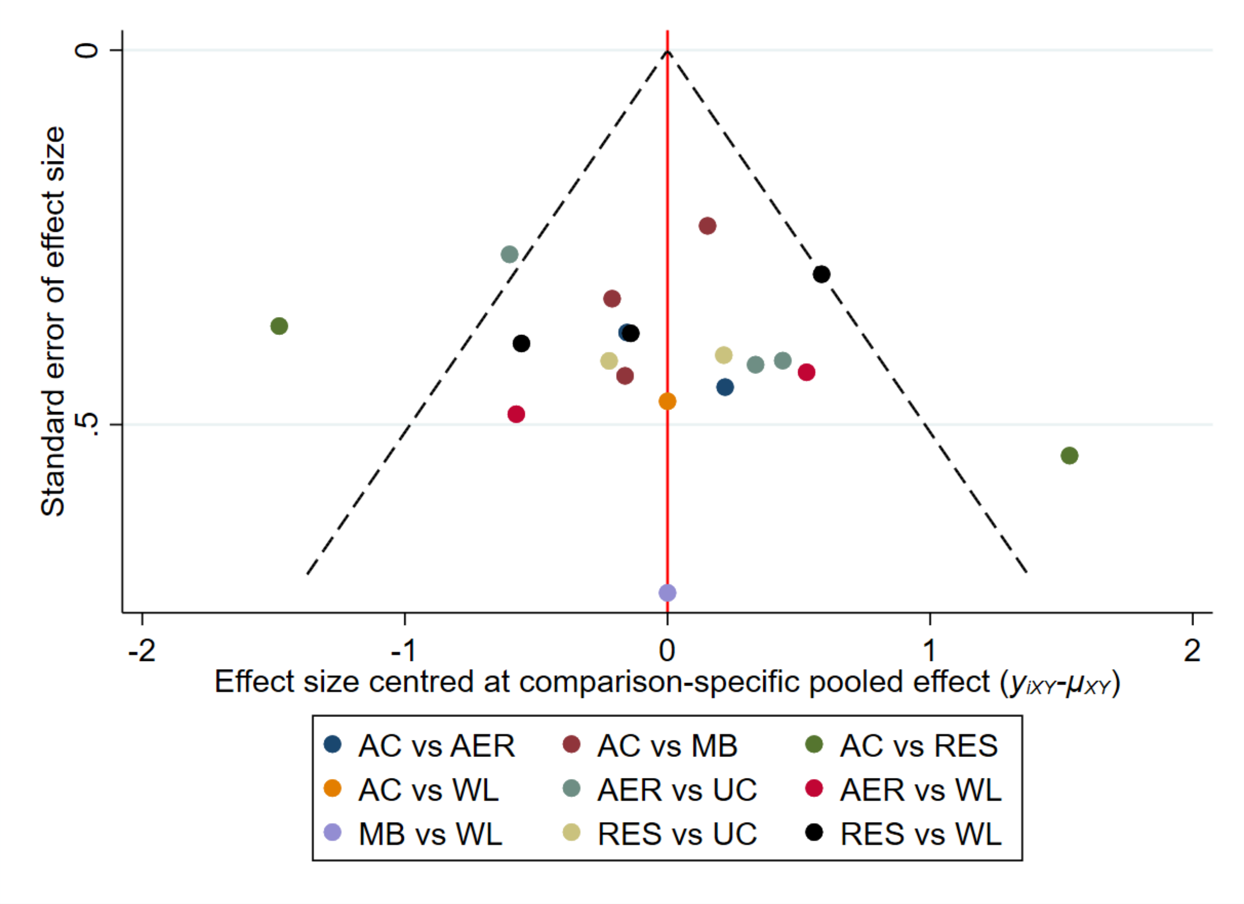

Figure 5.4. Comparison-adjusted funnel plot for the depressive symptoms network. The red line represents the null hypothesis that independent effect size estimates do not differ from the comparison-specific pooled estimates. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

5.4.8. GRADE assessment

Certainty of evidence was assessed with the GRADE approach (Salanti et al., 2014), which can be seen in *Table 5.2*. We found moderate-to-low certainty in the findings from the aerobic networks, which was downgraded due to imprecision from small sample sizes and a risk of detection bias. Findings from the resistance networks had low certainty due to imprecision from small sample sizes, risk of detection or attrition bias, and inconsistency in the network estimates. The mind-body networks were high-to-moderate certainty, with downgrading mainly due to imprecision from small samples sizes and a risk of attrition bias. Certainty in the indirect comparisons between the three exercise therapies was low or very low, which was downgraded because imprecision in the confidence intervals indicated that the true effect could potentially favour either condition.

5.5. Discussion

Despite a lack of significant differences between indirect comparisons, mind-body exercise showed the largest effect on depressive symptoms compared with control conditions (i.e., wait-list, usual care, attention-control), which was followed by aerobic and resistance exercise, respectively. Risk of bias was generally low for the included RCTs, however small sample sizes and imprecision in effect size estimates limited the confidence in the indirect comparisons between aerobic, resistance, and mind-body exercise interventions.

5.5.1. Theoretical implications for the current findings

The primary outcome of this network meta-analysis was depressive symptoms. In general, there was moderate confidence in the findings for aerobic and mind-body comparisons across all control conditions, while confidence in the resistance comparisons were downgraded to low certainty because of a high risk of bias and imprecision. Small samples sizes were primarily responsible for downgrading the certainty of the evidence. Furthermore, the dispersion in effect size estimates caused confidence intervals to become too wide to confidently conclude significant results, especially for the indirect comparisons between exercise interventions. Thus, it is conceivable that the certainty in evidence would be greatly improved if more RCTs on clinically depressed older adults (65 years or older) were available.

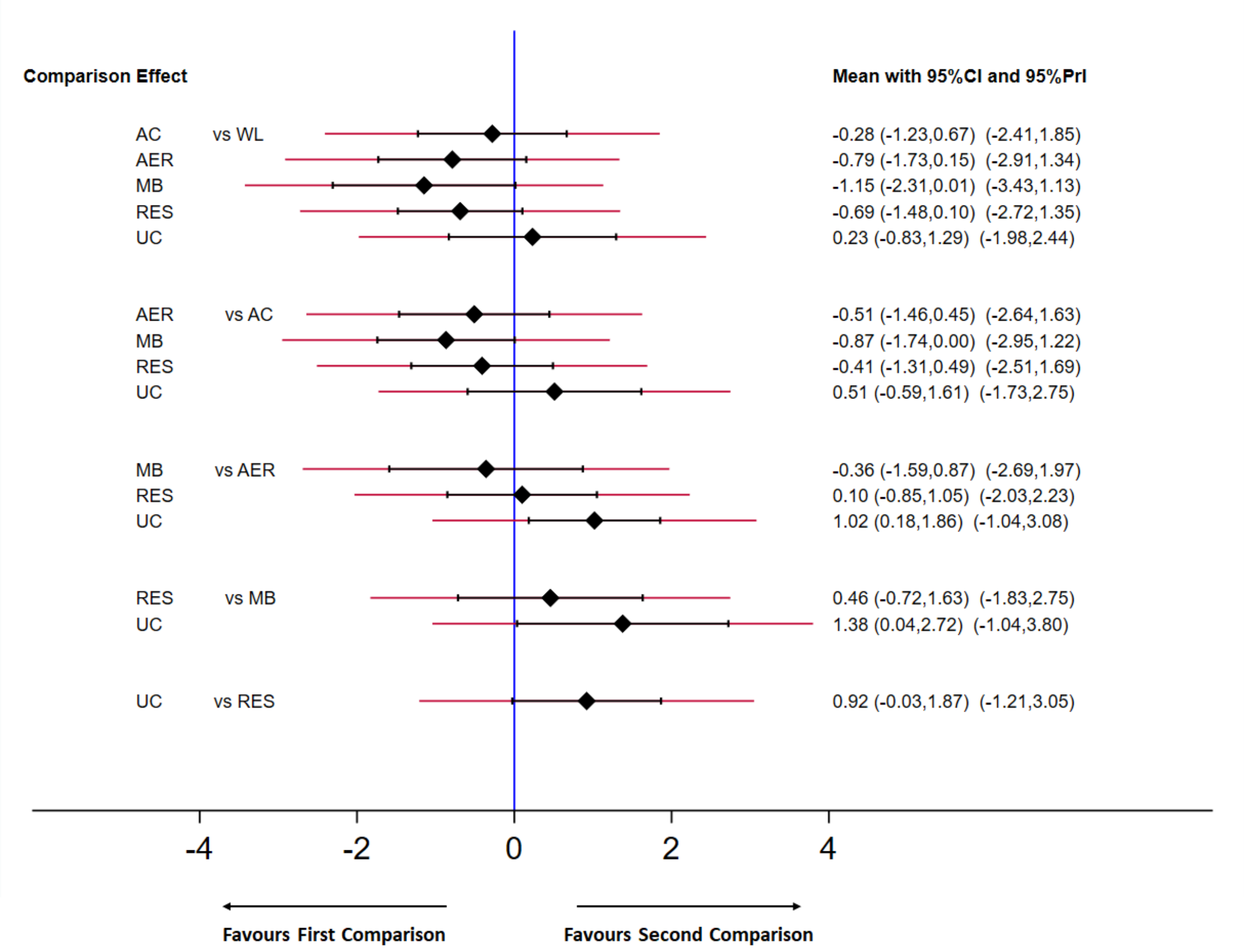

Figure 5.5. Predictive interval plot for the depressive symptoms network. The black diamonds represent the difference in the effect size estimate (Hedges' *g*). The narrow horizontal lines represent the confidence intervals (*CI*) and the wider horizontal lines represent the prediction intervals (*PrI*). The blue vertical line represents the null hypothesis (Hedges' *g* = 0). Negative scores indicate a greater decrease in depressive symptom for the comparison (left) group. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

Nevertheless, the current findings indicated that aerobic exercise had a slightly greater effect than resistance exercise (Hedges' g = -0.10, *PrI* = -2.23, 2.03), which is consistent with previous research (Penninx et al., 2002). Notably, the average length (weeks) for aerobic and resistance programs were comparable, whereas the average minutes spent per week (calculated as frequency multiplied by duration) was much higher in resistance conditions than aerobic conditions (170 minutes versus 117 minutes, respectively). This indicates that aerobic exercise can achieve a similar antidepressive treatment effect in a shorter duration than resistance exercise. Despite these trivial differences between aerobic and resistance exercise, both therapies appear to be effective in reducing clinical depression in older adulthood.

Five out of six aerobic RCTs used walking (Lok et al., 2017; McNeil et al., 1991; Patel, 2004; Prakhinkit et al., 2014; Williams & Tappen, 2008), while the remaining trial included ballroom dancing (Haboush et al., 2006). All five resistance RCTs used progressive weight training (Favilla, 1992; Sims et al., 2006, 2009; Singh et al., 1997, 2005), which is characterised by a gradual increase in the difficulty of exercises according to the individual's own capabilities. Since these pools of studies reflect relatively homogeneous modalities of exercise, the findings indicate that clinically depressed older adults may respond similarly to aerobic walking and progressive resistance training.

Table 5.2

Summary of GRADE assessment for the certainty in depressive symptoms estimates

Comparison Effect	**Number of Participants**	**Number of Direct Comparisons**	**Nature of Evidence**	**Certainty**	**Reason for Downgrading**
Aerobic vs. wait-list	20 vs. 22	2	Mixed	Moderate	Imprecision[a]
Aerobic vs. usual care	66 vs. 66	3	Mixed	Moderate	Risk of bias[b]
Aerobic vs. attention-control	27 vs. 22	2	Mixed	Low	Imprecision[ac]
Resistance vs. wait-list	65 vs. 44	3	Mixed	Low	Risk of bias[bd]
Resistance vs. usual care	35 vs. 19	2	Mixed	Low	Imprecision[a], risk of bias[d]
Resistance vs. attention-control	30 vs. 32	2	Mixed	Very low	Imprecision[ac], inconsistency[e]
Mind-body vs. wait-list	7 vs. 7	1	Mixed	Moderate	Imprecision[a]
Mind-body vs. usual care	0 vs. 0	0	Indirect	Moderate	Imprecision[a]
Mind-body vs. attention-control	81 vs. 63	3	Mixed	Moderate	Risk of bias[d]
Aerobic vs. resistance	0 vs. 0	0	Indirect	Low	Imprecision[ac]
Aerobic vs. mind-body	0 vs. 0	0	Indirect	Low	Imprecision[ac]
Resistance vs. mind-body	0 vs. 0	0	Indirect	Low	Imprecision[ac]

[a] Small sample size.

[b] Potential detection bias due to high number of studies without blinding of outcome.

[c] Wide confidence intervals favouring either treatment.

[d] Potential attrition bias due to high number of studies with incomplete outcome data.

[e] Evidence of inconsistency in the network.

Notable beneficial effects were observed for mind-body exercise, yet they did not reach the threshold for clinical significance when compared to aerobic and resistance exercise. In particular, interventions incorporating mind-body exercise therapy led to a relatively greater reduction in depressive symptoms than those involving either aerobic (Hedges’ g = -0.36, *PrI* = -2.69, 1.97) or resistance exercise (Hedges’ g = -0.46, *PrI* = -2.75, 1.83), supporting previous meta-analytic subgroup analyses (Heinzel et al., 2015). Since mind-body exercise is typically performed at a lower intensity than other exercise modes, it appears that intensity may not be primarily responsible for the reduction in depression. Instead, physical exercise combined with an internally directed focus on breathing and proprioception may result in stronger antidepressive effects than physical exercise alone (La Forge, 1997; Prakhinkit et al., 2014). Hence, mind-body exercise can allow older adults to manage their depressive symptoms through interoceptive states not normally available during aerobic and resistance activities (Paulus & Stein, 2010).

Four mind-body trials were included in the current pool of studies, including two interventions using tai chi (Cheng et al., 2012; Chou et al., 2004) and two using qigong (Tsang et al., 2006, 2013). The length of these programs was evidently longer, with mind-body interventions averaging more than three weeks longer than aerobic and resistance interventions. Thus, it is plausible that the greater improvement in depressive symptomology may be partially explained by participants experiencing a larger treatment dose.

Previously published clinical meta-analyses (Bridle et al., 2012; Heinzel et al., 2015; Schuch et al., 2016) included several studies which were not included in the current network meta-analysis. These studies were excluded because they did not fulfill our inclusion criteria, including a mean age lower than 65 years (Blumenthal et al., 2012; Mather et al., 2002) and incorporating a combination of exercise modalities in one condition (Brenes et al., 2007; Huang et al., 2015; Kerse et al., 2010). A further three studies were excluded because they used a multicomponent treatment that could have synergistically enhanced the treatment effect of exercise, such as medication (Murri et al., 2015), depression management (Ciechanowski et al., 2004), or laughter therapy (Lavretsky et al., 2011). Our findings therefore provide a more accurate representation of the comparative effectiveness between aerobic, resistance, and mind-body exercise interventions on depressive symptoms for clinically depressed older adults.

5.5.2. Practical implications

Secondary outcomes (i.e., adverse events, adherence, attrition) were used to evaluate overall compliance to exercise. No adverse events were identified in any studies, which means either (1) participants did not experience any major or minor adverse outcomes during exercise sessions, or (2) the researchers did not observe and/or record any adverse outcomes during the intervention period. Adherence was above 90 percent for all three exercise conditions, reflecting excellent adherence rates. Attrition rates were also compared between exercise interventions, which demonstrated slight discrepancies. Interestingly, highest dropout rates were observed for mind-body exercise, followed by resistance exercise. On the contrary, aerobic exercise had the lowest dropout rates, indicating that aerobic exercise is the best for high adherence to treatment while still maintaining a lower risk of attrition. Nevertheless, these outcomes demonstrate that older adults have very high compliance to physical exercise.

Our findings highlight the usefulness of all types of exercise as an effective adjunct therapy against depressive symptoms in clinically depressed older adults. Since non-compliance to antidepressant medication is a serious problem in older populations (Rossom et al., 2016; Stein-Shvachman et al., 2013), regular exercise can be incorporated into everyday life as a standalone treatment or an add-on strategy for other antidepressant therapies to further reduce depressive symptoms (Mura et al., 2014). This is particularly valuable for at-risk groups, such as those who are very old (Luppa et al., 2012), frail elderly (Soysal et al., 2017), people with dementia (De Souto Barreto et al., 2015), or residents in aged care facilities (Seitz et al. 2010), who might also benefit from the physiological and social aspects of group exercise.

Notably, there is an inherent form of inequity exists during the recruitment process for exercise-based trials. Participants are generally only selected for participation if they are healthy enough to meet the physical demands of the exercise intervention. This means that any person who presents significant illness or disability that prohibits them from completing the exercise intervention are likely to be excluded during the recruitment process, or alternatively, are likely to dropout once the trial has commenced. These conditions may include chronic diseases, physical disability, or cognitive impairment. In practice, clinicians can build a partnership with their patients to develop a modified exercise program to satisfy the physical needs, abilities, and personal interests of specific older individuals or groups. Several different types of exercise can also be concurrently used in an exercise program. Therefore, it is recommended that exercise programs are strategically developed to best suit the specific needs of older adults so that inequity can be addressed, allowing anyone to potentially benefit from a variety of exercise types and modalities.

5.5.3. Limitations and future directions

There were several noteworthy limitations in this network meta-analysis. Most importantly, the network meta-analysis was comprised of a relatively small group of participants (*n* = 596). Indeed, only two of the included RCTs had a sample size of over 30 participants for each comparison group (Lok et al., 2017; Tsang et al., 2006), introducing imprecision for the indirect comparisons. This is further exacerbated by the impossibility to blind participants and training personnel during exercise-based interventions, which introduced an inherent risk of performance bias. Risk of bias and GRADE assessments identified these factors as potential threats to the overall validity of the current findings. There was generally moderate-to-low confidence in the findings, and therefore, caution should be taken in the interpretation and implementation of the current findings.

It is also important to note that all exercise interventions from the included pool of RCTs lasted a maximum of 16 weeks, with an average length of 9.76 weeks (*SD* = 3.38 weeks). This is a rather short follow-up period, which is likely to reflect only the short-term impact of exercise on depressive symptoms. Despite this, exercise therapy seems to have a relatively strong impact on symptoms of clinical depression in older adults. The cumulative effect of long-term compliance to exercise therapy is still uncertain, and therefore, clinical applications are limited by the lack of available long-term research designs. This highlights the need for more high-quality clinical trials including intervention periods that are longer in duration.

Finally, treatment conditions using a combination of aerobic, resistance, and/or mind-body exercise were excluded during the screening process to prevent confounding effects of using more than one type of exercise within a single intervention group. While it is possible that a combination of exercise types may provide a synergistic or compound effect on depressive symptoms, this was beyond the scope of our review. Thus, it is recommended that future scientific reviews examine the effects of combined exercise modalities on depressive symptoms in clinically depressed older adults.

5.5.4. Conclusions

In summary, the current network meta-analysis shows substantial and comparable beneficial effects of aerobic, resistance, and mind-body exercise to reduce symptoms of clinical depression in older adults. This demonstrates that older adults can self-select their preferred exercise type in order to achieve therapeutic benefit on symptoms of depression. In coalition with high levels of compliance, these findings should be used to advise allied health professionals and stakeholders in clinical geriatrics that clinically depressed older adults can benefit from the antidepressant effect of either aerobic, resistance, or mind-body exercise as an adjunct therapy.

5.6. Chapter References

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CHAPTER VI

Aerobic, Resistance, and Mind-Body Exercise are Effective Treatments to Mitigate Symptoms of Depression in Older Adults: A Systematic Review and Network Meta-Analysis of Randomised Controlled Trials

Under Review

"**Miller, K. J.**, Areerob, P., Hennessy, D., Gonçalves-Bradley, D. C., Mesagno, C., & Grace, F. (2020). Aerobic, resistance, and mind-body exercise are effective treatments to mitigate symptoms of depression in older adults: A systematic review and network meta-analysis of randomised controlled trials. ***F1000 Research***."

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Supplementary Material: See *Appendix F* and *Appendix H*

Preface

The findings from Study 3 (Chapter V) establish a strong treatment effect for aerobic, resistance, or mind-body exercise to positively impact depressive symptoms in clinically older adults. It's worthy of note, however, that previous meta-analyses on RCTs have mainly focused on clinically depressed older adults (Bridle, Spanjers, Patel, Atherton, & Lamb, 2012; Heinzel, Lawrence, Kallies, Rapp, & Heissel, 2015; Netz, Wu, Becker, & Tenenbaum, 2005; Rhyner & Watts, 2016; Schuch et al., 2016). Whereas some meta-analyses on clinically depressed samples of older adults have concluded that mixed aerobic and resistance exercise are most effective for the treatment of clinical depression (Bridle et al., 2012; n = 7; Schuch et al., 2016; n = 8), others have concluded that mind-body exercise is the most effective (Heinzel et al., 2015; n = 18). Another recent meta-analysis (Rhyner & Watts, 2016; n = 41) concluded that all types of exercise are equally beneficial.

These discrepancies indicate that depression severity is an important effect modifier that threatens transitivity in exercise-based interventions. For instance, clinically depressed older adults are more likely to benefit from the antidepressant effects of exercise than their apparently healthy counterparts (Penninx et al., 2002; Rhyner & Watts, 2016), and therefore, it is necessary to differentiate between clinical depressed and apparently healthy older adults. In the follow-up network meta-analysis (Chapter VI), only older adults without clinically diagnosed depression (those samples that were excluded from the network meta-analysis performed in Chapter V) were examined. Thus, the purpose of the following study was to perform a systematic review and network meta-analysis of current evidence from RCTs to compare the effectiveness of three major exercise therapies (resistance, aerobic, or mind-body exercise) in apparently healthy older adults.

6.1. Abstract

6.1.1. Background

Recent demographic projections indicate that, within the next decade, there may be up to 200 million adults aged ≥ 65 years burdened with clinical depression worldwide. Physical exercise has been identified as an allied health strategy to support the management of depression in older adults, yet the relative effectiveness for individual exercise modalities is unknown. To meet this gap in knowledge, we present a systematic review and network meta-analysis of collective randomised controlled trials (RCTs) to simultaneously examine the head-to-head effectiveness of aerobic, resistance, and mind-body exercise to mitigate depressive symptoms in adults aged ≥ 65 years.

6.1.2. Methods

A PRISMA-NMA compliant review was undertaken on RCTs from inception to September 12th, 2019. Electronic databases were systematically searched for eligible trials enrolling adults aged ≥ 65 years, comparing one or more exercise intervention arms consisting either aerobic, resistance, or mind-body exercise, and which used valid measures of depressive symptomology. Comparative effectiveness was evaluated using network meta-analysis to combine direct and indirect evidence for all relative treatment effects, controlling for inherent variation in trial control groups.

6.1.3. Results

The systematic review included 81 RCTs, with 69 meeting eligibility for the network meta-analysis (*n* = 5,379 participants). Pooled analysis found each exercise type to be effective compared with controls (*g* = -0.27 to -0.51). Relative head-to-head comparisons were statistically comparable between exercise types: resistance versus aerobic (*g* = -0.06,

PrI = -0.91, 0.79), mind-body versus aerobic (*g* = -0.12, *PrI* = -0.95, 0.72), mind-body versus resistance (*g* = -0.06, *PrI* = -0.90, 0.79). High levels of compliance were demonstrated for each exercise treatment.

6.1.4. Conclusions

Aerobic, resistance, and mind-body exercise are each effective to mitigate symptoms of depression in older adults aged ≥ 65 years, with comparably encouraging levels of compliance to exercise treatment. When considered alongside comparable recent findings in clinically depressed older adults, these findings coalesce to provide general endorsement for stakeholders in ageing to encourage personal preference when prescribing exercise for depressive symptoms in older adults, irrespective of severity.

6.2. Introduction

At the close of this decade, the few remaining ‘baby boomers’ will transition to a peer cohort aged ≥ 65 years projected to comprise over one billion older adults (United Nations, 2019). Physical exercise has been proposed as a low-risk intervention for age-associated deterioration in mental health, such as dementia (Tari et al., 2019) and depression (Murri et al., 2018; Rhyner & Watts, 2016). In light of impending demographic shifts, and with the burden of age-associated depression estimated to affect ~20% of older adults (Barua, Ghosh, Kar, & Basilio, 2011; Pirkis et al., 2009; Volkert, Schulz, Harter, Wlodarczyk, & Andreas, 2013), this may confer a population of approximately 200 million adults aged ≥ 65 years with clinical depression by 2030. With this evolution of inevitable future demands on primary care systems (James et al., 2018), there is substantial value in supporting primary and allied health personnel to meet this challenge. Indeed, international public health consortia are in concert with the antidepressant effects of physical exercise as a low-risk adjunct for optimal mental health (American Psychiatric Association, 2010; Stubbs et al., 2018; World Health Organization, 2010). While we do not yet have the answers for low uptake of physical exercise in older adults (Knowles, Herbert, Easton, Sculthorpe, & Grace, 2015), it may in some way be due to nuanced regimen design, which in turn, may similarly impact compliance in exercise prescription by primary and stakeholders in aged care.

‘Exercise is Medicine’ is a global initiative promulgated through 40 member countries by the American College of Sports Medicine™ with a platform to promote and encourage exercise as a treatment for general health and a range of medical conditions. This manifesto encourages primary care physicians and health care providers to refer patients when prescribing treatment plans. Despite broad agreement for exercise as a preventative approach to geriatric depression, we are yet to establish antidepressant treatment effectiveness for individual exercise types. Perhaps a lesser appreciated obstacle to optimising exercise prescription for mental health in older adults lies with the ‘catch all’ characterisation of exercise. This is despite widely known metabolic, social, and environmental differences between modalities (i.e., running vs. weightlifting vs. yoga) that exist between exercise regimens. Such differences are not merely semantics, and only a few randomised controlled trials (RCTs) have deliberately compared the antidepressant effects of different exercise regimens in older adults (Martins et al., 2011; Penninx et al., 2002). Therefore, this begs the question, ‘are all exercise types equal?’. Surprisingly, this has not yet been adequately tested.

To progress a broader understanding of the antidepressant effect of exercise, some researches have deployed conventional pairwise meta-analysis (Bridle et al., 2012; Heinzel et al., 2015; Rhyner & Watts, 2016). While being useful, conventional meta-analytical techniques are confounded with systematic overestimation of effectiveness (Bucher, Guyatt, Griffith, & Walter, 1997) and collapsing (merging) different treatments to establish overall effect, meanwhile precluding direct (head-to-head) comparison between different exercise types and restricting interpretation for end-users wishing to prescribe exercise at the person/patient level. Of notable significance, conventional pairwise meta analyses also overlook important nuances between control treatment arms (i.e., wait-list, usual care, attention-control) of included trials (Pagoto et al., 2013), each of which coalesce to restrict accuracy of the defined outcome effect.

Where comparative effectiveness of multiple treatment comparisons are required, network meta-analysis is methodologically and statistically more appropriate to provide effect size estimates than may otherwise be achieved (Caldwell, Ades, & Higgins, 2005; Salanti, Higgins, Ades, & Ioannidis, 2008). For instance, comparative (head-to-head) effectiveness of exercise regimens (aerobic, resistance, and mind-body) may be performed while also comparing to individual control groups (wait-list, usual care, and attention-control), further correcting for known bias associated with small sample effects whilst avoiding the assumption of homogeneity across independent studies with different comparison groups.

Physical exercise regimens are broadly categorized into either aerobic, resistance, or mind-body exercise types (National Health Lung and Blood Institute, 2006; U.S. Department of Health and Human Services, 2018), and any individual exercise program may consist of multiple combinations of these activities. Extended description of these three exercise types can be found in *Appendix H*. Aerobic and resistance exercise each elicit a unique set of phenotypic changes, whereas mind-body exercise is unique in being an alternate low impact form of physical exercise. These, therefore, represent three fundamentally distinct forms of antidepressant treatment. Despite broad acceptance of the ‘Exercise is Medicine’ philosophy, investigation of individual treatment effects from aerobic, resistance, and mind-body exercise has not been undertaken to ascertain the true mitigation of depressive symptoms in older adults.

Recently, Miller and colleagues (2020) documented the comparative effectiveness of aerobic, resistance, and mind-body exercise using network meta-analytical interrogation of RCTs recruiting clinically depressed older adults. Due to binary threshold separating clinical diagnosis with subclinical depressive symptomology, it stands to reason that these diverse categories cannot be ‘merged’ into the same network. Similarly, should the projected 10-year population estimate of one billion adults aged ≥ 65 remain true (United Nations, 2019), the progression from symptom presentation to clinically diagnosed depression will become a significant public health challenge and a matter of clinical importance.

With these aspects in mind, the purpose of this systematic review and network meta-analysis was to quantitively assess the best evidence from RCTs to establish relative (head-to-head) effectiveness of resistance, aerobic, and mind-body exercise in adults aged ≥ 65 years below the clinical threshold for diagnosed depression. More specifically, we investigated whether (i) resistance, aerobic, and mind-body exercise training can induce substantive treatment effect on depressive symptoms in older adults, (ii) while considering relative treatment compliance to each exercise regimen, and further, (iii) to juxtapose the most feasible exercise treatment for all adults aged ≥ 65 years irrespective of depressive symptomology.

6.3. Methods

This review was prospectively registered with PROSPERO (registration number: CRD42018115866). The network meta-analysis extension for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-NMA) guidelines (Hutton et al., 2015) and the Cochrane Intervention Review that Compares Multiple Interventions (Cochrane Methods, 2014) each provided further support in guiding this review. Guidelines specific for geriatric meta-analyses (Shenkin, Harrison, Wilkinson, Dodds, & Ioannidis, 2017) were consulted to identify baseline characteristics, equity considerations, inclusion/exclusion criteria, known confounders, and potentially important effect modifiers.

6.3.1. Eligibility criteria

Studies were eligible for inclusion if they (i) followed an RCT protocol, (ii) used a wait-list, usual care, or attention-control group, (iii) included one or more aerobic, resistance, or mind-body exercise intervention arms, (iv) reported depressive symptoms as an outcome at baseline and during follow-up, (v) used one or more psychometrically validated depression questionnaires, (vi) recruited participants with a minimum mean sample age of 65 years. Studies were excluded when (i) the intervention condition used a multicomponent treatment including non-exercise components with the exercise condition, or (ii) the participants were diagnosed with clinical depression, defined by DSM or ICD criteria, or a clinical threshold on a questionnaire validated against a structured diagnostic interview prior to study enrollment.

6.3.2. Literature search

Studies were identified from computerised searches of the following databases: PubMed, Web of Science, Cumulative Index to Nursing and Allied Health Literature

(CINAHL), Health Source: Nursing/Academic Edition, PsycARTICLES, PsycINFO, and SPORTDiscus. Databases were searched for key terms pertaining to four main concepts: older adults, exercise, depressive symptoms, and RCTs. Search terms were identified using text mining procedures and an example of a search strategy is presented in detail in *Appendix H*. Published studies, systematic reviews, and meta-analyses (Blake, Mo, Malik, & Thomas, 2009; Bridle et al., 2012; Heinzel et al., 2015; Mura & Carta, 2013; Rhyner & Watts, 2016; Schuch et al., 2016; Sjosten & Kivela, 2006) were also screened for additional articles. Databases were searched up to and including September 12th, 2019.

6.3.3. Data extraction and coding

Detailed data extraction was undertaken independently by a minimum of two researchers (KJM, PA, and/or DH) in compliance with a data extraction form (See *Appendix H*), with any inconsistencies being arbitrated by another researcher (CM). Study characteristics are presented in *Table 6.1*. Methodological characteristics of each study were used to evaluate the quality of evidence, which included publication status, intention-to-treat principle, use of a cluster design, and validated measure(s) of depressive symptoms used.

Control groups within each individual study were further categorised as either wait-list, usual care, or attention-control. Participants undergoing wait-list conditions received the exercise intervention following trial completion. Participants randomised to usual care were those in sole receipt of conventional treatment during the trial. Participants randomised to attention-control conditions (also known as attention placebo control or active control) received activities unrelated to aerobic, resistance, or mind-body exercise during their respective trials (e.g., social activities, educational programs, etc.).

Table 6.1

Participant, intervention, and methodological characteristics of studies included in the systematic review

Author (year)	Treatment M_{age} (SD), females (%)	Control M_{age} (SD), females (%)	Source of participants	Inclusion criteria	Intention-to-treat	Cluster design	Treatment group	Control group	Length of intervention	Adherence (%)	Outcome measure(s)
Adler (2007)	72.8 (5.4) 100	70.8 (8.0) 87.5	Community	Osteoarthritis	Yes	N/R	*n* = 8 Mind-body (Tai Chi), supervised, group, low intensity, 1 time/week, 60 mins/session **Encouraged to practice at home at least 3 times per week for 15 minutes	*n* = 6 Attention-control (bingo)	10 weeks	85	CESD-20
Ángeles (2016)	65.0 (3.3) 80	69.3 (7.4) 70	N/R	N/R	N/R	No	*n* = 10 Mind-body (flexibility, toning, and balance - FlexToBa DVD), supervised, group, N/R, 3 times/week, 50 mins/session	*n* = 10 Usual care	12 weeks	N/R	POMS-D
Ansai (2015)	82.8 (2.8) 65.2	82.6 (2.6) 65.2	Community	Sedentary	Yes	No	*n* = 23 Resistance (strength exercises with machines), supervised, group, N/R, 3 times/week, 60 mins/session Adverse events: Mild muscle pain (*n* = 9)	*n* = 23 Usual care	16 weeks	N/R	GDS-15
Antunes (2005)	68.1 (5.5) 0	65.9 (3.8) 0	Community	Sedentary	N/R	No	*n* = 23 Aerobic (ergometric cycling), supervised, N/R, moderate intensity (50-60% VO_{2max}), 3 times/week, 20-60 mins/session	*n* = 23 Wait-list	6 months	N/R	GDS-30
Bernard (2015)	65.5 (4.0) 100	65.5 (4.4) 100	Community	N/R	Yes	No	*n* = 61 Aerobic (walking - Acti'March Program), supervised, individual, moderate intensity (40-75% HR_{max}), 2 times/week, 40 mins/session **One 40 minute unsupervised session	*n* = 60 Wait-list	6 months	53.8	BDI
Bethany (2005)	83.1 (4.8) 92.9		Community	N/R	N/R	No	*n* = 11 Aerobic (chair aerobics), supervised, group, N/R, 3 times/week, 30 mins/session	*n* = 10 Attention-control (social games)	6 weeks	71.7	BDI-II
							n = 10 Aerobic (walking), unsupervised, individual, N/R, 3 times/week, 30 mins/session			62.2	
							n = 11 Mind-body (chair yoga), supervised, group, N/R, 3 times/week, 30 mins/session			78.3	

Blumenthal (1991)	66.5 (4.3) 48.4	66.8 (4.3) 52.9	Community	Sedentary	N/R	No	*n* = 31 Aerobic (ergometric cycling, walking, jogging, and arm ergometry), supervised, group, moderate intensity (70% HR_{max}), 3 times/week, 60 mins/session	*n* = 32 Wait-list	16 weeks	95.8	CESD-20
	67.8 (5.9) 50						*n* = 34 Mind-body (yoga), supervised, group, low intensity, 2 times/week, 60 mins/session			100	
Bonura (2014)	77.0 (7.3) 69.8		Community	N/R	N/R	No	*n* = 33 Resistance (chair strength and balance), supervised, group, N/R, 1 time/week, 45 mins/session **Practice on their own for 15 minutes during non-class days	*n* = 32 Wait-list	6 weeks	83.8	GDS-30
							n = 33 Mind-body (chair yoga), supervised, group, N/R, 1 time/week, 45 mins/session **Practice on their own for 15 minutes during non-class days			95	
Boström (2016)	84.4 (6.2) 75.3	85.9 (7.8) 76.3	Residential	Dementia	N/R	Yes (36)	*n* = 83 Resistance (functional weight-bearing and balance - High-Intensity Functional Exercise Program), supervised, group, moderate-high intensity, 2.5 times/week, 45 mins/session	*n* = 80 Attention-control (seated social activities)	4 months	73	GDS-15; MADRS*
Bouaziz (2019)	72.9 (2.5) 70	74.3 (3.4) 76.6	Community	Sedentary	N/R	No	*n* = 27 Aerobic (cycle ergometry), supervised, individual, moderate intensity, 2 times/week, 30 mins/session	*n* = 29 Wait-list	9.5 weeks	94.7+	GADS-D
Brown (2009)	81.5 (6.9) 91.6	78.1 (6.4) 86.8	Community	N/R	Yes	Yes (8)	*n* = 26 Mind-body (flexibility and relaxation), supervised, group, low intensity, 2 times/week, 60 mins/session	*n* = 34 Usual care	6 months	44.8	GDS-30
Cancela (2016)	80.6 (8.3) 43.8	82.9 (7.4) 81	Residential	Dementia	Yes	No	*n* = 73 Aerobic (low resistance cycling), supervised, individual, N/R, 7 times/week, 15+ mins/session	*n* = 116 Attention-control (recreational activities)	15 months	88	CSDD
Chen (2009)	65.8 (4.3) 83.9	72.4 (6.0) 62.1	Community	N/R	N/R	Yes (8)	*n* = 62 Mind-body (silver yoga), supervised, group, N/R, 3 times/week, 70 mins/session	*n* = 66 Wait-list	6 months	87	TDQ

Chen (2015)	79.2 (7.0) 49.1		Residential	Wheelchair-bound	N/R	Yes (10)	$n = 59$ Aerobic (resistance bands, aerobic motion, and harmonic stretching - Wheelchair-bound Senior Elastic Band Program), supervised, group, N/R, 3 times/week, 40 mins/session	$n = 55$ Usual care	6 months	94.5	TDQ
Chen (2017)	80.7 (8.0) 58.5	81.6 (6.7) 54.8	Residential	Dementia; wheelchair-bound	N/R	Yes (8)	$n = 65$ Aerobic (resistance bands, aerobic motion, and harmonic stretching - Wheelchair-bound Senior Elastic Band Program), supervised, group, N/R, 3 times/week, 40 mins/session	$n = 62$ Usual care	15 months	96.9	CSDD
Chin A Paw (2004)	81.0 (5.8) 73.2	81.3 (4.4) 82.9	Residential	N/R	Yes	No	$n = 41$ Resistance (progressive resistance training), supervised, group, moderate intensity, 2 times/week, 45-60 mins/session Adverse events: Program was too intensive (n = 8)	$n = 35$ Attention-control (educational programs)	6 months	78	GDS-30
Choi (2018)	77.6 (5.69) 90.9	78.8 (5.83) 96.7	Residential	N/R	N/R	Yes (6)	$n = 33$ Mind-body (sitting yoga), supervised, group, moderate intensity (10-14/20 RPE), 4 times/week, 30-40 mins/session	$n = 30$ Wait-list	12 weeks	N/R	GDS-15
Clegg (2014)	79.4 (7.9) 73.3	78.0 (10.5) 69.2	Community	Frailty	Yes	No	$n = 40$ Resistance (strengthening exercises - Home-based Older People's Exercise Program), unsupervised, individual, N/R, 15 times/week, 15 mins/session Adverse events: Fell at least once ($n = 7$)	$n = 30$ Usual care	12 weeks	67	GDS-15
Collier (1997)	71 (N/R) 63	69 (N/R) 46.2	Community	N/R	N/R	No	$n = 25$ Resistance (strength exercises with machines), supervised, group, N/R, 3 times/week, 50 mins/session	$n = 13$ Usual care	10 weeks	N/R	GDS-30
Conradsson (2010)	85.3 (6.1) 73.6	84.2 (6.8) 72	Residential	N/R	Yes	Yes (34)	$n = 75$ Resistance (functional weight-bearing and balance - High-Intensity Functional Exercise Program), supervised, group, high intensity, 2.5 times/week, 45 mins/session	$n = 90$ Attention-control (seated social activities)	3 months	72	GDS-15
Cramer (2016)	68.7 (9.1) 37	67.8 (10.4) 40.7	Community	Colorectal cancer	Yes	No	$n = 27$ Mind-body (hatha yoga), supervised, group, N/R, 1 time/week, 90 mins/session Adverse events: Muscle soreness ($n = 3$), abdominal pain ($n = 1$), neck pain ($n = 1$), minor vertigo ($n = 1$), hip pain ($n = 1$)	$n = 27$ Wait-list	10 weeks	53	HADS-D

De Lima (2019)	66.2 (5.5) N/R	67.2 (5.2) N/R	Community	Parkinson's diease	N/R	No	*n* = 17 Resistance (free weights and machines), supervised, group, N/R, 2 times/week, 30-40 mins/session	*n* = 16 Usual care	20 weeks	N/R	HRSD
Donesky-Cuenco (2009)	72.2 (6.5) 73.3	67.7 (11.5) 71.4	Community	Chronic obstructive pulmonary disease	Yes	No	*n* = 14 Mind-body (yoga), supervised, group, N/R, 2 times/week, 60 mins/session	*n* = 15 Usual care	12 weeks	83.3	CESD-20
Dong (2013)	68.5 (N/R) 100		Community	N/R	N/R	No	*n* = 32 Mind-body (YiJinJing qigong), supervised, group, N/R, 3 times/week, 60 mins/session	*n* = 34 N/R	12 weeks	N/R	GDS-15
							n = 36 Mind-body (LiuZiJue qigong), supervised, group, N/R, 3 times/week, 60 mins/session			N/R	
Dorner (2007)	86.7 (6.1) 76.7	86.9 (5.7) 76.7	Residential	Frailty; cognitive impairment	N/R	No	*n* = 15 Resistance (resistance bands, soft weights, and balance), supervised, group, N/R, 3 times/week, 50 mins/session	*n* = 15 N/R	10 weeks	91.8	GDS-15
Emery (1990)	72 (6) 83.3		Community	N/R	N/R	No	*n* = 14 Aerobic (aerobic walking and rhythmic muscle strengthening), supervised, group, moderate intensity (70% HR_{max}) 3 times/week, 60 mins/session	*n* = 13 Wait-list *n* = 11 Attention-control (social games)	12 weeks	61-94	CESD-20
Eyigor (2009)	73.5 (7.6) 100	71.2 (5.5) 100	Community	N/R	N/R	N/R	*n* = 19 Aerobic (folkloric dance), supervised, group, N/R, 3 times/week, 60 mins/session **Walk for 30 minutes at least twice a week	*n* = 18 Usual care	8 weeks	N/R	GDS-30
Eyre (2017)	68.1 (8.7) 65.8	67.6 (8.0) 65.9	Community	Cognitive impairment	N/R	No	*n* = 29 Mind-body (kundalini yoga), supervised, group, N/R, 1 time/week, 60 mins/session Adverse events: Dizziness (*n* = 1) **Home meditation and finger movements for 12 minutes	*n* = 32 Attention-control (memory enhancement training)	12 weeks	59.4	GDS-30
Fakhari (2017)	69.2 (5.5) 48.1	69.3 (5.0) 58.6	Residential	Sedentary	N/R	No	*n* = 27 Mind-body (Tai Chi), supervised, group, N/R, 3 times/week, 20-25 mins/session	*n* = 29 Usual care	12 weeks	N/R	BDI-II

Fransen (2007)	70.8 (6.3) 67.9	69.6 (6.1) 82.9	Community	Osteoarthritis	Yes	No	*n* = 56 Mind-body (Tai Chi), supervised, group, N/R, 2 times/week, 60 mins/session	*n* = 41 Wait-list	12 weeks	N/R	DASS-D
Frye (2007)	69.2 (9.3) 64.3		Community	Sedentary	N/R	No	*n* = 23 Mind-body (Tai Chi), supervised, group, low-moderate intensity, 3 times/week, 60 mins/session **Tai Chi video to assist with home practice, but was not monitored	*n* = 21 Usual care	12 weeks	72.2-100	CESD-20
Gary (2004)	67 (11) 100	69 (11) 100	Community	Diastolic heart failure	N/R	No	*n* = 15 Aerobic (walking), supervised, individual, low-moderate intensity (40-60% HR_{max}), 3 times/week, 20-30 mins/session	*n* = 13 Attention-control (educational programs)	12 weeks	N/R	GDS-15
Gusi (2008)	71 (5) 100	74 (6) 100	Community	Moderate depression or overweight	N/R	No	*n* = 55 Aerobic (walking), supervised, group, N/R, 3 times/week, 50 mins/session	*n* = 51 Usual care	6 months	N/R	GDS-15
Hars (2014)	75 (8) 97	76 (6) 95.6	Community	Risk of falling	Yes	No	*n* = 66 Aerobic (aerobic training), supervised, group, N/R, 1 time/week, 60 mins/session	*n* = 68 Wait-list	6 months	79	HADS-D
Hsu (2016)	80.7 (9.7) 63.3	81.7 (6.3) 63.3	Residential	Wheelchair-bound	Yes	No	*n* = 30 Mind-body (seated Tai Chi), supervised, group, N/R, 3 times/week, 40 mins/session	*n* = 30 Usual care	26 weeks	85.3	GDS-15
Irwin (2012)	70.7 (5.9) 69.6	71.4 (7.7) 51.4	Community	N/R	Yes	No	*n* = 58 Mind-body (Tai Chi), supervised, group, N/R, 3 times/week, 40 mins/session	*n* = 53 Attention-control (health education)	16 weeks	83	BDI
Irwin (2014)	66.3 (7.4) 64.6	66.4 (7.7) 72	Community	Insomnia	Yes	No	*n* = 48 Mind-body (Tai Chi), supervised, group, N/R, 1 time/week, 120 mins/session	*n* = 25 Attention-control (sleep seminar education)	4 months	81	IDS-C
Kekäläinen (2018)	68.9 (2.7) 53.8	68.3 (2.3) 47.8	Community	N/R	Yes	No	*n* = 24 Resistance (progressive resistance training), supervised, group, N/R, 2 (month 1-3) and 1 (month 4-9) times/week, 60 mins/session	*n* = 19 Usual care	9 months	N/R	BDI-II
	67.7 (2.8) 59.6						*n* = 25 Resistance (progressive resistance training), supervised, group, N/R, 2 (month 1-3) and 2 (month 4-9) times/week, 60 mins/session			N/R	

	69.0 (3.3) 57.1						*n* = 27 Resistance (progressive resistance training), supervised, group, N/R, 2 (month 1-3) and 3 (month 4-9) times/week, 60 mins/session			N/R	
Kim (2019)	76.1 (3.85) 100	76.40 (3.27) 100	Community	N/R	N/R	No	*n* = 11 Resistance (strength exercises), N/R, N/R, moderate intensity (9-13/20 RPE), 3 times/week, 30-60 mins/session	*n* = 10 Usual care	24 weeks	N/R	GDS-15
Kohut (2005)	73.1 (5.6) 50	70.3 (5.6) 53.8	Community	Sedentary	N/R	No	*n* = 14 Aerobic (treadmills or ergometric cycling), supervised, group, high intensity (71% HR_{max}), 3 times/week, 20-30 mins/session	*n* = 13 Usual care	10 months	80+	GDS-30
Krishnamurthy (2007)	70.1 (8.3) 69.6	72.3 (7.4) 73.9	Residential	N/R	N/R	No	*n* = 18 Mind-body (yoga), supervised, group, N/R, 6 times/week, 75 mins/session	*n* = 20 Wait-list	24 weeks	N/R	GDS-15
Kuo (2018)	68.93 (3.81) 80	70.38 (5.22) 85.7	Clinical	N/R	N/R	No	*n* = 15 Aerobic (stepping exercises), supervised, N/R, moderate-high intensity (13-15/20 RPE; 60-80% HR_{max}), 2 times/week, 30 mins/session	*n* = 21 Usual care	8 weeks	N/R	GDS-15
Kupecz (2001)	74.3 (6.2) 5.1	73.6 (5.9) 13	Community	N/R	N/R	No	*n* = 30 Aerobic (walking), supervised, group, low-moderate intensity, 3 times/week, 45 mins/session Adverse events: Minor medical attention (*n* =2)	*n* = 35 Usual care	12 weeks	66	CESD-20
Li (2001)	73.2 (4.9) 76.5		Community	Sedentary	N/R	No	*n* = 40 Mind-body (Tai Chi), supervised, group, N/R, 2 times/week, 60 mins/session **Encouraged to practice at home	*n* = 32 Wait-list	24 weeks	90	CESD-20
Lin (2007)	77.1 (7.8) 51	76.2 (7.3) 51	Community	History of falling	N/R	No	*n* = 39 Resistance (muscle strengthening and balance), supervised, individual, N/R, 0.5 times/week, 40-60 mins/session **Instructed to practice exercises at least three times a week	*n* = 40 Attention-control (educational programs)	4 months	N/R	GDS-15
Lincoln (2011)	66.0 (7.9) 69	66.6 (7.4) 58.6	Community	Type 2 diabetes	N/R	No	*n* = 29 Resistance (progressive resistance training), supervised, N/R, high intensity, 3 times/week, 45 mins/session	*n* = 29 Attention-control (regular phone calls)	16 weeks	N/R	GDS-30

Ma (2018)	70.2 (10.3) 31.7	69.7 (10.8) 30.4	Community	Hypertension	Yes	No	$n = 79$ Mind-body (Tai Chi), supervised, group, N/R, 4 times/week, 60 mins/session	$n = 79$ Usual care	6 months	N/R	CESD-10
Maki (2012)	71.9 (4.1) 69.3	72.0 (3.9) 72	Community	N/R	Yes	No	$n = 66$ Aerobic (walking and group work), supervised, group, N/R, 1 time/week, 90 mins/session	$n = 67$ Attention-control (educational programs)	3 months	87.5	GDS-30
Martínez (2015)	76.1 (8.1) 89.7	72.5 (8.0) 86.2	Clinical	N/R	Yes	No	$n = 29$ Mind-body (qigong), supervised, group, N/R, 2 times/week, 90 mins/session	$n = 25$ Usual care	4 weeks	88.8	GDS-5
Martins (2011)	75.9 (7.0) 66.7	77.7 (8.8) 58.1	Residential	Sedentary	N/R	No	$n = 24$ Aerobic (rhythmic walking and stepping sequences), supervised, group, low-high intensity (40-85% HR_{max}), 3 times/week, 45 mins/session	$n = 31$ Usual care	16 weeks	N/R	POMS-SF-D
	73.4 (6.4) 56.5						$n = 23$ Resistance (resistance bands and calisthenics), supervised, group, moderate intensity, 3 times/week, N/R			N/R	
McMurdo (1993)	82.3 (6.9) 80	79.3 (6.2) 80.7	Residential	N/R	N/R	N/R	$n = 10$ Resistance (strengthening exercises), supervised, group, low intensity, 2 times/week, 45 mins/session	$n = 23$ Attention-control (reminiscence sessions)	7 months	91	GDS-30
Monga (2005)	68 (4.2) 0	70.6 (5.3) 0	Community	Prostate Cancer	N/R	No	$n = 11$ Aerobic (treadmill walking), supervised, group, moderate intensity (65% HR_{max}), 3 times/week, 45-50 mins/session	$n = 10$ Usual care	8 weeks	N/R	BDI
Mortazavi (2012)	71.7 (8.2) 64.1	71.7 (8.2) 61.3	Community	N/R	N/R	No	$n = 181$ Aerobic (upper, lower, and whole body movements), supervised, group, low intensity, 2 times/week, 45 mins/session **Pamphlet explaining details of each session for exercising at home	$n = 191$ Attention-control (physical activity pamphlets)	2 months	N/R	GHQ-D
Netz (1994)	70.7 (6.8) N/R	74.1 (8.9) N/R	Clinical	Cognitive or affective deterioration	N/R	No	$n = 15$ Aerobic (light callisthenic and rhythmic movements), supervised, group, low intensity, 3 times/week, 45 mins/session	$n = 15$ Attention-control (social intellectual activity)	8 weeks	N/R	GDS-30

Ng (2017)	70.3 (5.3) 56.2	70.1 (5.0) 56	Community	Frailty	Yes	No	$n = 48$ Resistance (functional strength and balance), supervised, group, moderate intensity, 2 times/week, 90 mins/session **Weeks 13-24 were instructed to participate at home	$n = 50$ Usual care	24 weeks	85	GDS-15
Oken (2006)	73.6 (5.1) 78.7	71.2 (4.4) 75	Community	Low activity (aerobic exercise less than 210 minutes per week)	N/R	No	$n = 38$ Aerobic (walking), supervised, group, moderate intensity (6-7/10 RPE; 70% HR_{max}), 1 time/week, 60 mins/session Adverse events: Hip pain ($n = 1$) **Exercise daily at least 5 times per week was strongly encouraged	$n = 42$ Wait-list	6 months	68.7	CESD-10*; POMS-D
	71.5 (4.9) 70.5						$n = 38$ Mind-body (hatha yoga), supervised, group, N/R, 1 time/week, 90 mins/session Adverse events: Groin muscle strain ($n = 1$) **Exercise daily at least 5 times per week was strongly encouraged			77.6	
Park (2016)	75.3 (7.5) 75		Community	Osteoarthritis	N/R	No	$n = 52$ Mind-body (chair yoga), supervised, group, N/R, 2 times/week, 45 mins/session	$n = 48$ Attention-control (health education)	8 weeks	95	PROMIS-EDD SF-8a
Payne (2008)	64.7 (6.3) 100		Community	Breast cancer	N/R	N/R	$n = 9$ Aerobic (walking), unsupervised, individual, moderate intensity, 4 times/week, 20 mins/session	$n = 9$ Usual care	12 weeks	N/R	CESD-20
Pedersen (2017)	79.2 (6.6) 52.6	81.3 (5.1) 50	Residential	N/R	N/R	N/R	$n = 19$ Resistance (resistance training), supervised, group, N/R, 2 times/week, 60 mins/session	$n = 12$ N/R	12 weeks	N/R	HADS-D
Penninx (2002)	68.7 (5.6) 70.1		Community	Osteoarthritis	Yes	N/R	$n = 149$ Aerobic (walking), supervised, N/R, moderate intensity (50-70% HR_{max}), 3 times/week, 60 mins/session **Months 4-18 were unsupervised	$n = 144$ Attention-control (health education)	18 months	N/R	CESD-6
							$n = 146$ Resistance (dumbbell and cuff weight exercises), supervised, N/R, N/R, 3 times/week, 60 mins/session ** Months 4-18 were unsupervised			N/R	

Pinniger (2013)	79.4 (N/R) 100		Community	Age-related macular degeneration	N/R	No	$n = 8$ Aerobic (tango dance), supervised, group, N/R, 2 times/week, 90 mins/session	$n = 9$ Wait-list	4 weeks	96.9	GDS-15
Ramanathan (2017)	68.9 (7.6) 100	68.2 (8.8) 100	Residential	N/R	N/R	No	$n = 20$ Mind-body (yoga), supervised, group, N/R, 2 times/week, 60 mins/session	$n = 20$ Wait-list	12 weeks	N/R	HRSD
Roswiyani (2019)	71.90 (8.57) 70.1	74.31 (9.57) 66.2	Residential	N/R	Yes	No	$n = 67$ Mind-body (qigong), supervised, group, N/R, 2 times/week, 90 mins/session	$n = 65$ Usual care	8 weeks	61.2	BDI-II
Sahin (2018)	84.5 (4.8) N/R	85.4 (4.7) N/R	Residential	Frailty	N/R	No	$n = 16$ Resistance (dumbbell and cuff weight exercises), supervised, N/R, low intensity (40% $1R_{max}$), 3 times/week, 40 mins/session	$n = 16$ Usual care	8 weeks	N/R	GDS-15
	84.2 (6.9) N/R						$n = 16$ Resistance (dumbbell and cuff weight exercises), supervised, N/R, high intensity (70% $1R_{max}$), 3 times/week, 40 mins/session			N/R	
Sattin (2005)	80.4 (3.1) 95.4	80.5 (3.2) 93.6	Residential	Frailty; history of falling	Yes	Yes (20)	$n = 158$ Mind-body (Tai Chi), supervised, group, N/R, 2 times/week, 60-90 mins/session	$n = 153$ Attention-control (health education)	48 weeks	76	CESD-20
Sola-Serrabou (2019)	71.9 (5.0) 76.5	74.8 (6.1) 77.8	Residential	Sedentary	N/R	No	$n = 18$ Resistance (strength exercises), supervised, N/R, moderate intensity (5-6/10 RPE), 2 times/week, 60 mins/session	$n = 17$ Usual care	24 weeks	90	GDS-15
Song (2019)	76.22 (5.76) 80	75.33 (6.78) 70	Community	Cognitive impairment; low activity (aerobic exercise less than 150 minutes per week)	Yes	No	$n = 60$ Aerobic (stepping exercises), supervised, group, moderate intensity (12-14/20 RPE), 3 times/week, 60 mins/session	$n = 60$ Attention-control (health education)	16 weeks	73.1	GDS-30
Sparrow (2011)	70.3 (7.5) 32.7	71.7 (7.2) 29.4	Community	Low activity (exercise less than 20 minutes per week)	Yes	N/R	$n = 49$ Resistance (resistance training - Telephone-Linked Computer-based Long-term Interactive Fitness Trainer), unsupervised, N/R, N/R, 3 times/week, 60 mins/session Adverse events: Musculoskeletal injury and discomfort ($n = 8$)	$n = 51$ Attention-control (health education)	12 months	54	BDI-II

Swoap (1994)	65.2 (4.2) 53.8	65.2 (4.2) 50	Community	Sedentary	N/R	No	$n = 24$ Aerobic (walking), supervised, group, moderate intensity (65-70% HR_{max}), 3 times/week, 30-65 mins/session	$n = 11$ Wait-list	26 weeks	N/R	GDS-30
	65.2 (4.2) 58.3						$n = 14$ Aerobic (walking), supervised, group, high intensity (80-85% HR_{max}), 3 times/week, 30-60 mins/session			N/R	
Tapps (2013)	76 (N/R) N/R		Residential	N/R	N/R	No	$n = 11$ Resistance (resistance band and chair exercises), supervised, group, N/R, 3 times/week, 30 mins/session	$n = 14$ Usual care	12 weeks	N/R	BDI-II
Taylor-Piliae (2014)	71.5 (10.3) 35.8	68.2 (10.3) 52.1	Community	History of stroke	Yes	No	$n = 53$ Mind-body (Yang-style Tai Chi), supervised, group, N/R, 3 times/week, 60 mins/session	$n = 48$ Usual care	12 weeks	82	CESD-20
Tsang (2003)	72.9 (9.5) 62.5	76.3 (8.4) 37.5	Residential	Chronic medical illness	N/R	No	$n = 24$ Mind-body (eight-section brocades qigong), supervised, group, N/R, 2 times/week, 60 mins/session **Practice daily for at least 30 minutes	$n = 26$ Attention-control (remedial rehabilitation activities)	12 weeks	N/R	GDS-30
Tsang (2013)	83.3 (6.3) 77	84.9 (6.0) 72.7	Clinical	Frailty	Yes	No	$n = 61$ Mind-body (Yan Chai Yi Jin ten-section brocades qigong), supervised, group, N/R, 2 times/week, 60 mins/session	$n = 55$ Attention-control (newspaper reading)	12 weeks	N/R	GDS-15
Tsutsumi (1998)	68.5 (6.1) 100		Community	Sedentary	N/R	N/R	$n = 12$ Resistance (strength exercises with machines), supervised, group, moderate intensity (55-65% $1R_{max}$), 3 times/week, N/R	$n = 12$ N/R	12 weeks	N/R	POMS-D
							$n = 12$ Resistance (strength exercises with machines), supervised, group, high intensity (75-85% $1R_{max}$), 3 times/week, N/R			N/R	
Vahlberg (2017)	72.6 (5.5) 20.6	73.7 (5.3) 27.3	Community	History of stroke	Yes	No	$n = 34$ Resistance (functional weight-bearing and balance - High-Intensity Functional Exercise Program), supervised, group, high intensity, 2 times/week, 55 mins/session	$n = 33$ Usual care	3 months	91	GDS-20

Vankova (2014)	83.4 (8.2) 91.6	82.9 (7.9) 92.4	Residential	N/R	N/R	No	$n = 79$ Aerobic (ballroom dance - Exercise Dance for Seniors Program), supervised, group, N/R, 1 time/week, 60 mins/session	$n = 83$ Wait-list	3 months	84.6	GDS-15
Wang (2009)	75.5 (9.2) 100	74.5 (8.1) 80	Community	N/R	N/R	No	$n = 7$ Mind-body (yoga), supervised, group, N/R, 2 times/week, 60 mins/session	$n = 10$ Attention-control (social group)	4 weeks	78.1	CESD-10
Witham (2005)	80 (6) 37	81 (4) 54	Community	Frailty; chronic heart failure	N/R	No	$n = 36$ Aerobic (progressive aerobic seated exercise with small weights), supervised, group, N/R, 2 times/week, 20 mins/session **Months 4-6 were home exercise 2-3 times per week with no face-to-face contact	$n = 32$ Usual care	6 months	82.7	HADS-D
Yang (2005)	72.6 (5.4) 68.4	72.7 (7.5) 90.5	Community	Chronic pain	N/R	No	$n = 19$ Mind-body (Chun Soo Energy Healing qigong), supervised, group, N/R, 2 times/week, 20 mins/session	$n = 21$ Wait-list	4 weeks	N/R	POMS-D
Yeh (2003)	65 (6) 40	66 (6) 40	Community	Chronic obstructive pulmonary disease	Yes	N/R	$n = 5$ Mind-body (Tai Chi), supervised, group, N/R, 2 times/week, 60 mins/session	$n = 5$ Usual care	12 weeks	74.2	CESD-20
Zanuso (2012)	74.3 (3.5) 50	67.1 (2.0) 50	Community	Sedentary	N/R	No	$n = 10$ Resistance (resistance training), supervised, N/R, moderate intensity, 3 times/week, 60 mins/session	$n = 10$ Wait-list	12 weeks	90.7	POMS-D

Note. N/R = not reported; n = Total participants included in intention-to-treat or post-treatment data analysis; HR_{max} = Heart rate maximum; VO_{2max} = Maximal oxygen uptake; $1R_{max}$ = One-repetition maximum; RPE = Rating of perceived exertion; BDI = Beck Depression Inventory; CESD = Center for Epidemiological Studies Depression Scale; CSDD = Cornell Scale for Depression in Dementia; DASS-D = Depression, Anxiety, and Stress Scale (depression subscale); GADS-D = Goldberg Anxiety and Depression Scale (depression subscale); GDS = Geriatric Depression Scale; GHQ-D = General Health Questionnaire (depression subscale); HADS-D = Hospital Anxiety and Depression Scale (depression subscale); HRSD = Hamilton Rating Scale for Depression; IDS-C = Inventory of Depression Symptomatology; MADRS = Montgomery-Asberg Depression Rating Scale; POMS-D = Profile of Mood States (depression subscale); PROMIS-EDD SF-8a = Patient Reported Outcome Measurement Information System - Emotional Distress and Depression Short Form-8a; TDQ = Taiwanese Depression Questionnaire.

*Outcome measure used in network meta-analysis.

**Additional unsupervised exercise component.

To evaluate the transitivity assumption, important participant and intervention characteristics were used to verify whether potential effect modifiers were similarly distributed across comparisons within the network. Participant characteristics were coded according to sample size, age (mean and standard deviation), percentage of females, and place of residence (community-dwelling, residential care, clinical setting). Relevant inclusion criteria (e.g., sedentary, dementia, etc.) were further used to assess the risk of bias from equity considerations (O'Neill et al., 2014).

Intervention characteristics were appropriately coded. Exercise types were categorised as aerobic, resistance, or mind-body exercise. Length of interventions were coded in weeks or months. Exercise intensities were coded according to ratings of perceived exertion (Borg, 1982), heart rate maximum (HR_{max}; low = <50%, moderate = 50-70%, high = >70%), maximal oxygen uptake (VO_{2max}; low = <40%, moderate = 40-60%, high = >60%) or one-repetition maximum ($1R_{max}$; low = <50%, moderate = 50-74%, high = >74%; Sigal, Kenny, Wasserman, & Castaneda-Sceppa, 2004), or where unavailable, this was estimated according to the assessment of the original author(s). Frequency was coded as total sessions per week. Duration was coded as the average number of minutes engaging in exercise per session. Format of program was dichotomously coded as exercise in a group or individual setting. Format of supervision was dichotomously coded as supervised or unsupervised exercise. Agreement between the three researchers was 91.3%.

6.3.4. Risk of bias and quality assessment

Risk of bias of the included RCTs was assessed using the Cochrane Collaboration’s Tool for Assessing Risk of Bias (Higgins et al., 2011), which were conducted by a minimum of two researchers (KJM, PA, and/or DH). Discrepancies were arbitrated by another co-author (CM). Appraisal for ‘other sources of bias’ were evaluated with consideration for small sample size ($n < 15$), low adherence (less than 80%), cluster randomisation, and inequity in the selection of the sample.

6.3.5. Summary of outcomes

Outcome statistics including means (*M*), standard deviations (*SD*), and sample sizes (*n*) for depressive symptoms were used to calculate the mean change in the primary outcome. Test statistics (i.e., *t*-, *F*-, and *p*-values) were used to estimate effect sizes when descriptive statistics were unavailable. Pairwise relative (head-to-head) treatment effects for depressive symptoms were estimated using Hedges’ *g* (Hedges, 1981), which corrects for overestimation biases due to small sample sizes ($n < 20$; Hedges & Olkin, 1985). Hedges’ *g* coefficients were interpreted according to Cohen’s conversions (Cohen, 1988), whereby effects were considered small (0.2), medium (0.5), and large (0.8). Independent subgroups (e.g., males vs. females) within studies were treated as independent effect size estimates (Borenstein, Hedges, Higgins, & Rothstein, 2009). When individual studies reported more than one post-treatment depression score for the same group of participants, only the initial post-treatment time-point was used. When studies reported depression scores on multiple outcome measures, the included depression measure was selected in compliance with clinical applicability (Costa et al., 2016; Smarr & Keefer, 2011).

Secondary outcome data were also extracted for study attrition, treatment adherence, and adverse events. Pairwise relative (head-to-head) treatment effects for study attrition were reported as odds ratios based on the pre-treatment sample size versus post-treatment dropout in the treatment and comparison conditions. Treatment adherence were reported as a percentage of total attendance in, or compliance to, the treatment condition. Adverse events were qualitatively reported according to the descriptive information provided in the transcript.

6.3.6. Data synthesis

One notable assumption of network meta-analysis relates to comparison group estimates, which are derived from pooling studies with homogenous between-study effect modifiers (Jansen & Naci, 2013). If the distribution of an effect modifier is heterogeneous across studies within a specific comparison group, the assumption of transitivity can be violated. In the context of this network meta-analysis, we separate exercise conditions (i.e., aerobic, resistance, mind-body) and control conditions (i.e., wait-list, usual care, attention-control) to account for the between-study variation of these effect modifiers. Given the intricacies of depression severity, a forest plot was generated to depict the juxtaposition of treatment effects between (i) participants in the present network meta-analysis with depressive symptomology but not clinically diagnosed and (ii) participants in a previous network meta-analysis with clinical depression (Miller et al., 2020).

Risk of bias assessment identified the potential for unit-of-analysis error within studies using a cluster design for treatment allocation. Thus, sample sizes were recalculated to account for error in cluster RCTs by determining a design effect (Higgins, Deeks, & Altman, 2008) with a conservative intracluster correlation coefficient of .05, in accordance with past studies (Bostrom et al., 2016; Underwood et al., 2013). The certainty of evidence contributing to network estimates was assessed according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Salanti, Del Giovane, Chaimani, Caldwell, & Higgins, 2014).

Data were analysed and figures were generated using STATA/SE 15.1 (StataCorp, 2017). Comparison-adjusted funnel plots were used to evaluate publication bias and small-study effects. Meta-regression was used to investigate modifying effects of age, gender, source of participants, length of intervention, exercise intensity, frequency, duration, and format of program, which have been identified as potential risks to transitivity in geriatric meta-analyses (Netz et al., 2005; Rhyner & Watts, 2016; Schuch et al., 2016).

A multivariate random-effects meta-analysis was conducted using the ‘mvmeta’ command (White, 2009). A random-effects model assumes variance both within and between studies, explaining the heterogeneity of treatment effects (Borenstein, Hedges, Higgins, & Rothstein, 2010). A common heterogeneity parameter was assumed across comparisons. Heterogeneity was evaluated using tau-squared (τ^2), which estimates the deviation in effect sizes across the population of studies (Borenstein et al., 2009). The 95% prediction interval (*PrI*) was also used to estimate the true dispersion of effect within two standard deviations of the mean effect size (Borenstein et al., 2009). The significance level was $p < .05$ for all analyses.

6.4. Results

6.4.1. Study selection

The initial systematic search yielded a total of 3,704 citations. When duplicate studies were removed (n = 1,395), 2,309 eligible records were identified. Titles and abstracts were screened by two independent researchers (KJM and DCGB) with an agreement of 91.9%. Subsequently, 356 full-text articles were assessed for compliance with inclusion criteria and outcome data. Full-text screening was performed independently by two researchers (KJM and PA) with an agreement of 81.8%, where discrepancies were arbitrated and resolved by consensus with a third researcher (CM). Studies using duplicate sample sets (*n* = 12) were identified, where the most informative publication with complete data being included in the quantitative analysis. Finally, 81 studies fulfilled all inclusion criteria to be included in the systematic review. In cases of missing data, authors were emailed by the first author (KJM). If authors failed to respond following two contact efforts, and there were insufficient data to calculate effect size estimates, the study was excluded from the quantitative analysis (*n* = 9). Additionally, three studies (Dong, Lee, Kim, & Kim, 2013; Dorner et al., 2007; Emery & Gatz, 1990) fulfilled all criteria but necessitated exclusion from the quantitative analysis due to control conditions being insufficiently defined, and the authors being unobtainable. *Figure 6.1* outlines study selection and additional exclusion criteria.

6.4.2. Characteristics of the studies

Data from a total of 5,379 participants (2,815 treatment and 2,564 control) across 69 studies were pooled in the quantitative analysis. Each study reported pre- and post-treatment measures of depression symptoms, and data from 60 of the 69 studies were obtained for post-treatment attrition. *Figure 6.2* illustrates the network of pairwise comparisons across all studies. Aerobic, resistance, and mind-body conditions had one or more direct comparison with each of the five comparison conditions. Direct comparisons for depressive symptoms were robustly characterised between intervention and corresponding control conditions (aerobic = 28, resistance = 22, mind-body = 32), with proportions being similar for study attrition (aerobic = 24, resistance = 21, mind-body = 25).

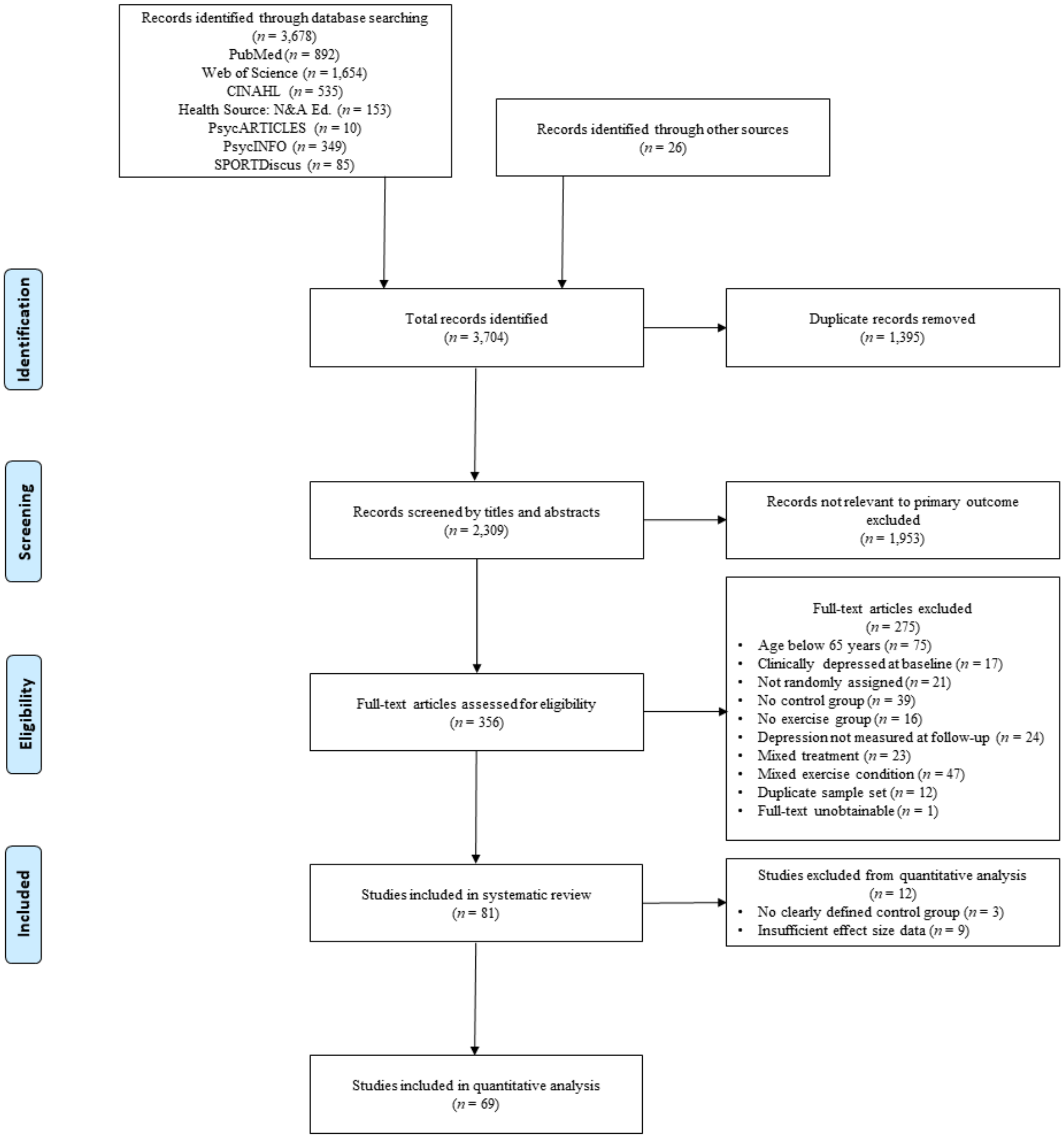

Figure 6.1. Flowchart of screening process.

From the 69 included studies, 43 studies enrolled young-old samples (65-75 years) and 26 studies enrolled old-old samples (>75 years). Participants were identified as either community-dwelling (*n* = 46), living in residential care (*n* = 18), clinical (*n* = 4), or uncategorised (*n* = 1). Twelve studies enrolled participants with sedentary lifestyles, while the remainder enrolled participants with a range of active and sedentary lifestyles. Some studies recruited older adults that were either frail (*n* = 5), wheelchair bound (*n* = 3), or identified as presenting with a risk of falling (*n* = 2). Participants with age-associated comorbidities were also recruited, including cardiovascular problems (*n* = 6), dementia (*n* = 3), cognitive impairment (*n* = 3), cancer (*n* = 2), and other chronic illness (*n* = 6).

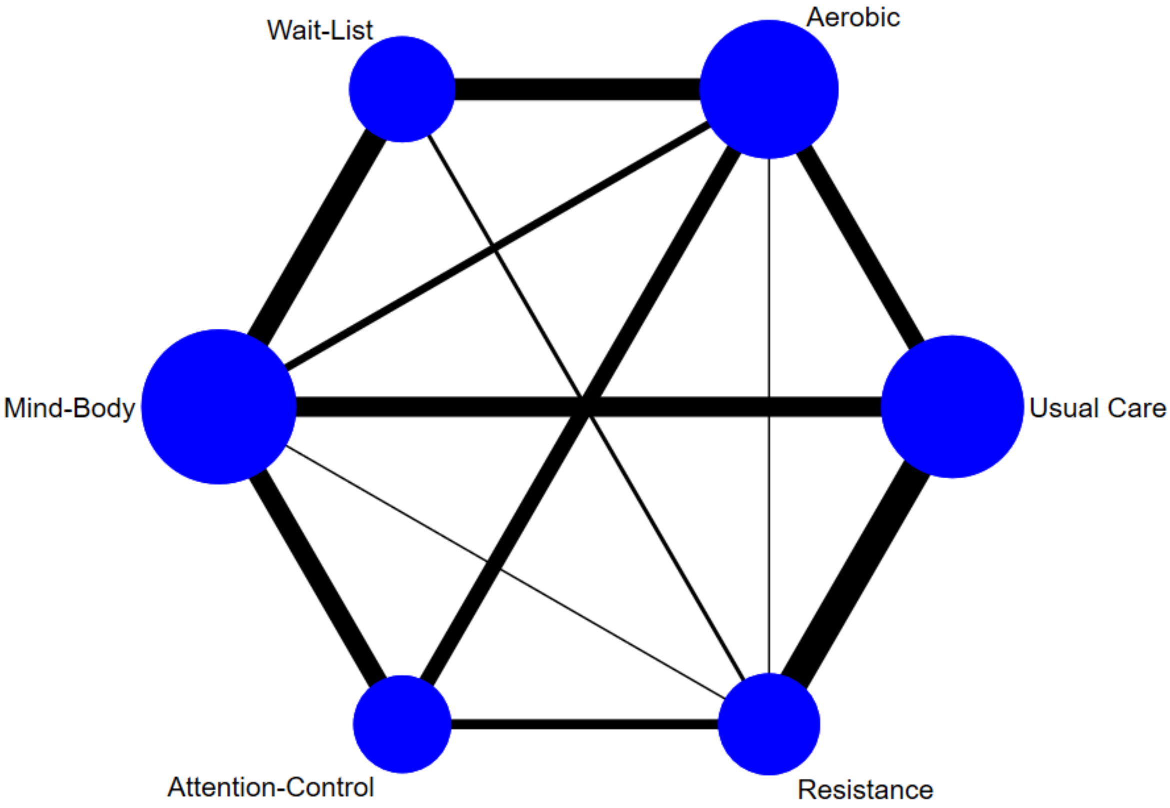

Figure 6.2. Network plot of comparisons for all studies included in the network meta-analysis. Line width is proportional to the number of pairwise effect size estimates and node size is proportional to the number of participants.

From 79 independent exercise interventions, the majority were supervised in group exercise classes (*n* = 64). The remainder were either individually supervised (*n* = 5), unsupervised in an individual format (*n* = 2), supervised in an undisclosed format (*n* = 1), or entirely undisclosed (*n* = 1). The average exercise program length (weeks) was shorter for mind-body (*M* = 13.67, *SD* = 6.77) than aerobic (*M* = 19.76, *SD* = 14.44) or resistance (*M* = 18.00, *SD* = 9.07). Average weekly exercise minutes (calculated as frequency multiplied by duration) were calculated for aerobic (*M* = 107.78, *SD* = 40.88), resistance (*M* = 126.90, *SD* = 50.28), and mind-body exercise (*M* = 132.75, *SD* = 76.07). Treatment adherence (*n* = 44) was comparable between aerobic (*M* = 81.01, *SD* = 13.72), resistance (*M* = 81.17, *SD* = 9.00), and mind-body exercise (*M* = 79.34, *SD* = 14.73). Adverse events were observed during several of the included trials, which are presented in *Table 6.2*.

Table 6.2

Adverse events from included studies

Exercise Group	**Study**	**Adverse Event(s)**
Aerobic	Kupecz (2001)	Minor medical attention (*n* = 2)
	Oken (2006)	Hip pain (*n* = 1)
Resistance	Ansai (2015)	Mild muscle pain (*n* = 9)
	Chin A Paw (2004)	Program was too intensive (*n* = 8)
	Clegg (2014)	Fell at least once (*n* = 7)
Mind-body	Cramer (2016)	Muscle soreness (*n* = 3), abdominal pain (*n* = 1), neck pain (*n* = 1), minor vertigo (*n* = 1), hip pain (*n* = 1)
	Eyre (2017)	Dizziness (*n* = 1)
	Oken (2006)	Groin muscle strain (*n* = 1)

6.4.3. Risk of bias and quality assessment

Risk of bias for each study is presented comprehensively in *Appendix H* (see *Figure H1*). Both blinding of participants and personnel to treatment was implausible due to the implicit nature of exercise training interventions, and thus, the remaining six criteria were used to assess the overall risk of bias within each study. Methodological quality of included studies can be considered low-to-moderate (M = 4.08/6, where low = 1, unclear, = 0.5, high = 0). Assessment of random sequence generation (selection bias), incomplete outcome data (attrition bias), and selective outcome reporting (reporting bias) may be considered adequate for most studies, whereas allocation concealment (selection bias) and blinding of outcome assessment (detection bias) were diverse. High ‘other sources of bias’ was due to low study adherence (n = 14), small sample sizes (n = 8), or both (n = 1). See *Figure 6.3* for a summary of the risk of bias in the included studies.

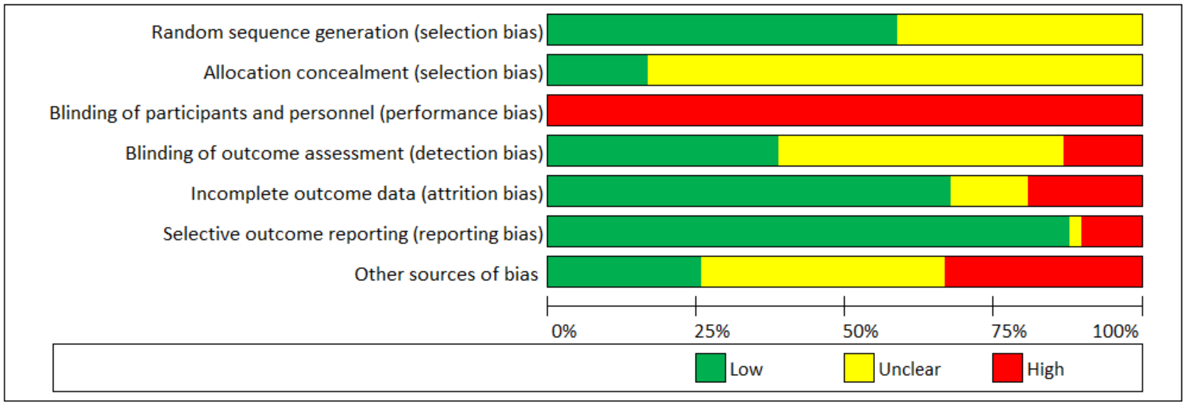

Figure 6.3. Risk of bias chart of studies included in the quantitative analysis.

6.4.4. Assessment of inconsistency

Inconsistency network models were used to test the global consistency of direct and indirect effects of pairwise and multi-arm comparisons. Assumption of consistency was satisfied for each treatment ($p > .05$). Tests for inconsistency between direct and indirect estimates were not significant ($p > .05$), thus indirect and direct estimates were not different to direct evidence. Inconsistency tables can be found in *Appendix H* (see *Tables S1* and *S2*).

Loop-specific heterogeneity was explored using inconsistency plots (see *Appendix H, Figure H7* and *H8*). Within the depressive symptoms network, inconsistency factors (*IF*) did not indicate high inconsistency ($IF = 0.00$ to 0.65) or loop-specific heterogeneity ($\tau^2 = 0.05$ to 0.28). The AER-MB-UC loop departed from the minimum lower-bound confidence interval (*CI*), yet fell short of presenting risk for heterogeneity ($IF = 0.54$, $\tau^2 = 0.05$, $CI = 0.04, 1.03$). Within the attrition network, the ratio of two odds ratios (*RoR*) indicated a high degree of inconsistency for the AER-RES-UC ($RoR = 1.87$) and MB-RES-UC ($RoR = 1.77$) loops. Each were interpreted as presenting elevated risk for heterogeneity, which were subsequently downgraded during GRADE assessment. All remaining loops satisfied assumption of consistency.

6.4.5. Publication bias and sensitivity analyses

Comparison-adjusted funnel plots were used to detect publication bias and small-study effects. Funnel plots were roughly symmetrical for both depressive symptoms and attrition, indicative of low publication bias from small-study effects. See *Figure 6.4* for the depressive symptoms network and *Appendix H* for the attrition network (see *Figure H9*).

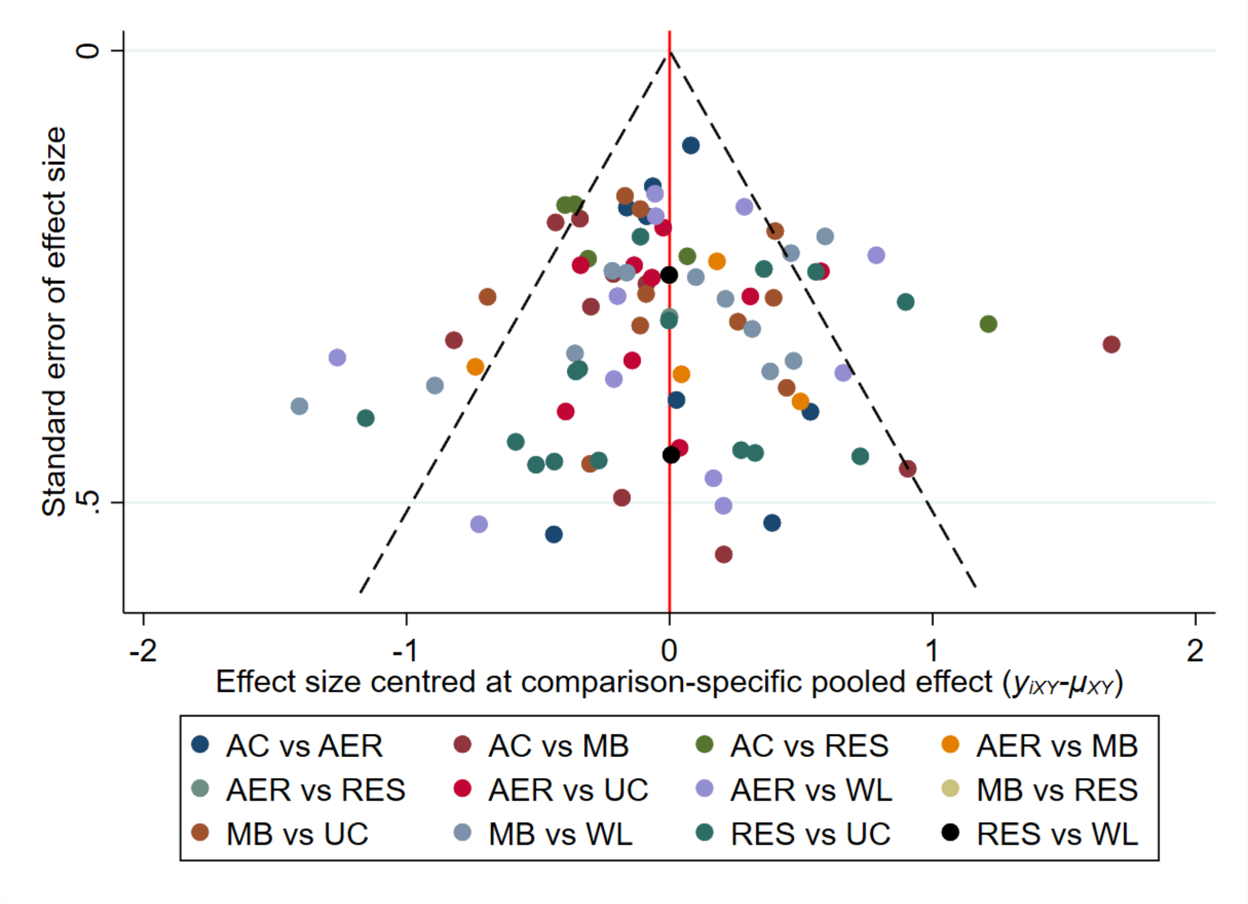

Figure 6.4. Comparison-adjusted funnel plot for the depressive symptoms network. The red line represents the null hypothesis that independent effect size estimates are not different to comparison-specific pooled estimates. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

In order to test transitivity across networks, potential effect modifiers were tested with meta-regression sensitivity analyses for the entire pool of studies and separately for each exercise comparison (aerobic vs. resistance vs. mind-body). No significant modifying effects were observed for the pool of studies or any separate exercise comparison for age, gender, source of participants, length of intervention, format of program, exercise intensity, frequency, duration, adherence, year of study, risk of bias, publication status, intention-to-treat analysis, nor cluster design, indicating that the assumption of transitivity was upheld. Full analyses are presented in *Appendix H* (see *Tables S6-S8*).

6.4.6. Results of the network meta-analysis

Data pooled from 69 eligible studies provided a total of 88 individual comparisons for depressive symptoms and 76 individual comparisons for study attrition. *Table 6.3* presents the network meta-analysis of depressive symptoms and attrition. Network estimates were calculated to establish relative effectiveness between pairs of comparisons.

Table 6.3

League table for head-to-head comparisons

Wait-List	-0.11 (-0.40, 0.17)	-0.45 (-0.77, -0.13)	-0.51 (-0.74, -0.27)	-0.39 (-0.63, -0.14)	-0.12 (-0.41, 0.18)
1.10 (0.48, 2.48)	**Usual Care**	-0.34 (-0.57, -0.10)	-0.39 (-0.62, -0.16)	-0.27 (-0.51, -0.04)	-0.00 (-0.27, 0.27)
0.74 (0.30, 1.83)	0.68 (0.37, 1.26)	**Resistance**	-0.06 (-0.33, 0.22)	0.06 (-0.22, 0.35)	0.33 (0.05, 0.61)
1.00 (0.50, 2.01)	0.92 (0.47, 1.77)	1.35 (0.61, 2.99)	**Mind-Body**	0.12 (-0.12, 0.35)	0.39 (0.15, 0.63)
1.03 (0.50, 2.14)	0.94 (0.48, 1.84)	1.39 (0.62, 3.10)	1.03 (0.51, 2.07)	**Aerobic**	0.27 (0.02, 0.52)
1.03 (0.41, 2.57)	0.94 (0.41, 2.12)	1.38 (0.60, 3.19)	1.02 (0.47, 2.23)	1.00 (0.46, 2.15)	**Attention-Control**

Note. Depressive symptoms (upper) are reported as Hedges' *g* and 95% confidence intervals. Negative scores indicate a greater decrease in depressive symptom for the column group. Attrition (lower) is reported as odds ratios and 95% confidence intervals. An odds ratio lower than 1 indicate a greater attrition for the column-defining comparison.

Each exercise type effectively reduced depressive symptoms compared with control conditions (see *Figure 6.5*). Ranking of treatments for depressive symptoms are presented on SUCRA plots of ranked mean values, which can be found in *Appendix H* (see *Figure H11* and *Table H3*). Ranked order of quantitative values determined mind-body exercise to be the most effective type of exercise to mitigate depressive symptoms, followed closely by resistance and aerobic exercise, respectively. The magnitude of study effect did not reach statistical threshold to favour any individual exercise treatment.

Resistance exercise demonstrated the highest study compliance compared with each of the other comparison groups, but the dispersion of effect estimates presented a level of heterogeneity that confounded any substantive differences. Comprehensive reporting of study attrition can be found in *Appendix H* (see *Figure H10*) in addition to SUCRA plots and ranked order (see *Figure H12* and *Table H4*).

6.4.7. Effectiveness vs. attrition

A two-dimensional clustered ranking plot was employed to illustrate the average reduction in depressive symptoms for each comparison, relative to average attrition rate. *Figure 6.6* presents the ranking of the exercise conditions with respective control conditions in conjunction with SUCRA values for depressive symptoms (effectiveness) and attrition. The three exercise conditions amalgamated a single cluster and were more effective than control conditions.

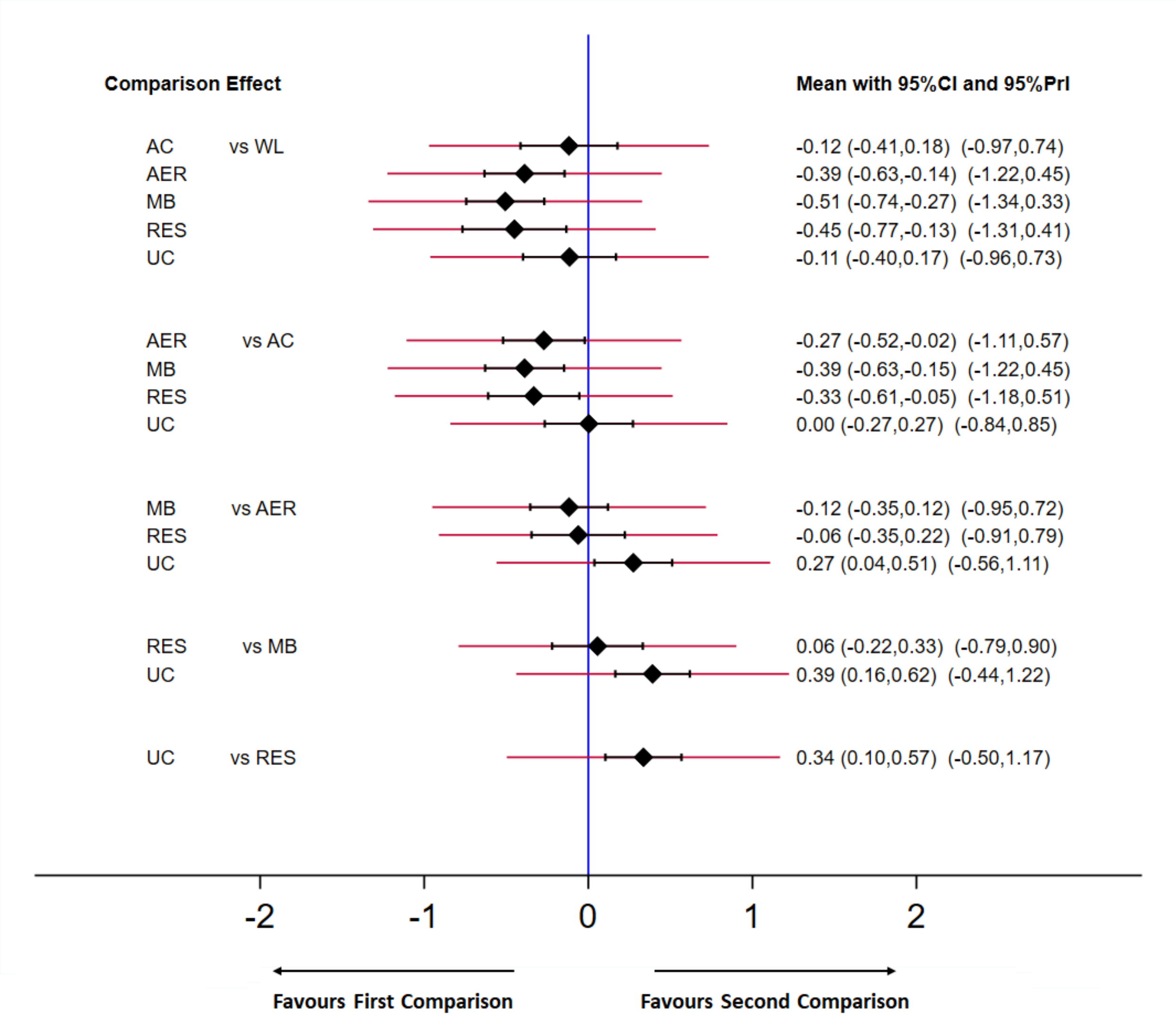

Figure 6.5. Predictive interval plot for the depressive symptoms network. Black diamonds represent the difference in the effect size estimate (Hedges' *g*). Narrow horizontal lines represent the confidence intervals (*CI*) and the wider horizontal lines represent the prediction intervals (*PrI*). The blue vertical line represents the null hypothesis (Hedges' *g* = 0). Negative scores indicate a greater decrease in depressive symptom for the comparison (left) group. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

6.4.8. GRADE assessment

The certainty of evidence was assessed with the GRADE approach (Salanti et al., 2014). All control comparisons in the depressive symptoms network were rated as high or moderate certainty, which were downgraded due to small sample size or potential risks of bias (i.e., attrition bias, detection bias, or bias resulting from low adherence). Comparisons between exercise interventions were moderate-to-low certainty, resulting from imprecision in confidence intervals and small sample sizes. Detailed summary of the depressive symptoms network is presented in *Table 6.4*. Estimates of the attrition network were downgraded due to inconsistency and imprecision, which reflect moderate to very low confidence this outcome (see *Supplementary File H1, Table H5*).

6.4.9. Generalisation for all adults aged ≥ 65 years

Figure 6.7 presents collective representation for all adults aged ≥ 65 years. This comparison employs scaled distribution (Hedges' *g*) for the present data and that of clinically depressed older adults (Miller et al., 2020).

6.5. Discussion

The present review offers new information for general exercise prescription to support mental health outcomes for adults aged ≥ 65 years. Specifically, (i) aerobic, resistance, and mind-body each demonstrate equivalent benefit to mitigate symptoms of depression in adults aged ≥ 65 years, (ii) compliance to exercise treatment is notably encouraging for each exercise types, and (iii) when combined with the pool of data from clinically depressed older adults (Miller et al., 2020), the effectiveness of aerobic, resistance, and mind-body exercise is comparably consistent for all adults aged ≥ 65 years, irrespective of depression severity. These findings should provide reassurance for personnel and stakeholders in healthy ageing to encourage exercise prescription from a point of pragmatism and in collaboration with patient preference.

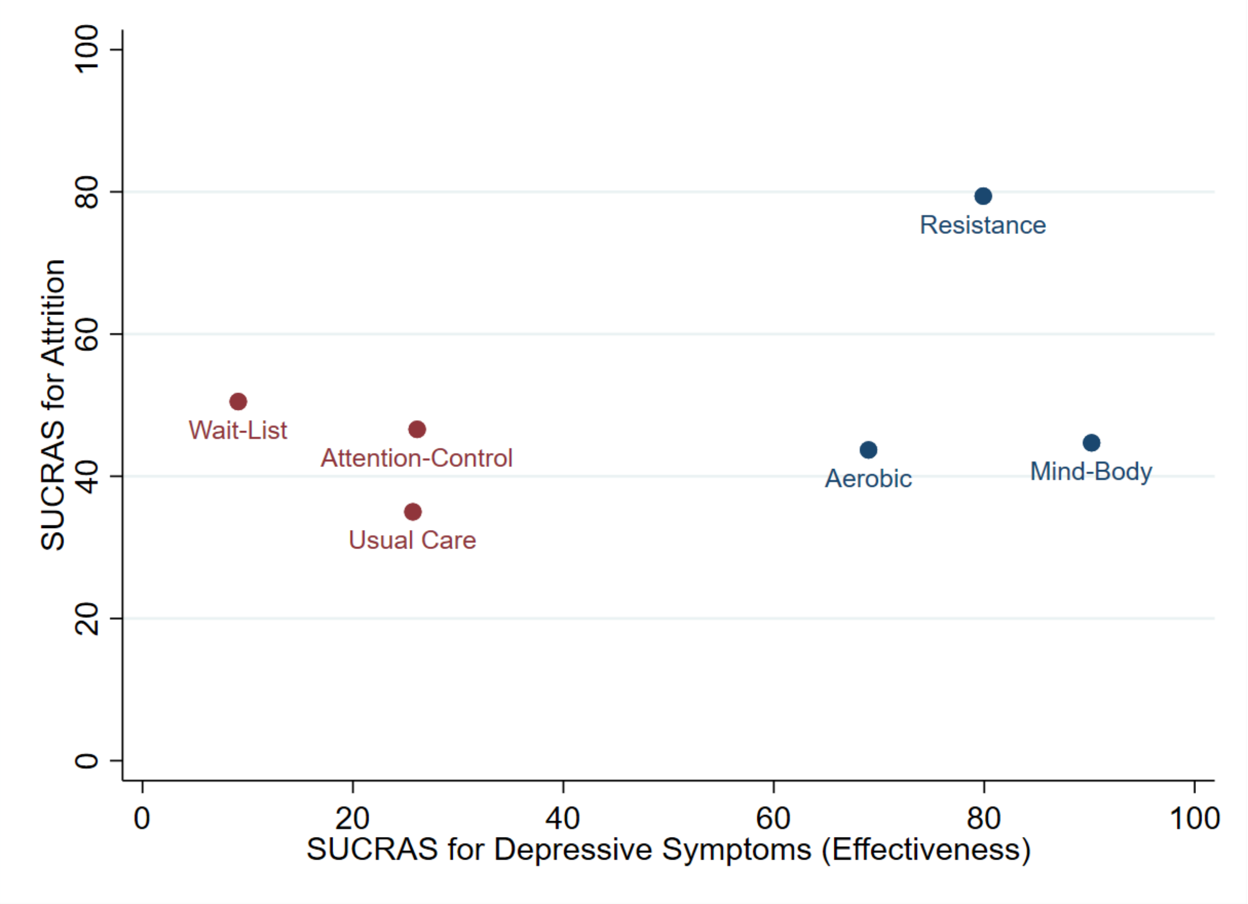

Figure 6.6. Clustered ranking plot of the network based on clustered analysis of SUCRA values for depressive symptoms (effectiveness) and attrition outcomes. Each colour represents a group of treatments that belong to the same cluster. Treatments in the upper right corner represent effective treatments with low attrition.

6.5.1. Theoretical implications for the current findings

In agreement with findings from previous research (Martins et al., 2011; Penninx et al., 2002; Schuch et al., 2016), aerobic and resistance exercise demonstrated similar treatment effectiveness in older samples aged ≥ 65 years (Hedges' g = -0.06, *PrI* = -0.91, 0.79). Exercise characteristics (i.e., intensity, frequency, duration, etc.) are often similar between aerobic and resistance exercise, representing two sides of the same coin. Meta-analytical data (Bridle et al., 2012) on older adults with existing clinical depression observed that exercise programs incorporating a combination of aerobic and resistance training were most beneficial. Although the synergistic effects of combined exercise types were beyond the scope of the current review, it is conceivable that aerobic and resistance exercise may complement one another in an exercise intervention.

Pooled direct and indirect estimates marginally favoured treatment with mind-body exercise over either aerobic (Hedges' g = -0.12, *PrI* = -0.95, 0.72) or resistance exercise (Hedges' g = -0.06, *PrI* = -0.90, 0.79). However, it must be noted that the magnitude of effect falls short of being statistically different between groups. Certainty of evidence is moderate, due to the dispersion in effect size estimates resulting in imprecision. Direct comparisons from multi-arm RCTs have offered mind-body exercise to be more effective than aerobic (Oken et al., 2006) or resistance (Bonura & Tenenbaum, 2014) exercise. Moreover, subgroup analyses (Heinzel et al., 2015) have indicated that clinically depressed older adults respond more favourably to mind-body exercise, but this hypothesis has not be substantiated (Rhyner & Watts, 2016).

Table 6.4

Summary of GRADE assessment for the certainty in depressive symptoms estimates

Comparison Effect	**Number of Participants**	**Number of Direct Comparisons**	**Nature of Evidence**	**Certainty**	**Reason for Downgrading**
Aerobic vs. wait-list	371 vs. 357	11	Mixed	High	None
Aerobic vs. usual care	309 vs. 310	9	Mixed	Moderate	Risk of bias[a]
Aerobic vs. attention-control	431 vs. 472	8	Mixed	High	None
Resistance vs. wait-list	43 vs. 42	2	Mixed	Moderate	Imprecision[b]
Resistance vs. usual care	358 vs. 272	15	Mixed	High	None
Resistance vs. attention-control	267 vs. 274	5	Mixed	Moderate	Risk of bias[c]
Mind-body vs. wait-list	380 vs. 363	12	Mixed	High	None
Mind-body vs. usual care	358 vs. 356	10	Mixed	Moderate	Risk of bias[d]
Mind-body vs. attention-control	298 vs. 265	10	Mixed	High	None
Aerobic vs. resistance	24 vs. 23	1	Mixed	Low	Imprecision[be]
Aerobic vs. mind-body	90 vs. 83	4	Mixed	Moderate	Imprecision[e]
Resistance vs. mind-body	33 vs. 33	1	Mixed	Low	Imprecision[be]

[a] Potential attrition bias due to high number of studies with incomplete outcome data.

[b] Small sample size.

[c] Potential risk of bias due to high number of studies with low adherence.

[d] Potential detection bias due to high number of studies without blinding of outcome.

[e] Confidence intervals include values favouring either treatment.

Since mind-body exercise engages low intensity muscular activity (i.e., yoga, tai chi, qigong), the novel evidence in the current systematic analysis challenge the idea that intensity is the primary mechanism for the antidepressive effect of exercise. Rather, mind-body exercise combines the mental and physical aspects of exercise, which may result in similar antidepressive effects to higher intensity physical exercise (La Forge, 1997; Prakhinkit et al., 2014). Critical to these mental aspects is interoceptive sensations such as an internally directed focus on breathing and proprioception, which have previously been linked to the resilience of depressive states (Avery et al., 2014; Paulus & Stein, 2010). Thus, it is plausible that mind-body exercise allows older adults to regulate negative mood states, which is not normally possible during aerobic and resistance activities.

Other important determinants of successful programming include study attrition, adherence rate, and adverse events. Here, we hypothesised that each exercise conditions would demonstrate lower compliance to treatment than wait-list, usual care, and attention-control comparisons. Contrary to expectations, pooled direct and indirect estimates indicated that study attrition was comparable for all comparisons apart from resistance exercise, which offered a higher degree of compliance. However, on deeper scrutiny of absolute sample size, any differences observed in attrition become abrogated due to relatively smaller participant numbers within the resistance exercise studies (*n* = 705) compared with aerobic (*n* = 1,143) or mind-body (*n* = 1,005). Thus, in consideration of the wide dispersion in effect size estimates and a moderate risk of bias in individual studies, there are limitations in the certainty to confidently conclude substantive difference in study attrition between any comparisons.

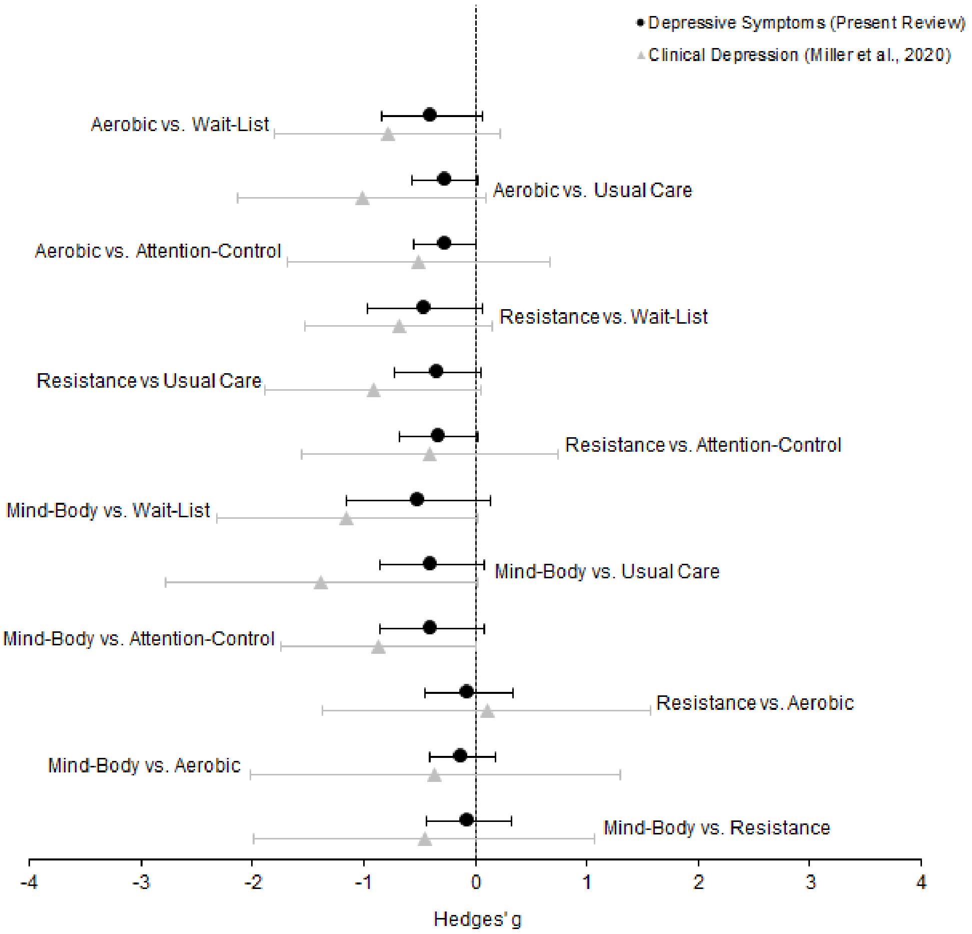

Figure 6.7. Forest plot depicting juxtaposed collective RCT evidence of older adults (*n* = 5,975) in the depressive symptoms network. Circles represent the difference in the effect size estimate (Hedges' *g*) for those with depressive symptomology but not diagnosed with clinical depression (*n* = 5,379). Triangles represent the difference in the effect size estimate (Hedges' *g*) for those with clinical depression (*n* = 596; effect sizes adapted from Miller et al., 2020). Horizontal lines represent the confidence intervals (*CI*). The dotted vertical line represents the null hypothesis (Hedges' *g* = 0). Negative scores indicate a greater decrease in depressive symptom for the left group, and vice versa.

Each of the three types of exercise had similar adherence rates and time spent per week (calculated as frequency multiplied by duration). Interestingly, mind-body exercise had relatively shorter intervention length than either aerobic or resistance exercise (M_{diff} = 6.09 and 4.33 weeks, respectively) despite having a greater reduction in depressive symptoms. This could be explained by (i) mind-body exercise having the same antidepressive effects in a shorter time than aerobic and resistance exercise, or (ii) a potential plateau effect whereby the antidepressive effects reach a maximum threshold during the first 10-15 weeks of an exercise program and are then maintained during the remaining weeks. Either way, it seems plausible that mind-body exercise provides a slightly more effective intervention against depressive symptoms in older populations without clinical depression, but that these treatment effects are not substantive enough to constitute statistical difference.

6.5.2. Practical considerations

With consideration to projected population estimates over the next decade and the consequential demand on healthcare services (James et al., 2018; United Nations, 2019), the findings from this network meta-analysis offer a message of support for exercise prescription to promote mentally healthy ageing. When considering the collective findings of the present review in conjunction with the recent network meta-analysis in clinically depressed adults aged ≥ 65 years (Miller et al., 2020), stakeholders in healthy ageing and exercise prescription have encouraging pooled RCT evidence for the antidepressant effects of either aerobic, resistance, or mind-body exercise for older adults across the mental health continuum.

Treatment safety is a matter of ongoing importance in gerontological health, and exercise treatment programs are no different. Systematic scrutiny of the included RCTs found that study participants reported no major adverse events and only a few minor somatic complaints (*n* = 28). Taken together, this provides encouraging support for personnel wanting to safely prescribe exercise-based intervention programs in older populations. Of course, there is always a possibility of underreporting adverse events in clinical trials, and the present review was no exception. Therefore, the importance of reporting event outcomes, adverse or otherwise, cannot be understated. In fact, there is a known phenomenon in geriatric exercise research whereby adverse events are often underreported because authors do not consider minor adverse events to be noteworthy and/or essential to the primary purpose of the trial (Liu & Latham, 2010), giving rise to an ongoing issue that will not be corrected until all studies routinely report event outcomes.

Nevertheless, participants engaging in aerobic exercise reported the least adverse events (*n* = 3), including minor medical attention and hip pain. Amongst studies included in this meta-analysis, aerobic exercise predominantly involved walking and stationary cycling, which may reflect a safe and natural form of exercise for older adults. Resistance exercise was typically associated with participants experiencing mild muscular pain and falls (*n* = 16), which may be explained by the progressive overloading of resistance-based training. Notably, incidents of falling were reported in an unsupervised exercise program. Finally, mind-body exercise was typically associated with different types of muscular pain and body strain (*n* = 9). It is speculated that the higher rates of injury in mind-body exercise are predominantly because it incorporates flexibility, balance, and stability movements, which may be unique to older bodies. In general, exercise seems to be a relatively safe intervention for older adults living in both the local community and residential aged care, although intensity and supervision, particularly for resistance training, should be monitored to ensure falls and injury do not occur.

The present review has some notable advantages above a traditional pairwise meta-analysis. RCTs with considerable non-exercising components, such as those using a multicomponent exercise intervention, were excluded because they may have overestimated the magnitude of the true effect in past reviews. Specifically, it is likely that multicomponent exercise interventions such as laughter therapy (Hirosaki et al., 2013), depression awareness training (Underwood et al., 2013), or self-efficacy training (Resnick, Luisi, & Vogel, 2008) may have introduced a risk of bias by inflating the observed effectiveness of the exercise program on depressive symptoms through a secondary, complementary treatment effect. Pairwise meta-analysis also assumes that all control groups are the same, which is not always the case (Pagoto et al., 2013). To manage heterogeneity from this assumption, control groups were separated into individual network comparisons. Taken together, the current findings provide a more accurate estimate of the true effects of exercise on depressive symptoms in adults aged ≥ 65 years.

6.5.3. Limitations and future directions

The present network meta-analysis is not without limitations. As study participants and personnel cannot be successfully blinded, there is an inherent risk of performance bias. It is also believed that many exercise-based interventions have a small number of participants, shorter follow-up, and do not adequately conceal randomisation (Daley & Jolly, 2012), which are all likely to reduce the quality of RCTs and increase the risk of bias. However, we mitigated the impact of this by comparing relative effects with multiple control groups in order to increase reliability and specificity. This, combined with the relatively low risk of bias in individual RCTs, were extremely important in minimising overall risk of bias and achieving accurate effect comparisons in the present review.

Since most RCTs did not explicitly describe the exclusion of participants with ongoing diagnosis of clinical depression, there was potential contamination with data from participants with existing clinical diagnosis and medical treatment that went unreported. This was primarily managed by separating (i) participants with depressive symptomology but not clinically diagnosed in the present review from (ii) participants with clinical depression in a previous network meta-analysis (Miller et al., 2020). Within this review, we further mitigated this effect modifier by only including RCTs, where this risk would be balanced by control participants. We recommended that ageing researchers encourage the reporting all ongoing pharmacological regimens in trials recruiting older participants.

Although modifying effects were explored using meta-regression, important participant (e.g., age, gender) and exercise (e.g., fitness improvements, length of program, session frequency and duration, exercise intensity, supervision, group format) modifiers were outside the scope of our network meta-analysis. There has been a modicum of such exploration in subgroup and meta-regression analyses of previous reviews (Heinzel et al., 2015; Rhyner & Watts, 2016; Schuch et al., 2016), providing researchers with an encouraging opportunity in their planning of future similar work. Future meta-analyses with extensive subgroup analyses should explain the heterogeneity of effect sizes between similar exercise intervention studies in older persons.

6.5.4. Conclusions

Pooled RCT evidence highlights that each individual exercise mode (aerobic, resistance, and mind-body) can effectively mitigate symptoms of depression in older adults, irrespective of depression severity. As each exercise treatment demonstrated encouraging levels of treatment compliance, we endorse personnel and stakeholders in healthy ageing to encourage individual/patient preference when prescribing exercise to older adults ≥ 65 years presenting with depressive symptomology.

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CHAPTER VII

Thesis Hypotheses and Realisation of Aims

Hypothesis 1a (H_1): Aerobic capacity (VO_{2max}) will change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong athletic control

Previously sedentary older adults who continued regular aerobic exercise (*n* = 11) improved aerobic capacity during the 4-year period by 5.9%, which was comparable to the 5.4% improvement in lifelong exercisers (*n* = 12). As might be expected, sedentary participants who continued regular aerobic exercise had lower aerobic fitness during baseline and 4-year follow-up (*M* = 29.4 vs. 30.8 ml kg min^{-1}) compared to lifelong exercisers (*M* = 39.5 vs. 41.9 ml kg min^{-1}). Based on this preliminary evidence, continued regular exercise does improve the aerobic capacity of older adults. Therefore, the null hypothesis (H_0) was rejected, and the alternative hypothesis (H_1) was accepted.

Hypothesis 1b (H_1): Aerobic capacity (VO_{2max}) will change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong sedentary control

Lifelong sedentary older adults who did not exercise (*n* = 6) had a 7.5% decrease over 4-years in aerobic capacity compared with a converse 5.9% improvement for those who continued regular aerobic exercise (*n* = 11). Interestingly, sedentary participants who continued regular aerobic exercise had higher aerobic fitness during both baseline and 4-year follow-up (*M* = 29.4 vs. 30.8 ml kg min^{-1}) compared to lifelong sedentary older adults (*M* = 23.8 vs. 22.2 ml kg min^{-1}). Given this preliminary evidence, continued regular aerobic exercise does maintain the aerobic capacity of older adults and can counteract the natural decline of aerobic fitness that is typically associated with ageing. Therefore, the null hypothesis (H_0) was rejected, and the alternative hypothesis (H_1) was accepted.

It is worthy of note that lifelong exercisers that ceased exercise lost a substantial 20.9% aerobic capacity over the 4-year non-training period (M = 36.3 vs. 28.8 ml kg min^{-1}). Although this was not aligned with a specific hypothesis, these novel findings provide further support to the benefit of long-term exercise on aerobic capacity. Taken together, results from this study offers preliminary evidence for the benefits of physical exercise on cardiorespiratory function even when it is adopted later in life.

Hypothesis 2a (H_1): Self-perceived HRQL will change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong athletic control

Previously sedentary older adults who continued regular aerobic exercise (n = 11) had general improvements in HRQL during the 4-year period (M = 79.3% vs. 87.3%), whereas lifelong exercisers (n = 12) tended to maintain their HRQL (M = 86.8% vs. 85.2%). Sedentary participants who continued regular aerobic exercise predominantly had improvements in physical functioning (M_{diff} = +16.4%), whereas lifelong exercisers perceived role limitations due to physical health as being most detrimental to their quality of life (M_{diff} = -12.5%). These findings support the benefits of long-term exercise on HRQL in older adulthood. Therefore, the null hypothesis (H_0) was rejected, and the alternative hypothesis (H_1) was accepted.

Hypothesis 2b (*H_1*): Self-perceived HRQL will change after four years of regular aerobic exercise in sedentary ageing men compared with age-matched lifelong sedentary control

Lifelong sedentary older adults who did not exercise (*n* = 6) generally had lower self-rated perceptions of HRQL over 4-years (*M* = 75.5% vs. 73.7%) compared with those who continued regular aerobic exercise (*n* = 11; *M* = 79.3% vs. 87.3%). Lifelong sedentary older adults perceived worsening general health (M_{diff} = -10.8%), pain (M_{diff} = -7.5%), role limitations due to physical health (M_{diff} = -13.5%), and role limitations due to emotional problems (M_{diff} = -9.7%) as being most detrimental to their quality of life. These findings offer preliminary evidence for the HRQL benefits of commencing exercise in later life. Therefore, the null hypothesis (H_0) was rejected, and the alternative hypothesis (H_1) was accepted.

Notably, lifelong exercisers that ceased exercise showed a substantial decrease in all eight domains of HRQL, as well as a general worsening in quality of life over the 4-year non-training period (*M* = 89.4% vs. 82.3%). Taken together, findings from Study 1 demonstrate preliminary proof of concept for exercise-induced benefits on cardiorespiratory function and perceived HRQL in ageing men. In light of the lack of existing longitudinal research, the data from Chapter III provide evidence as to how the physiological effects of exercise can cultivate long-term improvements in psychological well-being.

Hypothesis 3a (H_0): Exercise behaviour will not predict depressive symptoms in community-dwelling older adults, when controlling for mood, self-efficacy, social support, health status, physical functioning, age, and gender

Contrary to expectations, exercise behaviour (measured as the number of calories expended per week) did not significantly predict depressive symptoms in a sample of community-dwelling older adults ($n = 586$). This indicates that the physical characteristics of exercise, such as calorie expenditure and time spent in activities, do not add any additional predictive value beyond mood states, self-efficacy, and social support. Therefore, the null hypothesis (H_0) was accepted, and the alternative hypothesis (H_1) was rejected.

Hypothesis 3b (H_1): Exercise-induced mood will significantly predict depressive symptoms in community-dwelling older adults, when controlling for exercise behaviour, self-efficacy, social support, health status, physical functioning, age, and gender

Exercise-induced mood significantly predicted depressive symptoms in a sample of community-dwelling older adults ($n = 586$). Exercise-induced mood uniquely explained 3.2% of the variance in depressive symptomology. This indicates that positive mood states induced by exercise can predict lower depressive symptoms, whilst negative mood states can predict greater depressive symptoms. Therefore, the null hypothesis (H_0) was rejected, and the alternative hypothesis (H_1) was accepted.

Hypothesis 3c (H_1): Exercise self-efficacy will significantly predict depressive symptoms in community-dwelling older adults, when controlling for exercise behaviour, mood, social support, health status, physical functioning, age, and gender

Exercise self-efficacy significantly predicted depressive symptoms in a sample of community-dwelling older adults (n = 586). Exercise self-efficacy uniquely explained 0.4% of the variance in depressive symptomology. This indicates that healthier self-efficacy beliefs about exercise can predict lower depressive symptomology, and vice versa. Therefore, the null hypothesis (H_0) was rejected, and the alternative hypothesis (H_1) was accepted.

Hypothesis 3d (H_1): Social support will significantly predict depressive symptoms in community-dwelling older adults, when controlling for exercise behaviour, mood, self-efficacy, health status, physical functioning, age, and gender

Social support significantly predicted depressive symptoms in a sample of community-dwelling older adults (n = 586). Social support uniquely explained 15.4% of the variance in depressive symptomology. Taking into account the confines of existing research, this indicates that stronger social support is the best predictor of lower depressive symptomology, and vice versa. Therefore, the null hypothesis (H_0) was rejected, and the alternative hypothesis (H_1) was accepted.

Notably, in a subsequent analysis of interaction effects, a modest two-way interaction effect between exercise-induced mood and social support. No interaction effects were found for exercise-induced mood × exercise self-efficacy, nor exercise self-efficacy × social support. Although these interaction effects were not pertinent to the hypotheses, this demonstrates that when social support is low, positive mood states from exercise have a slightly stronger association with depressive symptoms in older adults.

To date, Study 2 provides the largest quantitative examination of exercise-related factors to predict depressive symptomology in older adults aged 65 years and over. Taken together, these data demonstrate that the combination of exercise behaviour, exercise-induced mood, exercise self-efficacy, and social support explain approximately of 26% of the variability in depressive symptoms. Hierarchical comparisons indicate that social support is the strongest predictor of depressive symptomology in community-dwelling older adults, followed by exercise-induced mood states, and exercise self-efficacy.

Hypothesis 4a (H_1): Collective RCT evidence will demonstrate that exercise training is more effective to treat depressive symptoms compared with control conditions in clinically depressed older adults

Pooled evidence from 596 participants (321 treatment and 275 controls) across 15 studies demonstrated that aerobic exercise (g = -0.51 to -1.02), resistance exercise (g = -0.41 to -0.92), and mind-body exercise (g = -0.87 to -1.38) were all significantly more effective for older adults with pre-existing clinical depression than control conditions (i.e., wait-list, usual care, attention-control). Therefore, the null hypothesis (H_0) was rejected, and the alternative hypothesis (H_1) was accepted.

Hypothesis 4b (H_0): Collective RCT evidence will demonstrate that mind-body exercise is equally as effective to treat depressive symptoms as aerobic or resistance exercise in clinically depressed older adults

Greater beneficial effects were observed for mind-body exercise, but they did not reach the threshold for clinical significance when compared to aerobic and resistance exercise: aerobic versus resistance (g = -0.10, *PrI* = -2.23, 2.03), mind-body versus aerobic (g = -0.36, *PrI* = -2.69, 1.97), or mind-body versus resistance (g = -0.46, *PrI* = -2.75, 1.83). Pooled RCT evidence failed to establish a hierarchy of therapeutic effectiveness in older adults with pre-existing clinical depression. Therefore, the null hypothesis (H_0) was accepted, and the alternative hypothesis (H_1) was rejected.

Hypothesis 5a (H_1): Collective RCT evidence will demonstrate that exercise training is more effective to reduce depressive symptoms compared with control conditions in apparently healthy older adults

Pooled evidence from 5,379 participants (2,815 treatment and 2,564 control) across 69 studies indicated that aerobic exercise (g = -0.27 to -0.39), resistance exercise (g = -0.33 to -0.45), and mind-body exercise (g = -0.39 to -0.51) were all significantly more effective for older adults with pre-existing clinical depression than control conditions (i.e., wait-list, usual care, attention-control). Therefore, the null hypothesis (H_0) was rejected, and the alternative hypothesis (H_1) was accepted.

Hypothesis 5b (H_0): Collective RCT evidence will demonstrate that mind-body exercise is equally as effective to reduce depressive symptoms as aerobic or resistance exercise in apparently healthy older adults

By employing network meta-analytical techniques, Studies 4 identified comparable effectiveness for all three major exercise types: aerobic versus resistance (Hedges' *g* = -0.06, *PrI* = -0.91, 0.79), mind-body versus aerobic (Hedges' *g* = -0.12, *PrI* = -0.95, 0.72), mind-body versus resistance (Hedges' *g* = -0.06, *PrI* = -0.90, 0.79). Pooled RCT evidence failed to establish a hierarchy of effectiveness in apparently health older adults without pre-existing clinical depression. Therefore, the null hypothesis (H_0) was accepted, and the alternative hypothesis (H_1) was rejected.

Hypothesis 6 (H_0): Collective RCT evidence will demonstrate equal levels of attrition in exercise conditions compared with control conditions in apparently healthy older adults

A sufficiently large sample size in the network meta-analysis allowed the comparison of attrition rates across exercise and control groups. Both aerobic and mind-body exercise had similar levels of attrition as the three control conditions (i.e., wait-list, usual care, attention-control). On the contrary, resistance exercise showed slightly lower levels of attrition than all other groups. After scrutiny of absolute sample size, it appeared that any difference observed in attrition was abrogated by wide dispersion in effect size estimates in combination with relatively smaller participant numbers within the resistance exercise studies (*n* = 705) compared to aerobic (*n* = 1,143) or mind-body (*n* = 1,005). Therefore, the null hypothesis (H_0) was accepted, and the alternative hypothesis (H_1) was rejected.

Taking the results from Studies 3 and 4 together, these data demonstrate that all three major exercise types are effective treatments for both clinical and subthreshold symptoms of geriatric depression, and that no single type is more effective than the others. In coalition with high levels of compliance, these findings endorse personal exercise preference when prescribing either aerobic, resistance, or mind-body exercise as a treatment adjunct for depression in older adults with pre-existing clinical depression or apparently healthy older adults without pre-existing depression.

CHAPTER VIII

Summary Discussion

Components of original research findings have been discussed within respective chapters. Therefore, this final chapter will begin with a brief theoretical synthesis of potential mechanisms for the antidepressive effects of physical exercise and followed by the practical consideration, and thus implications, of these thesis findings. To conclude this chapter, limitations related to the overarching thesis findings will be summarised to highlight potential new lines of inquiry for future research in order to further advance exercise regimens for optimal mental health in persons aged 65 years and older.

8.1. Theoretical Implications of the Current Work

Preliminary evidence from Study 1 (Chapter III) identified that both aerobic capacity (as determined by VO_{2max}) and self-perceived general health (a component of health-related quality of life) were higher for older adults who engage in regular aerobic exercise during a 4-year period compared with their lifelong sedentary counterparts. Study 2 (Chapter IV) subsequently demonstrated that exercise-induced mood, exercise self-efficacy, and social support were important predictors of depressive symptoms within a cross-sectional analysis of survey data from a sample of community-dwelling older adults. Studies 3 and 4 (Chapters V and VI) employed network meta-analytical procedures to compare the effectiveness of three major types of exercise training (aerobic, resistance, and mind-body). Both studies demonstrated that aerobic, resistance, and mind-body exercise are all effective for reducing depressive symptoms in older adults, with no single exercise type being quantitatively more effective than another.

Taken together, these data provide encouraging support for a holistic model of psychological well-being incorporating both physiological and psychosocial mechanisms. Physical exercise can facilitate notable change in physiological health, and in response, promote meaningful changes in psychological well-being. In the current thesis, regular exercise gradually improved cardiorespiratory fitness, which may lessen depressive symptomology via two speculative biological processes (Paluska & Schwenk, 2000). The monoamine hypothesis offers that exercise-related changes in cardiorespiratory fitness may produce a systemic release of monoamine neurotransmitters (dopamine, noradrenaline, and serotonin), in an effect similar to that of antidepressant medications (Hirschfeld, 2000). Similarly, the endorphin hypothesis offers that improved fitness may reduce symptoms of depression by increasing the secretion of endorphins throughout the body, effectively reducing the sensation of pain associated with an induced state of euphoria (Dinas et al., 2011).

Increased monoamine neurotransmitters and endorphins correspond with enhanced positive mood states. Therefore, it is plausible that elevated exercise-induced mood states support the antidepressive effects of physical exercise in older age. By applying causal inference from the distraction theory (Bahrke & Morgan, 1978; Festinger & Maccoby, 1964), it is speculated that the biological responses to exercise training elicit these positive mood states by providing a distraction from a painful stimulus, which lead to a subsequent reduction in negative dispositions such as depression.

Despite a physiological basis for the antidepressive effects of physical exercise, psychosocial theories offer longer-term explanations of the exercise-depression relationship that cannot be explained by the biological or physiological responses to sustained bouts of exercise. Self-efficacy was also found to partially account for the antidepressive effects of exercise (Chapter IV). In this regard, exercise mediates symptoms of depression by improving fitness levels, physical functioning, and independent living. These physical improvements, in turn, increase one's efficacy beliefs in being able to perform specific tasks, which are then transferred to other everyday tasks (Bandura, 1997).

Findings from Study 2 (Chapter IV) shows that social support is the strongest predictor of depressive symptomology in older adults aged 65 and over. Indeed, preliminary experimental evidence from Study 1 (Chapter III) indicated that perceived social functioning was greater in those who commenced exercise compared with those who remained sedentary. In compliance with the social interaction hypothesis, social interaction and support derived from exercise training may relieve depressive symptoms (Ransford, 1982). Accordingly, group-based exercise may well be the best way to integrate social aspects into exercise, which has been shown to have significantly greater antidepressive effects than individual-based exercise programs (McAuley, Blissmer, Katula, & Duncan, 2000; Schuch et al., 2016).

8.2. Practical Considerations for Stakeholders in Clinical Geriatrics

Successful ageing is a key challenge of geriatric health research, which is primarily focused on prolonging physiological health and maintaining psychosocial well-being (Bowling & Dieppe, 2005). Findings from this thesis support the tenet that these domains can be maintained and/or improved by adopting regular exercise habits in later life. Since structured exercise is known confer additional benefits than antidepressant medications alone (Mura & Carta, 2013; Mura et al., 2014), therapeutic exercise can be used as a cost-effective adjunct to traditional cognitive-behavioural treatments of geriatric depression.

Exercise-related health outcomes (i.e., physiological fitness, quality of life, and late-life depression) are currently diagnosed and treated as somewhat separate entities, even though it is known that medical comorbidity greatly increases with ageing (Burroughs et al., 2006; Haigh, Bogucki, Sigmon, & Blazer, 2018). Instead, these outcomes should be holistically viewed in terms of interrelated constructs whereby physiological and mental factors can have reciprocal and compounding impact on psychological well-being. Similarly, it is reasonable to suggest that interrelated factors may be useful to effectively identify and/or treat those most susceptible to geriatric depression, including age, gender, perceived general health, exercise motivations, exercise habits (or lack thereof), mood, self-efficacy, and social support.

In the past, a ‘one size fits all’ approach has been assumed when prescribing exercise for older adults. Specifically, exercise has been used as a ‘catch all’ despite the inherently diverse metabolic challenges associated with different exercise types. Thus, the prevailing narrative is that exercise regimens should be modified to meet the physical needs, abilities, and personal interests of aged populations. By encouraging a personalised selection of exercise types and modalities, clinicians and allied health professionals can assist older adults to take advantage of the physiological and psychosocial benefits associated with an active lifestyle.

8.3. Limitations of the Work Presented Herein

As with any body of research, there are several limitations to the present work that should be considered in this thesis. Most notably, this thesis had a focus on the psychosocial mechanisms surrounding the potential antidepressant effect of exercise, and provides limited interrogation of physiological mechanisms. Nevertheless, the physiological effects of exercise are well established within the exercise science literature, and with support generated from the preliminary evidence in Study 1 (Chapter III), potential influences of these physiological mechanisms were considered.

Despite the small margin of progress made in the current thesis, further interrogation of the temporal sequence of exercise-related factors and depressive symptoms is required before causality may be presented with confidence. Study 1 (Chapter III) did not monitor exposure to treatment dosages of physical exercise (i.e., intensity, frequency, duration), limiting the causal inferences that could be derived from the results. In addition, Study 2 (Chapter IV) did not deduce causal inference as an inherent function of study design and data collected. This limitation highlights the importance of objectively measuring physical exercise, such as using accelerometry, to accurately determine the dosage effects of exercise.

On reflection of the data from the first two lines of inquiry, it became apparent that the body of literature has not been synthesised to a position of consistency. Therefore, in the intentions of scientific progression, it was decided that it would be most beneficial to pool the current RCT evidence so that potential points of interest could be identified in exercise-based interventions. While an overall treatment effect was ultimately established for exercise types in Studies 3 and 4 (Chapters V and VI) via network meta-analysis, there were many exercise-related factors that offer additional research merit, but that a thorough examination of these factors was beyond the scope of this thesis (i.e., length of intervention, format of program, intensity, frequency, duration). Therefore, each of these factors should be used to generate new theories with the purpose of developing new lines of inquiry, highlighting particular areas of evidence synthesis, and informing future experimental research.

8.4. Future Directions in Gerontology Research

Given the projected population growth in adults aged 65 and over, there is evidently a need for more geriatric research. This thesis has expanded on some founding theories in gerontology and revealed new lines of inquiry within the area of geriatric depression. Nevertheless, there are still several key aspects that require further development before the progress of this area reflects a level of scientific inquiry that is similar in comparison to other age groups.

Notably, cardiorespiratory fitness declines at a rate of 1-2% per year (Fleg et al., 2005; Hollenberg, Yang, Haight, & Tager, 2006) and certain aspects of HRQL (i.e., physical functioning, pain tolerance, general health, vitality, and emotional well-being) may diminish by up to 5-10% per year (Esain, Gil, Bidaurrazaga-Letona, & Rodriguez-Larrad, 2019). However, the cumulative effect of long-term compliance to physical exercise during middle-to-older age is yet to be fully elucidated for psychosocial well-being. Since practical implications are limited by the lack of available longitudinal research designs, this highlights the need for additional high-quality clinical trials that involve longer intervention periods before definitive conclusions can be drawn.

Although exercise types were categorically compared, investigating other important exercise characteristics was beyond the scope of this thesis. Nevertheless, preliminary evidence indicates that several exercise characteristics may have markedly different treatment effects for geriatric depression. For example, Study 1 identified potential differences between moderate and vigorous intensity exercise, Study 2 alluded to the social impact of individual and group exercise formats, and Studies 3 and 4 explored potential influences between different exercises dose effects (i.e., length of program, session frequency and duration, adherence, and compliance). Thus, it is recommended that future scientific investigations examine the effects of other exercise characteristics on depressive symptoms in depressed older adults.

8.5. Conclusions of the Thesis

In summary, the current thesis provides new knowledge relating to the dynamic interactions between variables of exercise and mental health. This evidence can be used to inform clinicians and allied health professions of the clinical applications of exercise prescription. Most notably, older adults can self-select their preferred exercise modalities to best target a range of key predictors for geriatric depression, including cardiorespiratory health, quality of life, mood, self-efficacy, and social support. This thesis provides encouraging evidence for physical exercise as an adjunct treatment for clinical and subthreshold symptoms of depression in persons aged 65 years and over.

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Appendix A: Ethics Approval for Chapter III

PRIFYSGOL CYMRU
Y Drindod Dewi Sant
UNIVERSITY OF WALES
Trinity Saint David

Yr Athro/Professor Medwin Hughes DL DPhil DPS FRSA FLSW
Is-Ganghellor/Vice-Chancellor

Swyddfa Ymchwil Ôl-raddedig /
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Dr Peter Herbert
Faculty of Business and Management

15 February 2016

Annwyl / Dear Peter

Ganlyniad Pwyllgor Moeseg / Ethics Committee Outcome

Orosiect Ymchwil y Staff / Staff Research Project:

A Follow-up study to: 'The Effects of Low Volume, Infrequent, High Intensity Exercise Training on Cardio-Respiratory, Functional and Health Related Quality of Life In Ageing Men', conducted in 2012.

Yr wyf yn falch o gadarnhau bod y Pwyllgor wedi cymeradwyo eich cais moeseg	I am pleased to confirm that the Committee approved your research application.
Peidiwch ag oedi cyn cysylltu â mi os ydych angen unrhyw wybodaeth bellach.	Please do not hesitate to contact me should you require any further information.

Yr eiddoch yn gywir / Yours sincerely

Alison Sables MSc
Senior Administrative Officer
Uwch Swyddog Gweinyddol

BUDDSODDWYR MEWN POBL | INVESTORS IN PEOPLE

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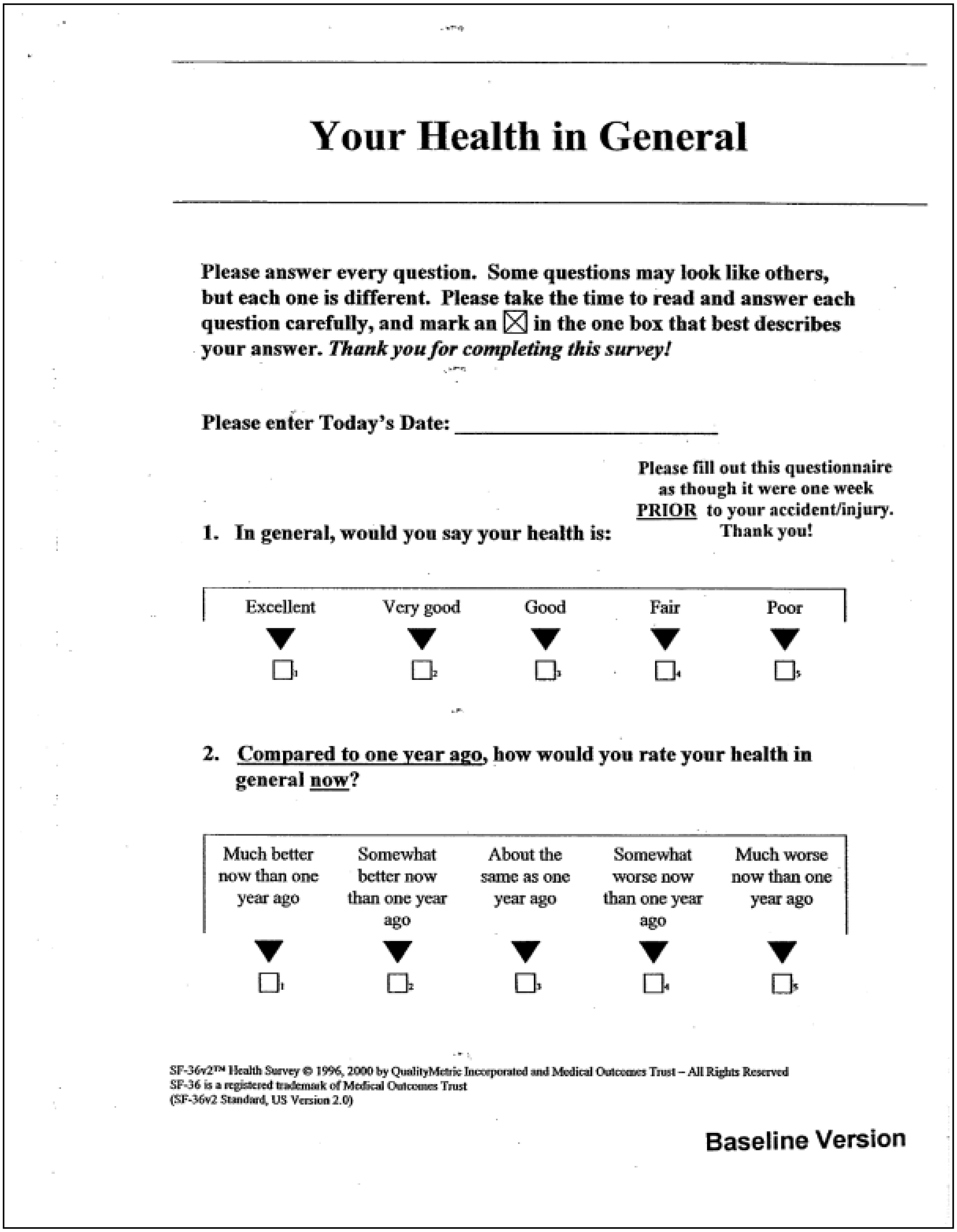
Appendix B: Questionnaires for Chapter III



Your Health in General

Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully, and mark an ☒ in the one box that best describes your answer. ***Thank you for completing this survey!***

Please enter Today's Date: ________________________

Please fill out this questionnaire as though it were one week <u>PRIOR</u> to your accident/injury. Thank you!

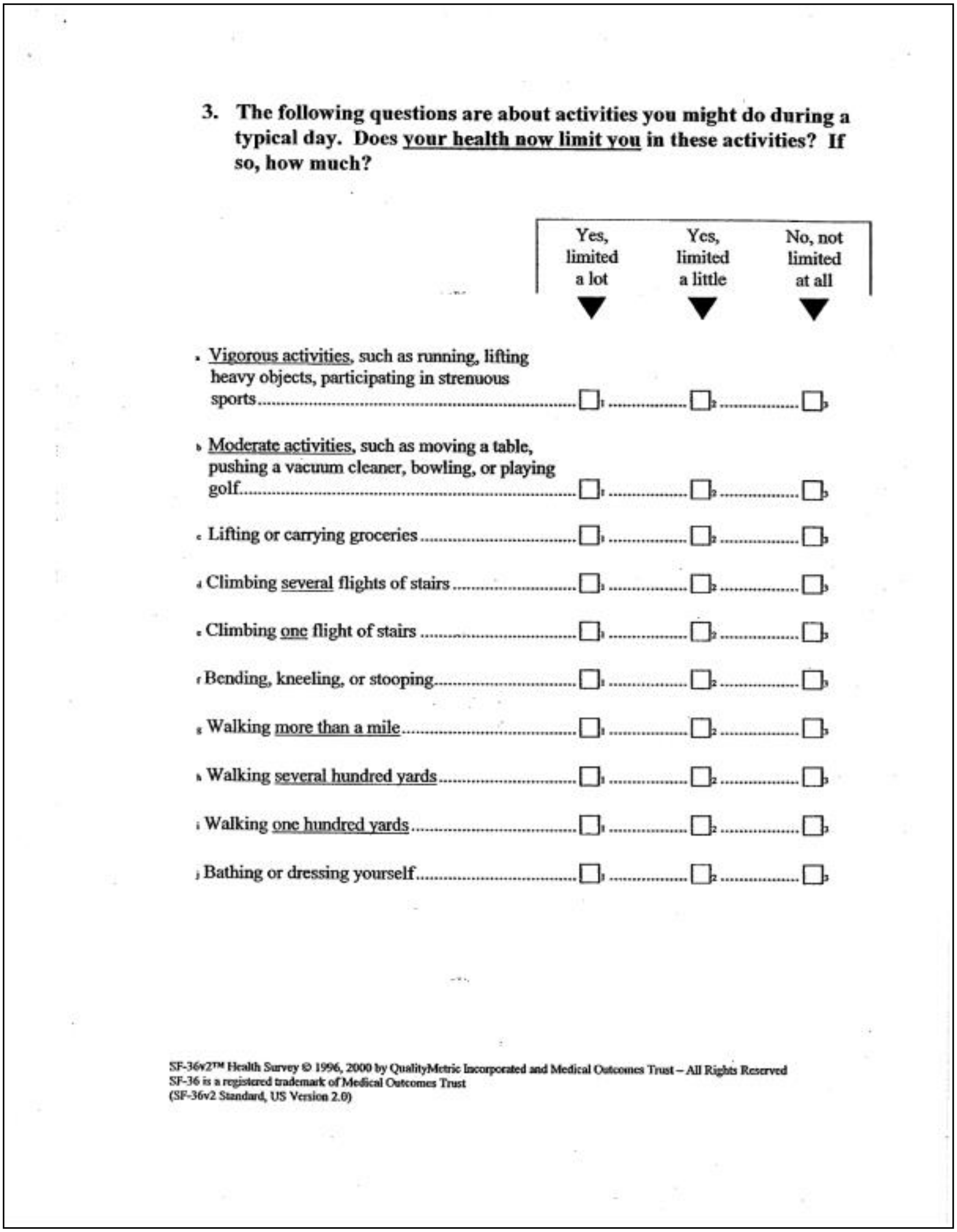
1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. <u>Compared to one year ago</u>, how would you rate your health in general <u>now</u>?

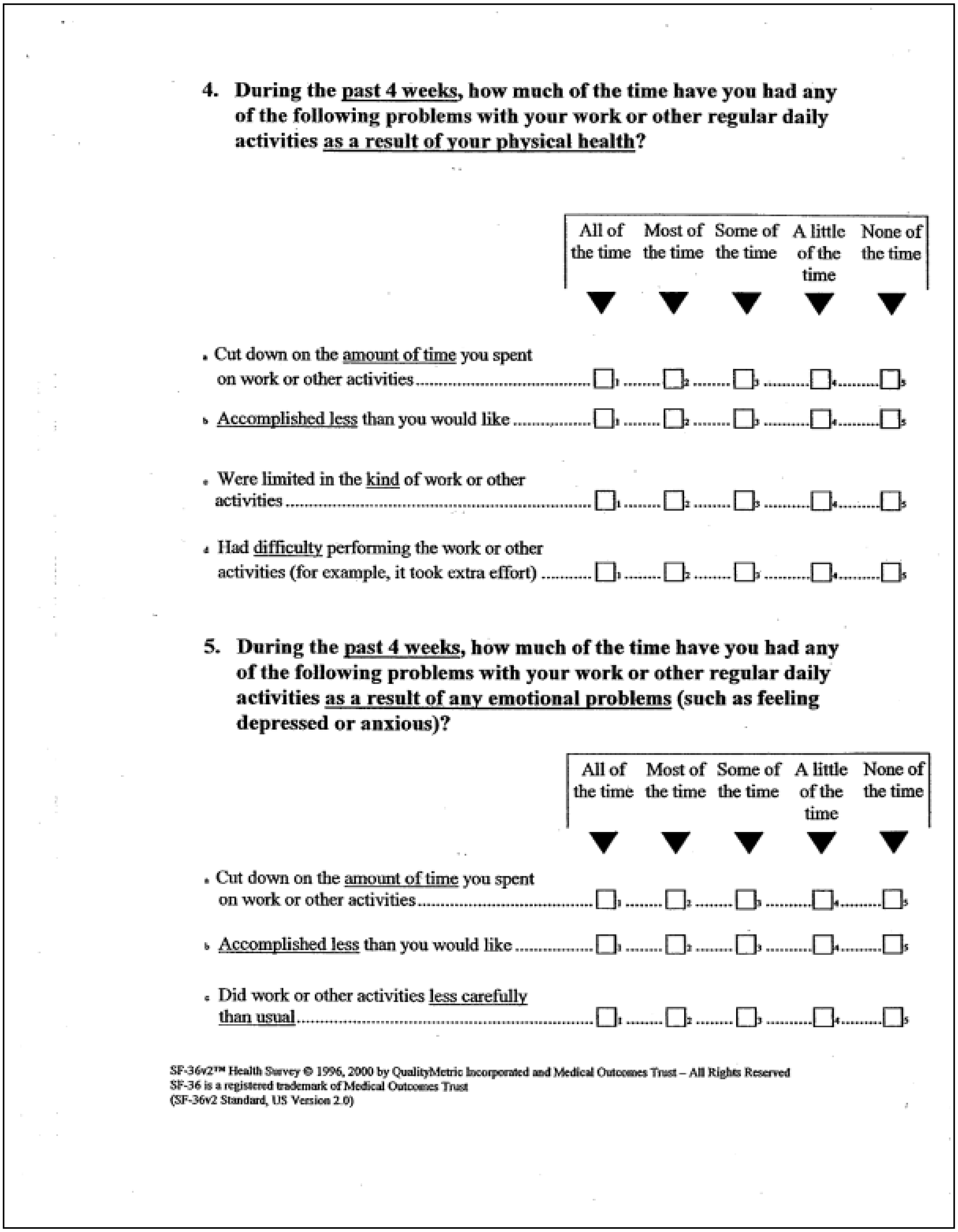
Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Baseline Version



3. **The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?**

	Yes, limited a lot ▼	Yes, limited a little ▼	No, not limited at all ▼
a Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
b Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d Climbing several flights of stairs	☐ 1	☐ 2	☐ 3
e Climbing one flight of stairs	☐ 1	☐ 2	☐ 3
f Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g Walking more than a mile	☐ 1	☐ 2	☐ 3
h Walking several hundred yards	☐ 1	☐ 2	☐ 3
i Walking one hundred yards	☐ 1	☐ 2	☐ 3
j Bathing or dressing yourself	☐ 1	☐ 2	☐ 3



4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
	▼	▼	▼	▼	▼
a Cut down on the amount of time you spent on work or other activities	☐1	☐2	☐3	☐4	☐5
b Accomplished less than you would like	☐1	☐2	☐3	☐4	☐5
c Were limited in the kind of work or other activities	☐1	☐2	☐3	☐4	☐5
d Had difficulty performing the work or other activities (for example, it took extra effort)	☐1	☐2	☐3	☐4	☐5

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
	▼	▼	▼	▼	▼
a Cut down on the amount of time you spent on work or other activities	☐1	☐2	☐3	☐4	☐5
b Accomplished less than you would like	☐1	☐2	☐3	☐4	☐5
c Did work or other activities less carefully than usual	☐1	☐2	☐3	☐4	☐5

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

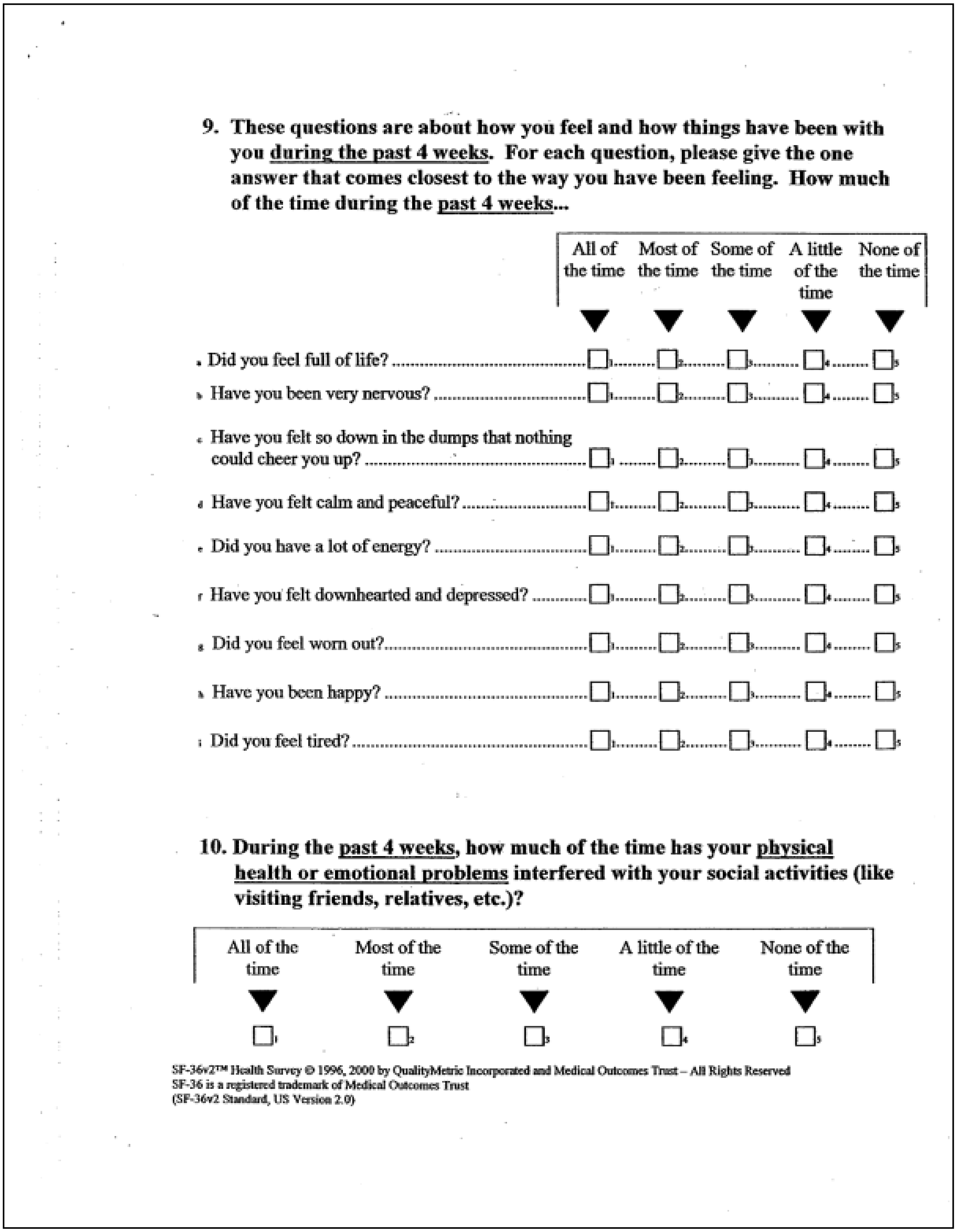
Not at all	Slightly	Moderately	Quite a bit	Extremely
▼	▼	▼	▼	▼
☐1	☐2	☐3	☐4	☐5

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very Severe
▼	▼	▼	▼	▼	▼
☐1	☐2	☐3	☐4	☐5	☐6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
▼	▼	▼	▼	▼
☐1	☐2	☐3	☐4	☐5

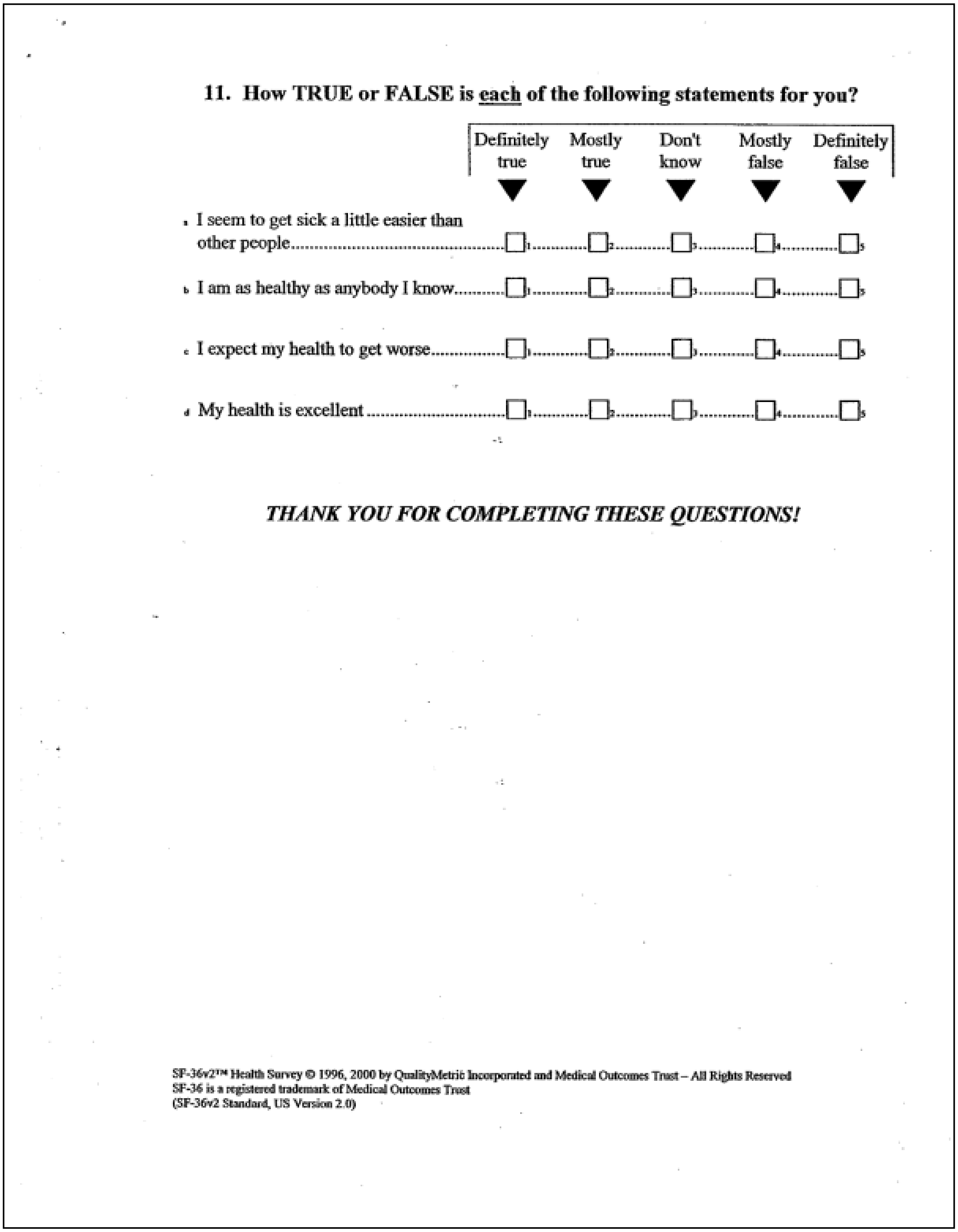


9. These questions are about how you feel and how things have been with you <u>during the past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the <u>past 4 weeks</u>...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Did you feel full of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Have you been very nervous?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f Have you felt downhearted and depressed?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h Have you been happy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. During the <u>past 4 weeks</u>, how much of the time has your <u>physical health or emotional problems</u> interfered with your social activities (like visiting friends, relatives, etc.)?

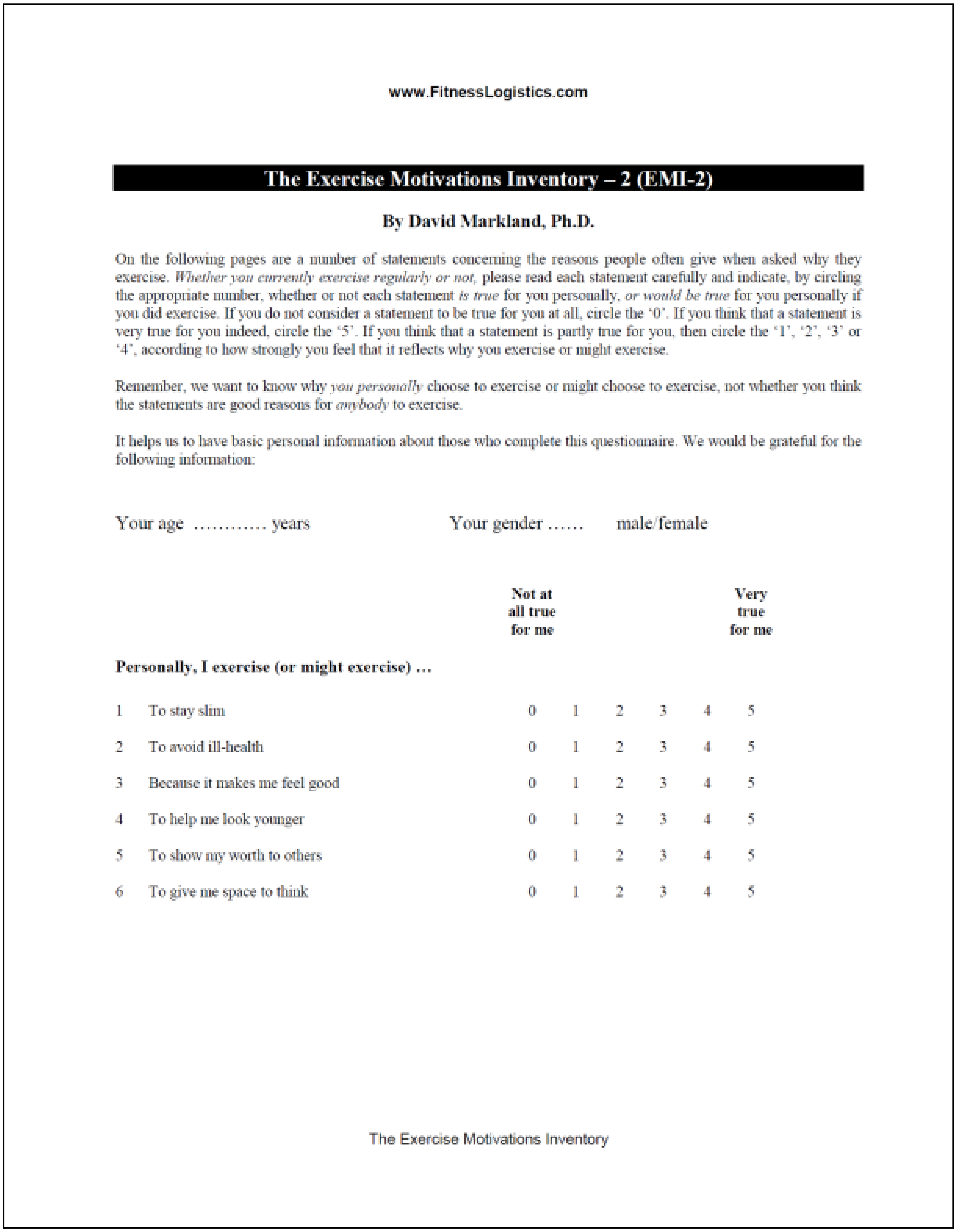
All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5



11. How TRUE or FALSE is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a I seem to get sick a little easier than other people	☐1	☐2	☐3	☐4	☐5
b I am as healthy as anybody I know	☐1	☐2	☐3	☐4	☐5
c I expect my health to get worse	☐1	☐2	☐3	☐4	☐5
d My health is excellent	☐1	☐2	☐3	☐4	☐5

THANK YOU FOR COMPLETING THESE QUESTIONS!



www.FitnessLogistics.com

The Exercise Motivations Inventory – 2 (EMI-2)

By David Markland, Ph.D.

On the following pages are a number of statements concerning the reasons people often give when asked why they exercise. *Whether you currently exercise regularly or not,* please read each statement carefully and indicate, by circling the appropriate number, whether or not each statement *is true* for you personally, *or would be true* for you personally if you did exercise. If you do not consider a statement to be true for you at all, circle the '0'. If you think that a statement is very true for you indeed, circle the '5'. If you think that a statement is partly true for you, then circle the '1', '2', '3' or '4', according to how strongly you feel that it reflects why you exercise or might exercise.

Remember, we want to know why *you personally* choose to exercise or might choose to exercise, not whether you think the statements are good reasons for *anybody* to exercise.

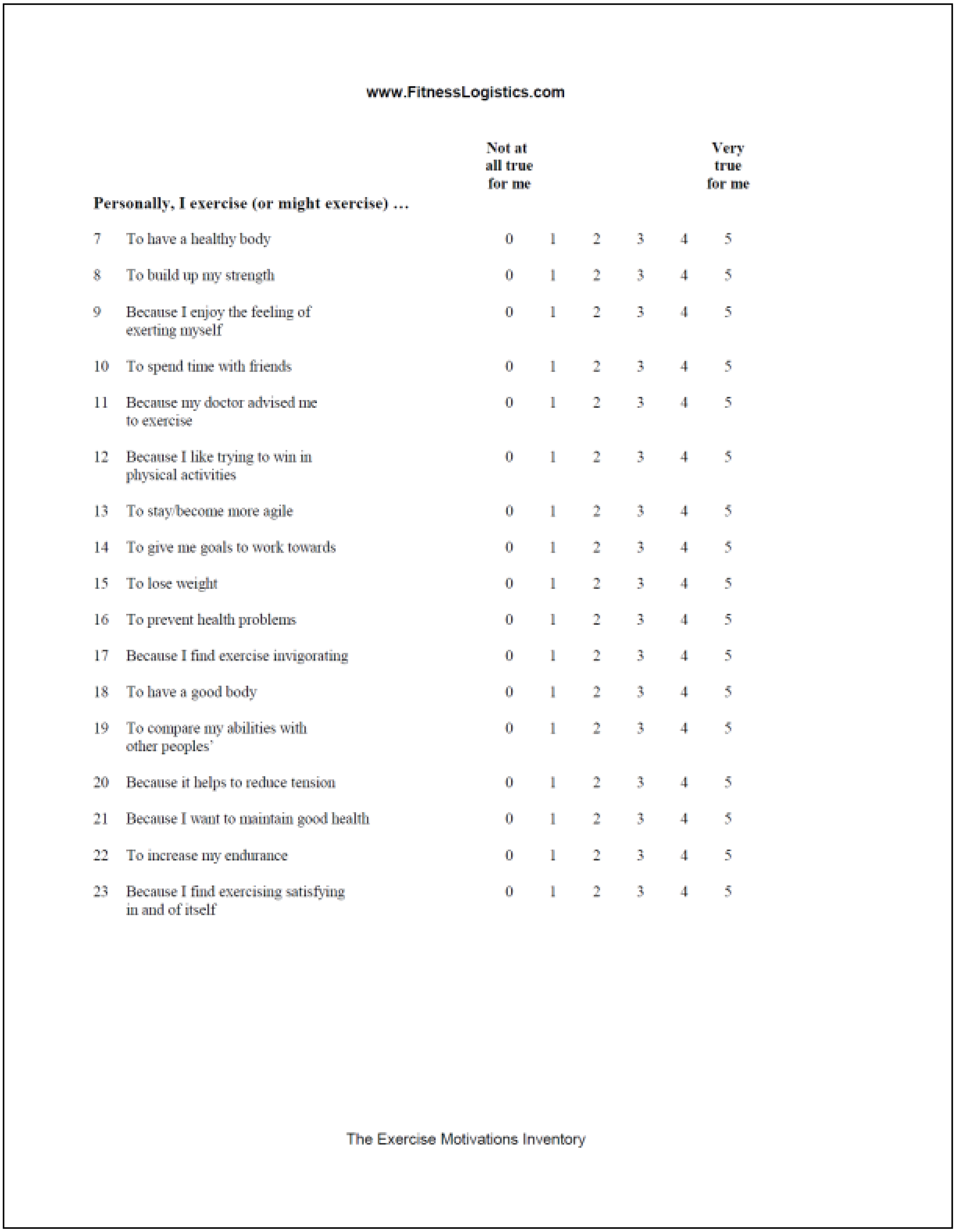
It helps us to have basic personal information about those who complete this questionnaire. We would be grateful for the following information:

Your age ………… years

Your gender …… male/female

		Not at all true for me					**Very true for me**
Personally, I exercise (or might exercise) …							
1	To stay slim	0	1	2	3	4	5
2	To avoid ill-health	0	1	2	3	4	5
3	Because it makes me feel good	0	1	2	3	4	5
4	To help me look younger	0	1	2	3	4	5
5	To show my worth to others	0	1	2	3	4	5
6	To give me space to think	0	1	2	3	4	5

The Exercise Motivations Inventory



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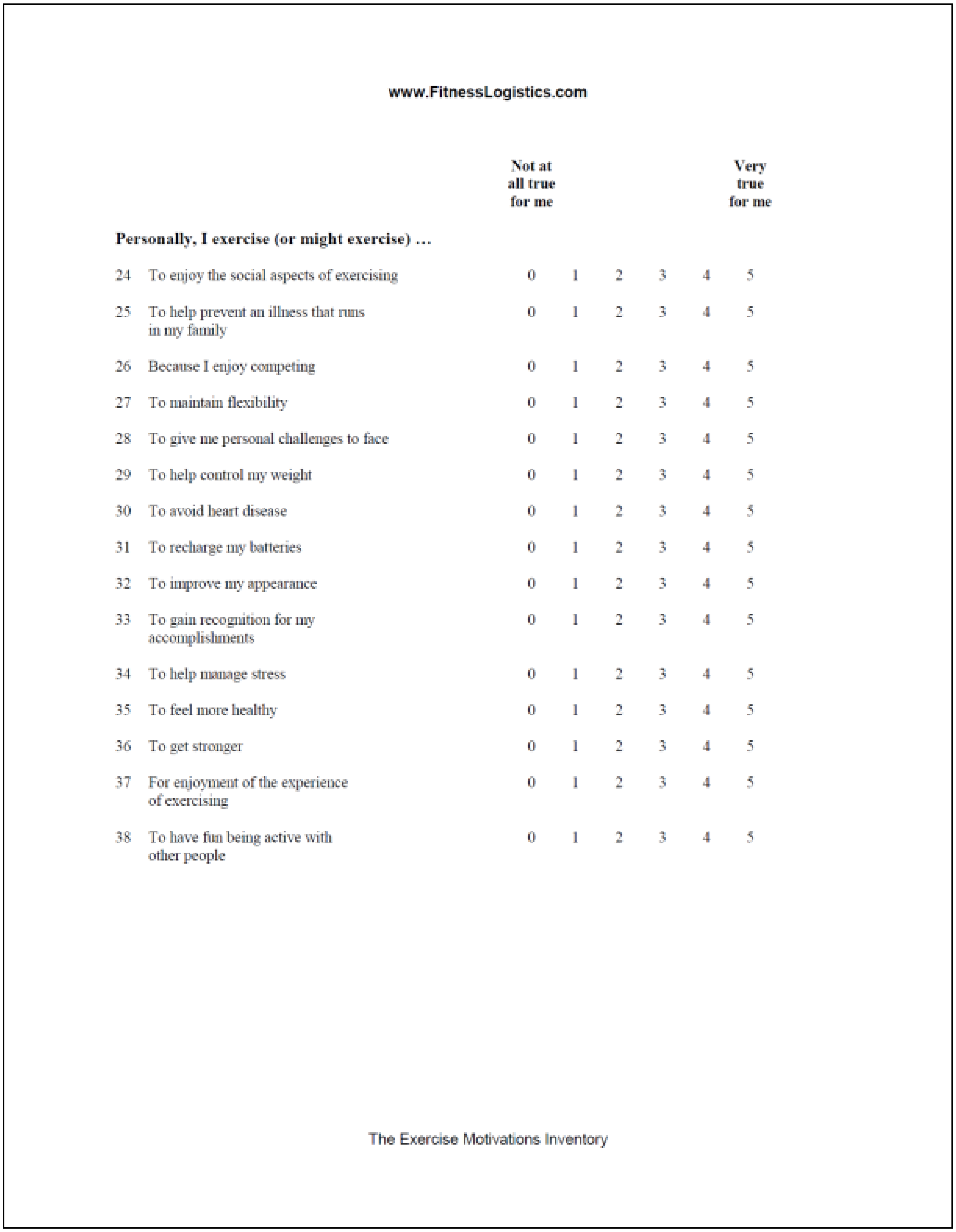
Personally, I exercise (or might exercise) …

		Not at all true for me					**Very true for me**
7	To have a healthy body	0	1	2	3	4	5
8	To build up my strength	0	1	2	3	4	5
9	Because I enjoy the feeling of exerting myself	0	1	2	3	4	5
10	To spend time with friends	0	1	2	3	4	5
11	Because my doctor advised me to exercise	0	1	2	3	4	5
12	Because I like trying to win in physical activities	0	1	2	3	4	5
13	To stay/become more agile	0	1	2	3	4	5
14	To give me goals to work towards	0	1	2	3	4	5
15	To lose weight	0	1	2	3	4	5
16	To prevent health problems	0	1	2	3	4	5
17	Because I find exercise invigorating	0	1	2	3	4	5
18	To have a good body	0	1	2	3	4	5
19	To compare my abilities with other peoples'	0	1	2	3	4	5
20	Because it helps to reduce tension	0	1	2	3	4	5
21	Because I want to maintain good health	0	1	2	3	4	5
22	To increase my endurance	0	1	2	3	4	5
23	Because I find exercising satisfying in and of itself	0	1	2	3	4	5

The Exercise Motivations Inventory

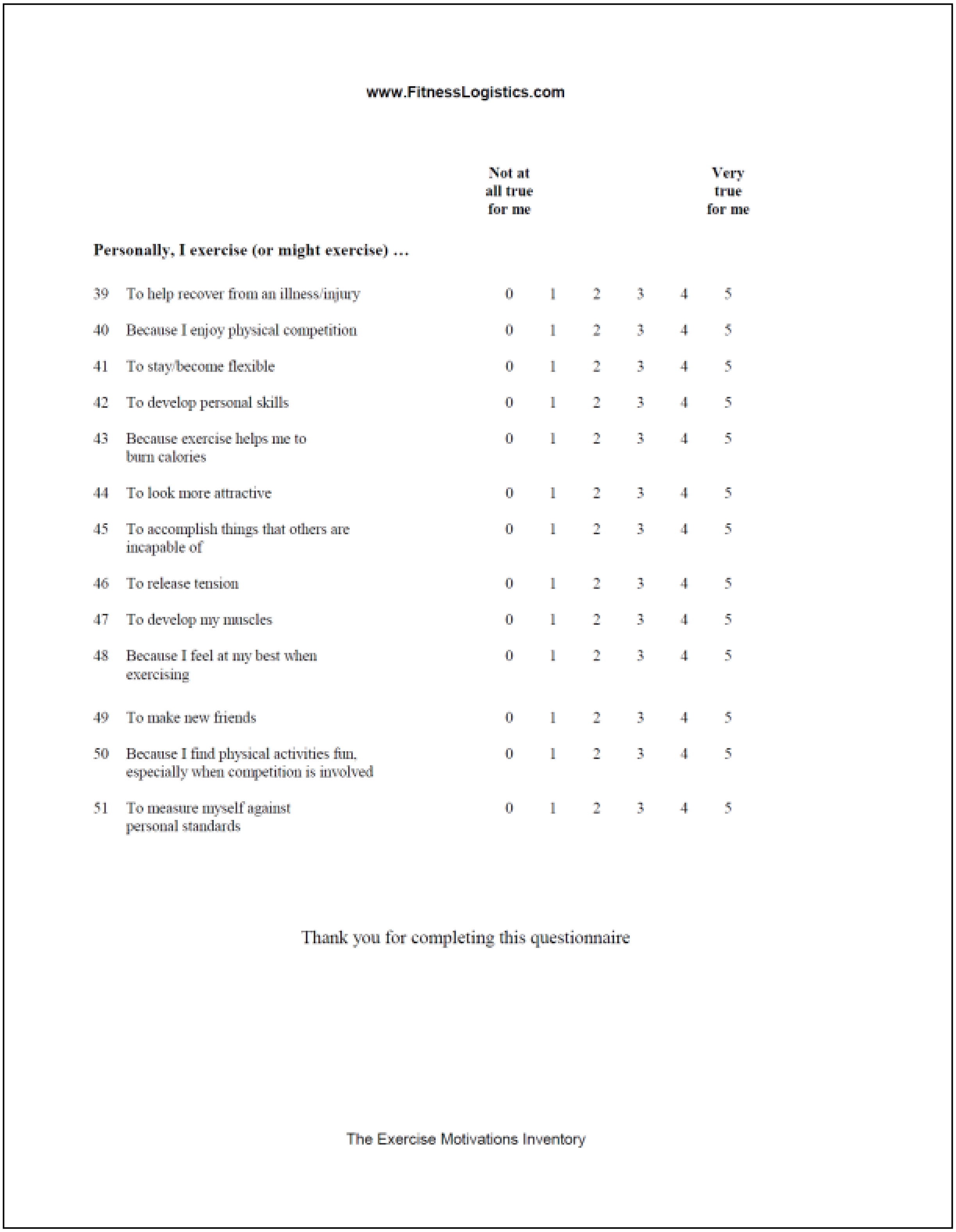


www.FitnessLogistics.com

Personally, I exercise (or might exercise) …

		Not at all true for me					Very true for me
24	To enjoy the social aspects of exercising	0	1	2	3	4	5
25	To help prevent an illness that runs in my family	0	1	2	3	4	5
26	Because I enjoy competing	0	1	2	3	4	5
27	To maintain flexibility	0	1	2	3	4	5
28	To give me personal challenges to face	0	1	2	3	4	5
29	To help control my weight	0	1	2	3	4	5
30	To avoid heart disease	0	1	2	3	4	5
31	To recharge my batteries	0	1	2	3	4	5
32	To improve my appearance	0	1	2	3	4	5
33	To gain recognition for my accomplishments	0	1	2	3	4	5
34	To help manage stress	0	1	2	3	4	5
35	To feel more healthy	0	1	2	3	4	5
36	To get stronger	0	1	2	3	4	5
37	For enjoyment of the experience of exercising	0	1	2	3	4	5
38	To have fun being active with other people	0	1	2	3	4	5

The Exercise Motivations Inventory



www.FitnessLogistics.com

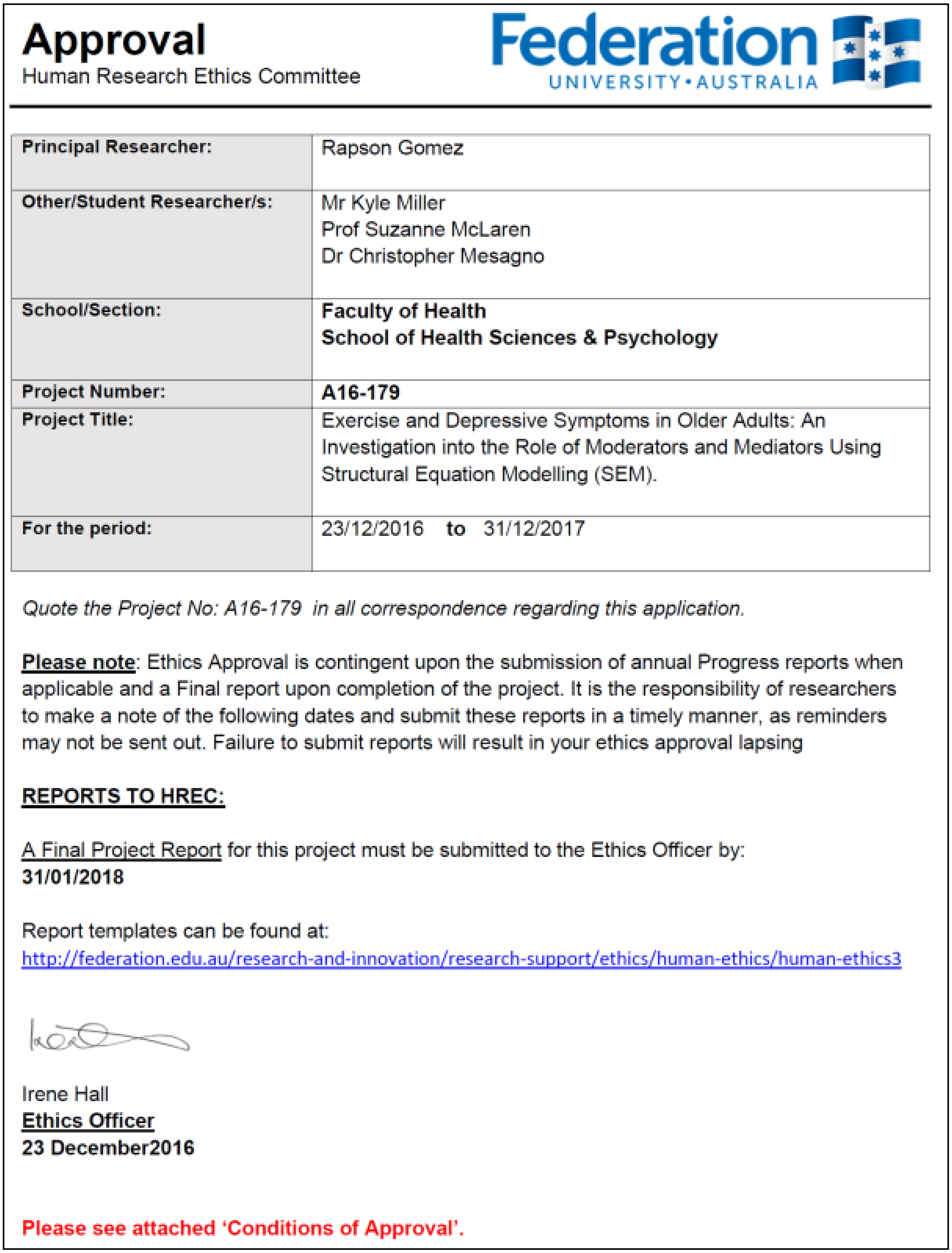
Personally, I exercise (or might exercise) …

		Not at all true for me					Very true for me
39	To help recover from an illness/injury	0	1	2	3	4	5
40	Because I enjoy physical competition	0	1	2	3	4	5
41	To stay/become flexible	0	1	2	3	4	5
42	To develop personal skills	0	1	2	3	4	5
43	Because exercise helps me to burn calories	0	1	2	3	4	5
44	To look more attractive	0	1	2	3	4	5
45	To accomplish things that others are incapable of	0	1	2	3	4	5
46	To release tension	0	1	2	3	4	5
47	To develop my muscles	0	1	2	3	4	5
48	Because I feel at my best when exercising	0	1	2	3	4	5
49	To make new friends	0	1	2	3	4	5
50	Because I find physical activities fun, especially when competition is involved	0	1	2	3	4	5
51	To measure myself against personal standards	0	1	2	3	4	5

Thank you for completing this questionnaire

The Exercise Motivations Inventory

Appendix C: Ethics Approval for Chapter IV



Approval

Human Research Ethics Committee

Federation UNIVERSITY • AUSTRALIA

Principal Researcher:	Rapson Gomez
Other/Student Researcher/s:	Mr Kyle Miller Prof Suzanne McLaren Dr Christopher Mesagno
School/Section:	**Faculty of Health** **School of Health Sciences & Psychology**
Project Number:	**A16-179**
Project Title:	Exercise and Depressive Symptoms in Older Adults: An Investigation into the Role of Moderators and Mediators Using Structural Equation Modelling (SEM).
For the period:	23/12/2016 **to** 31/12/2017

Quote the Project No: A16-179 in all correspondence regarding this application.

Please note: Ethics Approval is contingent upon the submission of annual Progress reports when applicable and a Final report upon completion of the project. It is the responsibility of researchers to make a note of the following dates and submit these reports in a timely manner, as reminders may not be sent out. Failure to submit reports will result in your ethics approval lapsing

REPORTS TO HREC:

A Final Project Report for this project must be submitted to the Ethics Officer by:
31/01/2018

Report templates can be found at:
http://federation.edu.au/research-and-innovation/research-support/ethics/human-ethics/human-ethics3

Irene Hall
Ethics Officer
23 December2016

Please see attached 'Conditions of Approval'.

Approval

Human Research Ethics Committee

Federation UNIVERSITY·AUSTRALIA

Principal Researcher:	Prof Fergal Grace	
Other/Student Researcher/s:	Mr Kyle Miller Prof Rapson Gomez Prof Suzanne McLaren	Dr Christopher Mesagno Dr Beyon Miloyan
School/Section:	**Faculty of Health - Psychology**	
Project Number:	**A18-045**	
Project Title:	**Exercise and depressive Symptoms in Older Adults: An investigation into the role of Moderators and Mediators Using Structural Equation Modelling (SEM).**	
For the period:	07/05/2018 **to** 31/12/2018	

Quote the Project No: A18-045 in all correspondence regarding this application.

Approval has been granted to undertake this project in accordance with the proposal submitted for the period listed above.

Please note: It is the responsibility of the Principal Researcher to ensure the Ethics Office is contacted immediately regarding any proposed change or any serious or unexpected adverse effect on participants during the life of this project.

In Addition: Maintaining Ethics Approval is contingent upon adherence to all Standard Conditions of Approval as listed on the final page of this notification

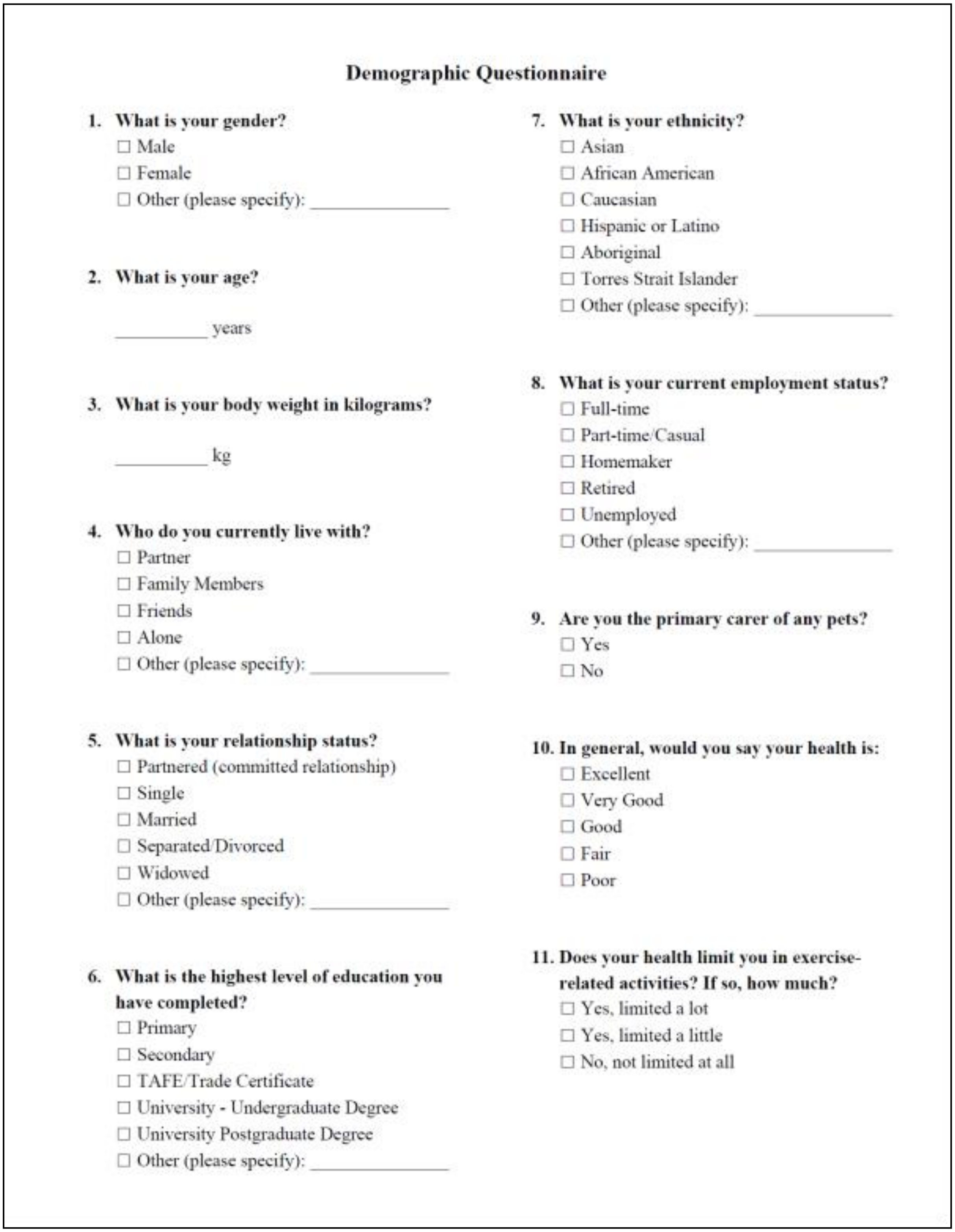
COMPLIANCE REPORTING DATES TO HREC:

Final project report:
31 January 2019

The combined annual/final report template is available at:
http://federation.edu.au/research-and-innovation/research-support/ethics/human-ethics/human-ethics3

Fiona Koop
Ethics Officer
7 May 2018
Please note the standard conditions of approval on Page 2:

Appendix D: Questionnaires for Chapter IV



Demographic Questionnaire

1. **What is your gender?**
   ☐ Male
   ☐ Female
   ☐ Other (please specify): _______________

2. **What is your age?**

   __________ years

3. **What is your body weight in kilograms?**

   __________ kg

4. **Who do you currently live with?**
   ☐ Partner
   ☐ Family Members
   ☐ Friends
   ☐ Alone
   ☐ Other (please specify): _______________

5. **What is your relationship status?**
   ☐ Partnered (committed relationship)
   ☐ Single
   ☐ Married
   ☐ Separated/Divorced
   ☐ Widowed
   ☐ Other (please specify): _______________

6. **What is the highest level of education you have completed?**
   ☐ Primary
   ☐ Secondary
   ☐ TAFE/Trade Certificate
   ☐ University - Undergraduate Degree
   ☐ University Postgraduate Degree
   ☐ Other (please specify): _______________

7. **What is your ethnicity?**
   ☐ Asian
   ☐ African American
   ☐ Caucasian
   ☐ Hispanic or Latino
   ☐ Aboriginal
   ☐ Torres Strait Islander
   ☐ Other (please specify): _______________

8. **What is your current employment status?**
   ☐ Full-time
   ☐ Part-time/Casual
   ☐ Homemaker
   ☐ Retired
   ☐ Unemployed
   ☐ Other (please specify): _______________

9. **Are you the primary carer of any pets?**
   ☐ Yes
   ☐ No

10. **In general, would you say your health is:**
    ☐ Excellent
    ☐ Very Good
    ☐ Good
    ☐ Fair
    ☐ Poor

11. **Does your health limit you in exercise-related activities? If so, how much?**
    ☐ Yes, limited a lot
    ☐ Yes, limited a little
    ☐ No, not limited at all

Instructions: This questionnaire is about activities that you may have done in the past 4 weeks. The questions on the following pages are similar to the example shown below.

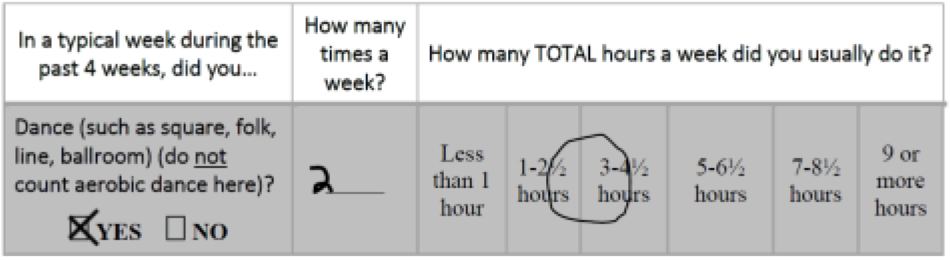
If you DID the activity in the past 4 weeks:

Step #1 Check the YES box.

Step #2 Think about how many TIMES a week you usually did it, and write your response in the space provided.

Step #3 Circle how many TOTAL HOURS in a typical week you did the activity.

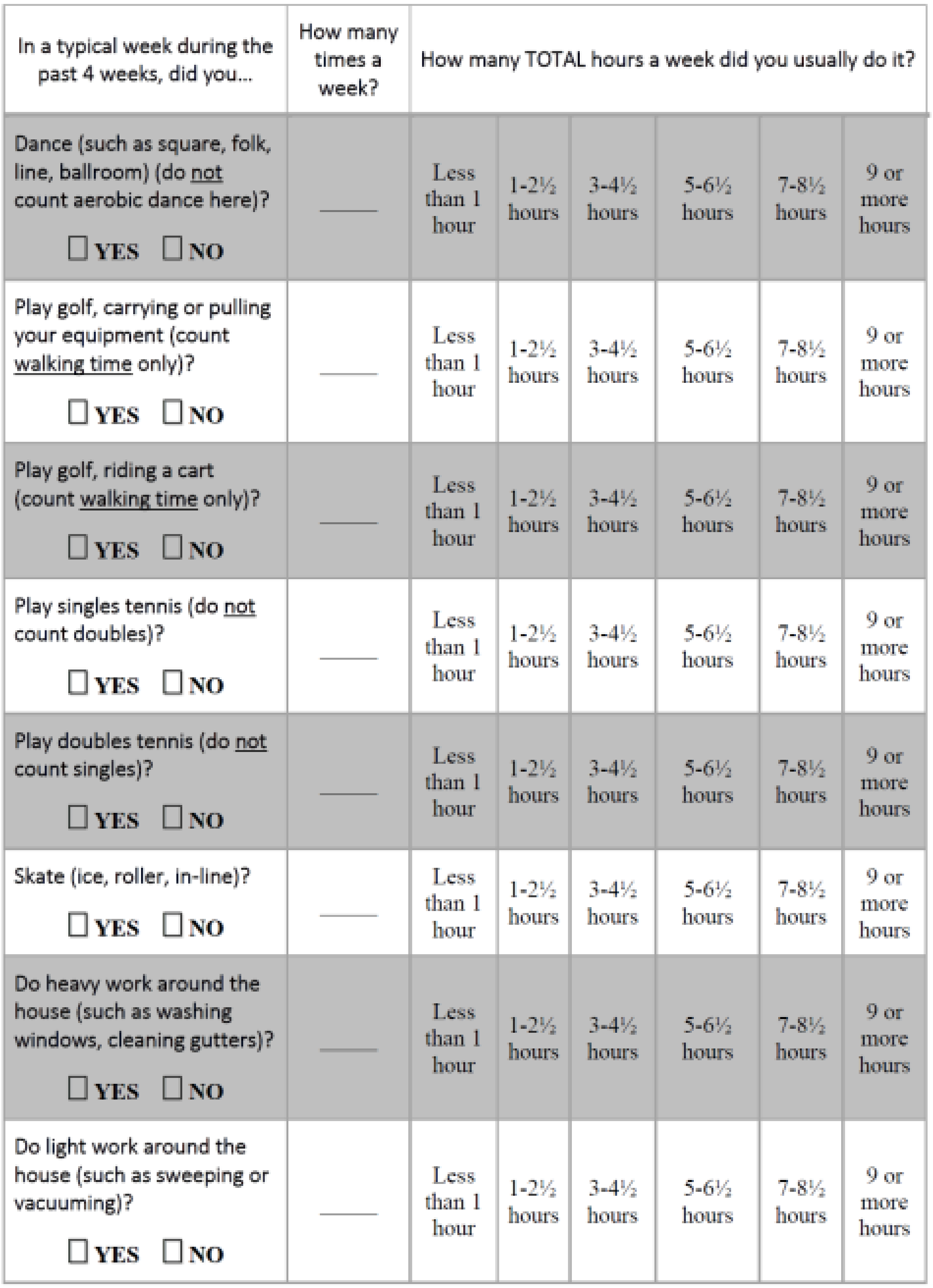
Here is an example of how Mrs. Jones would answer question #1: Mrs. Jones usually goes dancing with her friends twice a week. She usually spends one hour on Monday folk dancing with Maria and two hours on Wednesday square dancing with Olga. Therefore, the total hours a week that she goes dancing with friends is 3 hours a week.



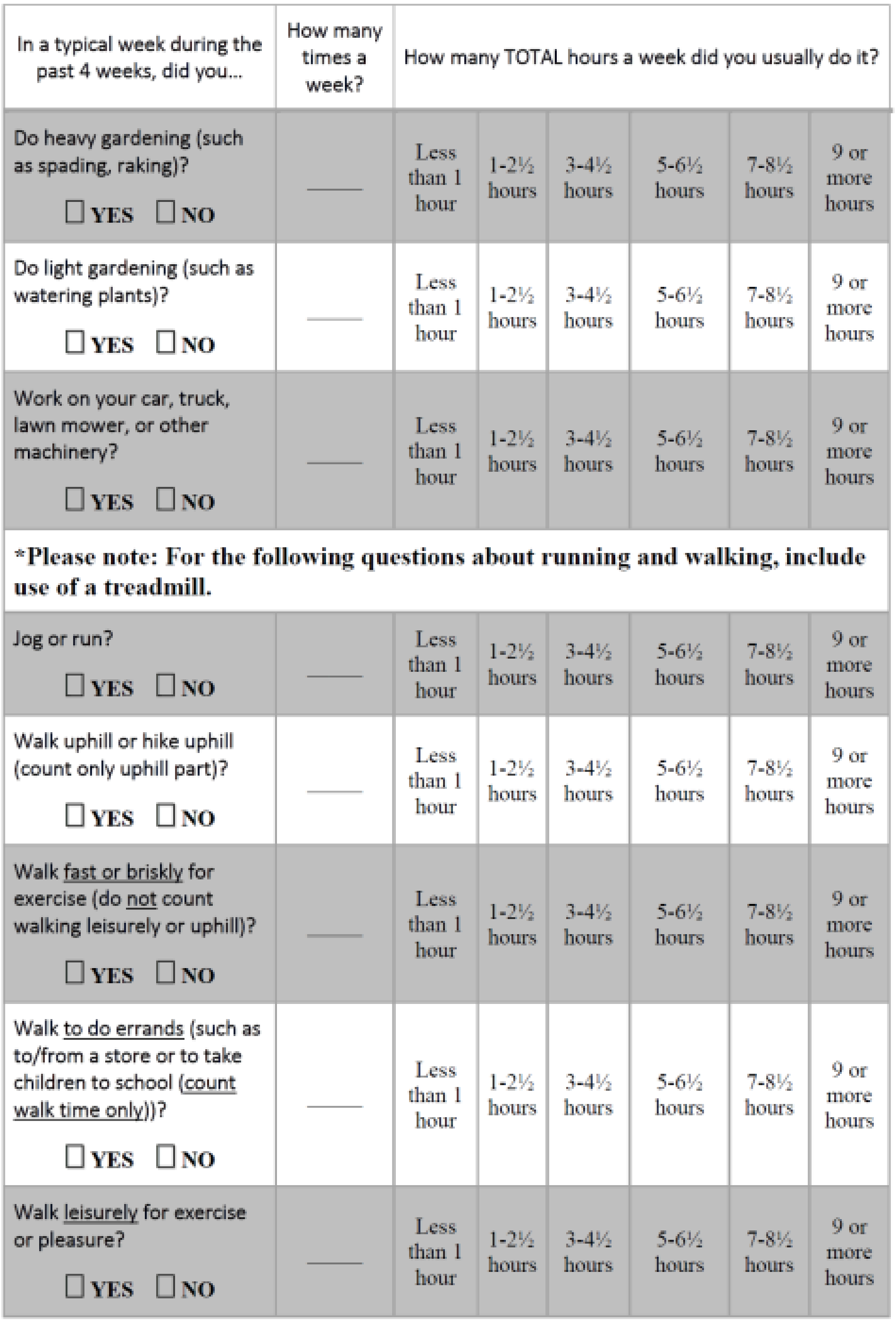
In a typical week during the past 4 weeks, did you…	How many times a week?	How many TOTAL hours a week did you usually do it?					
Dance (such as square, folk, line, ballroom) (do not count aerobic dance here)? ☒YES ☐NO	2	Less than 1 hour	1-2½ hours	[✓ 3-4½ hours]	5-6½ hours	7-8½ hours	9 or more hours

If you DID NOT do the activity:

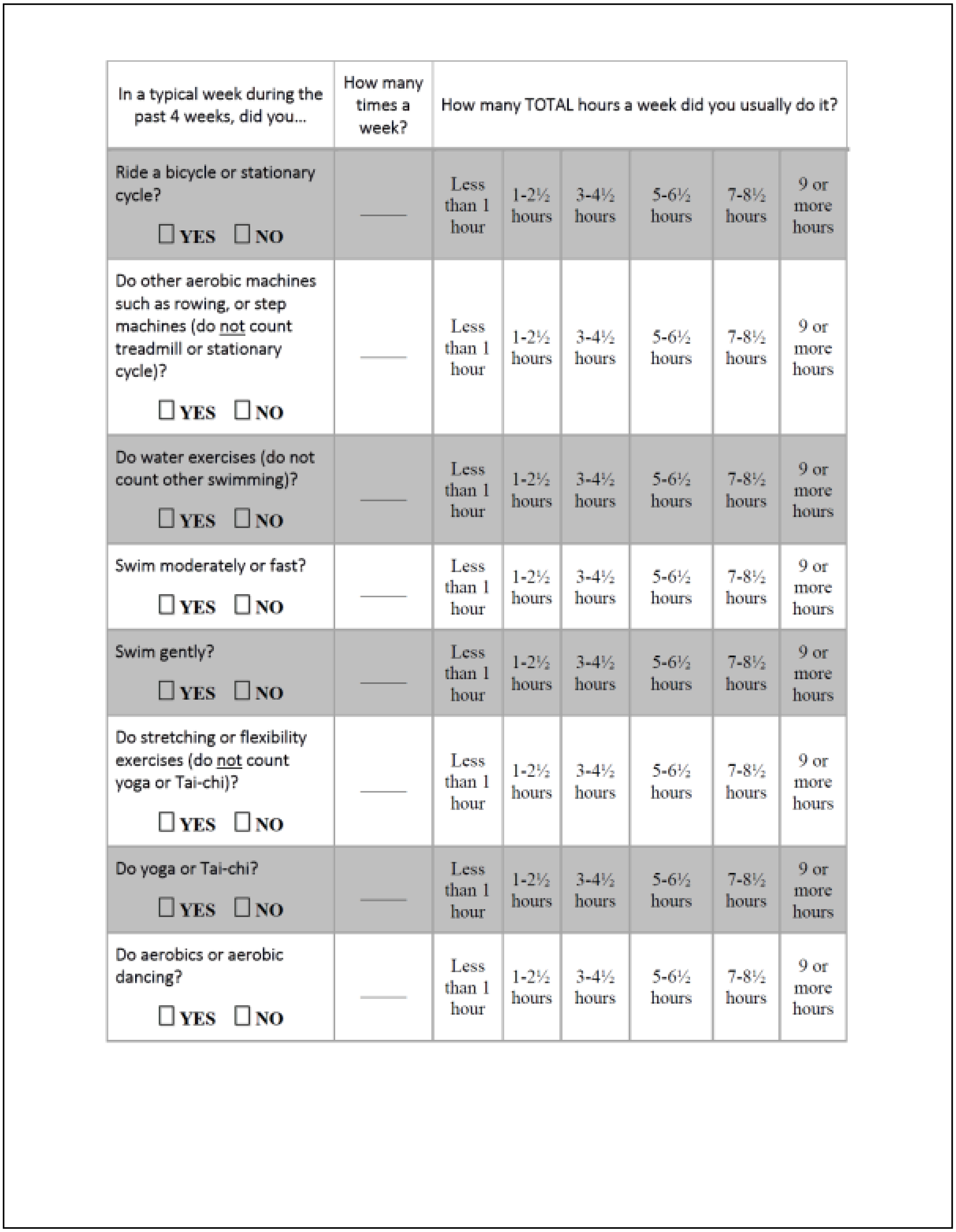
- Check the NO box and move to the next question.



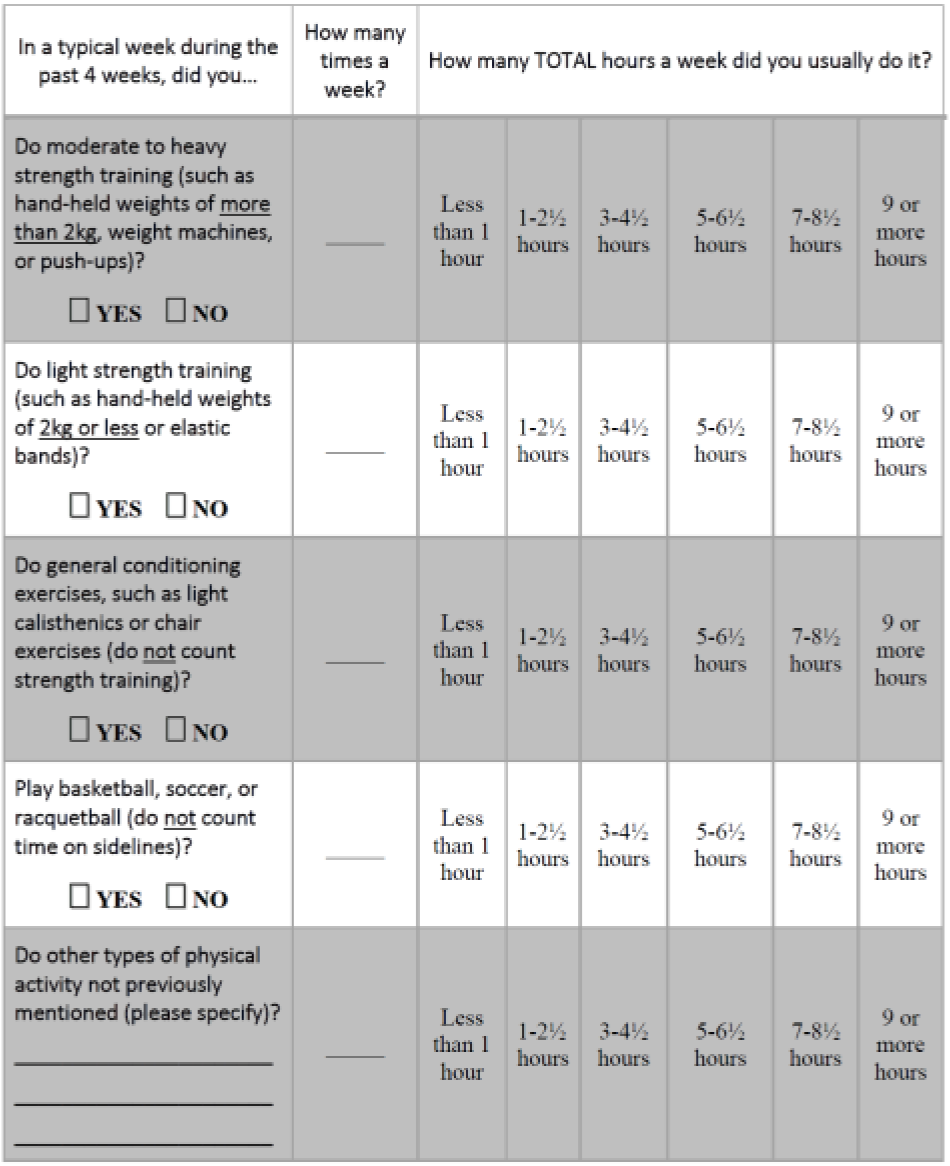
In a typical week during the past 4 weeks, did you…	How many times a week?	How many TOTAL hours a week did you usually do it?					
Dance (such as square, folk, line, ballroom) (do not count aerobic dance here)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Play golf, carrying or pulling your equipment (count walking time only)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Play golf, riding a cart (count walking time only)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Play singles tennis (do not count doubles)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Play doubles tennis (do not count singles)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Skate (ice, roller, in-line)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do heavy work around the house (such as washing windows, cleaning gutters)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do light work around the house (such as sweeping or vacuuming)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours



In a typical week during the past 4 weeks, did you…	How many times a week?	How many TOTAL hours a week did you usually do it?					
Do heavy gardening (such as spading, raking)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do light gardening (such as watering plants)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Work on your car, truck, lawn mower, or other machinery? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
***Please note: For the following questions about running and walking, include use of a treadmill.**							
Jog or run? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Walk uphill or hike uphill (count only uphill part)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Walk fast or briskly for exercise (do not count walking leisurely or uphill)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Walk to do errands (such as to/from a store or to take children to school (count walk time only))? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Walk leisurely for exercise or pleasure? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours



In a typical week during the past 4 weeks, did you…	How many times a week?	How many TOTAL hours a week did you usually do it?					
Ride a bicycle or stationary cycle? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do other aerobic machines such as rowing, or step machines (do not count treadmill or stationary cycle)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do water exercises (do not count other swimming)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Swim moderately or fast? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Swim gently? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do stretching or flexibility exercises (do not count yoga or Tai-chi)? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do yoga or Tai-chi? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do aerobics or aerobic dancing? ☐ YES ☐ NO	______	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours

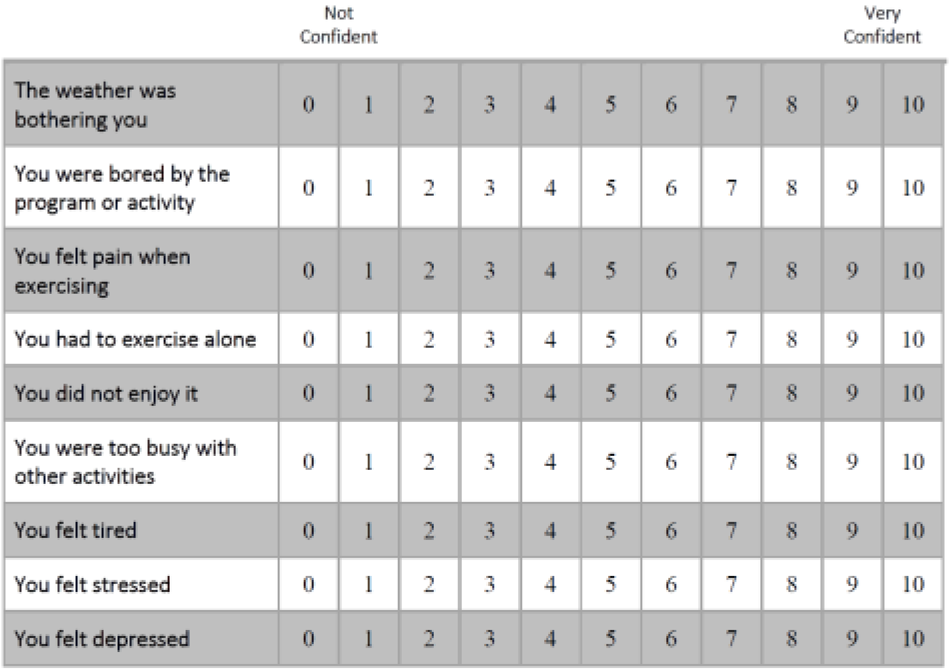


In a typical week during the past 4 weeks, did you…	How many times a week?	How many TOTAL hours a week did you usually do it?					
Do moderate to heavy strength training (such as hand-held weights of more than 2kg, weight machines, or push-ups)? ☐ YES ☐ NO	____	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do light strength training (such as hand-held weights of 2kg or less or elastic bands)? ☐ YES ☐ NO	____	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do general conditioning exercises, such as light calisthenics or chair exercises (do not count strength training)? ☐ YES ☐ NO	____	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Play basketball, soccer, or racquetball (do not count time on sidelines)? ☐ YES ☐ NO	____	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
Do other types of physical activity not previously mentioned (please specify)? ____________________ ____________________ ____________________	____	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours

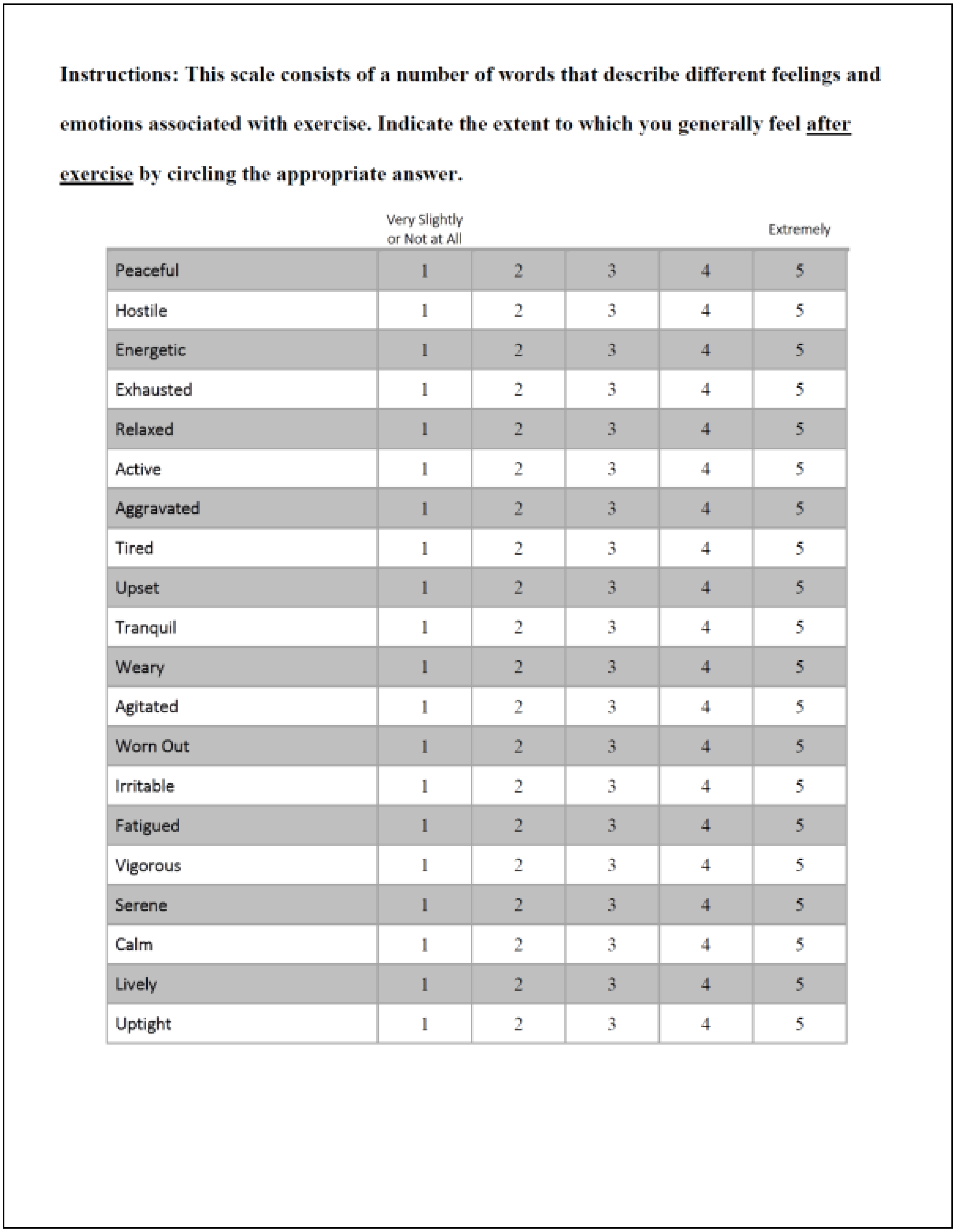
Instructions: Below is a list of the ways you might have felt or behaved. Please circle the response that reflects how often you have felt this way <u>during the past 4 weeks</u>.

	Rarely or None of the Time	Some or a Little of the Time	Occasionally or a Moderate Amount of Time	Most or All of the Time
I was bothered by things that usually don't bother me	0	1	2	3
I did not feel like eating; my appetite was poor	0	1	2	3
I felt that I could not shake off the blues even with help from my family or friends	0	1	2	3
I felt that I was just as good as other people	0	1	2	3
I had trouble keeping my mind on what I was doing	0	1	2	3
I felt depressed	0	1	2	3
I felt that everything I did was an effort	0	1	2	3
I felt hopeful about the future	0	1	2	3
I thought my life had been a failure	0	1	2	3
I felt fearful	0	1	2	3
My sleep was restless	0	1	2	3
I was happy	0	1	2	3
I talked less than usual	0	1	2	3
I felt lonely	0	1	2	3
People were unfriendly	0	1	2	3
I enjoyed life	0	1	2	3
I had crying spells	0	1	2	3
I felt sad	0	1	2	3
I felt that people dislike me	0	1	2	3
I could not get "going"	0	1	2	3

Instructions: By circling the corresponding number below for each statement, how confident are you right now that you could exercise three times per week for 20 minutes if:



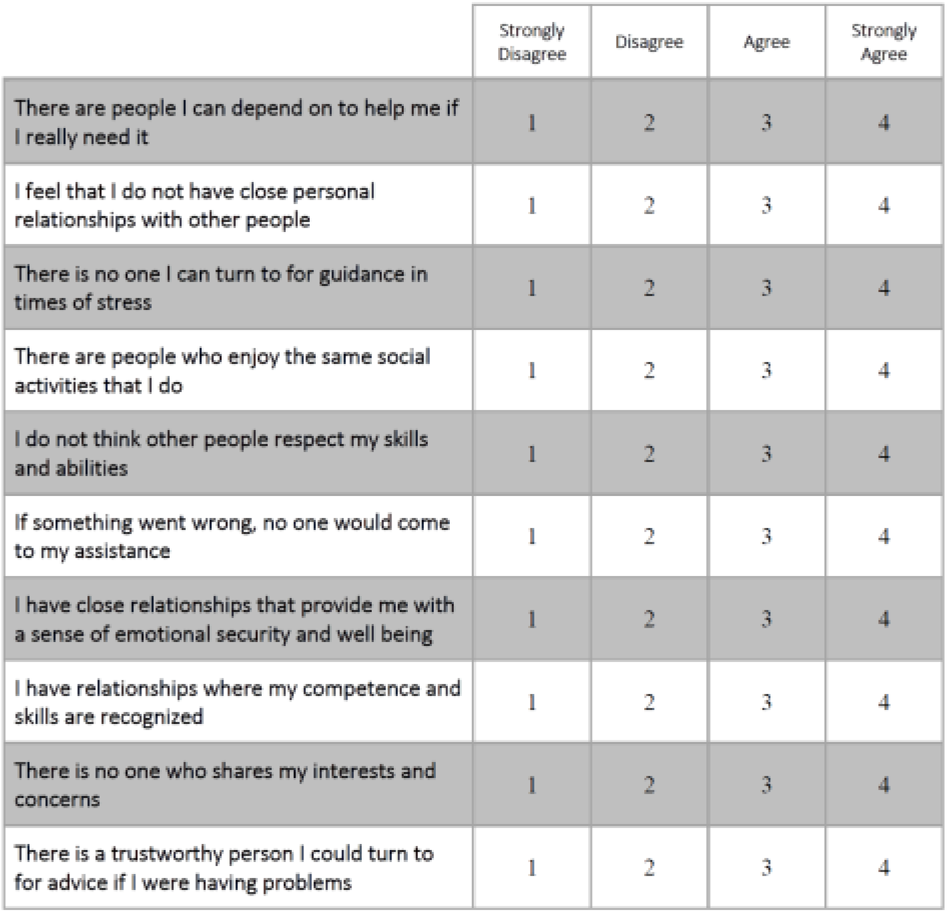
	Not Confident										Very Confident
The weather was bothering you	0	1	2	3	4	5	6	7	8	9	10
You were bored by the program or activity	0	1	2	3	4	5	6	7	8	9	10
You felt pain when exercising	0	1	2	3	4	5	6	7	8	9	10
You had to exercise alone	0	1	2	3	4	5	6	7	8	9	10
You did not enjoy it	0	1	2	3	4	5	6	7	8	9	10
You were too busy with other activities	0	1	2	3	4	5	6	7	8	9	10
You felt tired	0	1	2	3	4	5	6	7	8	9	10
You felt stressed	0	1	2	3	4	5	6	7	8	9	10
You felt depressed	0	1	2	3	4	5	6	7	8	9	10



Instructions: This scale consists of a number of words that describe different feelings and emotions associated with exercise. Indicate the extent to which you generally feel <u>after exercise</u> by circling the appropriate answer.

	Very Slightly or Not at All				Extremely
Peaceful	1	2	3	4	5
Hostile	1	2	3	4	5
Energetic	1	2	3	4	5
Exhausted	1	2	3	4	5
Relaxed	1	2	3	4	5
Active	1	2	3	4	5
Aggravated	1	2	3	4	5
Tired	1	2	3	4	5
Upset	1	2	3	4	5
Tranquil	1	2	3	4	5
Weary	1	2	3	4	5
Agitated	1	2	3	4	5
Worn Out	1	2	3	4	5
Irritable	1	2	3	4	5
Fatigued	1	2	3	4	5
Vigorous	1	2	3	4	5
Serene	1	2	3	4	5
Calm	1	2	3	4	5
Lively	1	2	3	4	5
Uptight	1	2	3	4	5

Instructions: In answering the following questions, think about your current relationships with friends, family members, co-workers, community members, and so on. Please circle to what extent each statement describes your current relationships with other people.



	Strongly Disagree	Disagree	Agree	Strongly Agree
There are people I can depend on to help me if I really need it	1	2	3	4
I feel that I do not have close personal relationships with other people	1	2	3	4
There is no one I can turn to for guidance in times of stress	1	2	3	4
There are people who enjoy the same social activities that I do	1	2	3	4
I do not think other people respect my skills and abilities	1	2	3	4
If something went wrong, no one would come to my assistance	1	2	3	4
I have close relationships that provide me with a sense of emotional security and well being	1	2	3	4
I have relationships where my competence and skills are recognized	1	2	3	4
There is no one who shares my interests and concerns	1	2	3	4
There is a trustworthy person I could turn to for advice if I were having problems	1	2	3	4

Appendix E: Supplementary Data for Chapter IV

1.a. Literature Search Procedures

Two separate computerised searches were performed in the PubMed database using MeSH terms and keywords pertinent to three main concepts: age group, depression, and exercise. During the initial search, age group MeSH terms were used (i.e., ‘aged’, ‘middle aged’, ‘younger adult’, ‘adolescent’, ‘child’, and ‘infant’) in combination with depression-related MeSH terms (i.e., ‘depressive disorder’ and ‘depression’) and depression-related keywords (i.e., ‘depress*’ and ‘dysthymi*’). A secondary search was then performed with the addition of exercise-related keywords (i.e., ‘exercise’, ‘physical activity’, ‘weight training’, ‘weight lifting’, ‘resistance training’, ‘strength training’, ‘balance training’, ‘aerobic training’, ‘anaerobic training’, ‘yoga’, ‘tai chi’, ‘taiji’, ‘qigong’, ‘walk*’, ‘jog*’, ‘run*’, ‘swim*’, ‘danc*’, and ‘cycl*’). Total search results were determined based on the total number of retrieved records from inception up to and including May, 2019.

1.b. Initial Search Results

Older Adults Search Strategy #1

(aged[Mesh]) AND (depressive disorder[Mesh] OR depression[Mesh] OR depress*[Title/Abstract] OR dysthymi*[Title/Abstract])

Total Search Results = 92,108

Younger Adults Search Strategy #1

(middle aged[Mesh] OR young adult[Mesh]) AND (depressive disorder[Mesh] OR depression[Mesh] OR depress*[Title/Abstract] OR dysthymi*[Title/Abstract])

Total Search Results = 150,320

Children and Adolescents Search Strategy #1

(adolescent[Mesh] OR child[Mesh] OR infant[Mesh]) AND (depressive disorder[Mesh] OR depression[Mesh] OR depress*[Title/Abstract] OR dysthymi*[Title/Abstract])

Total Search Results = 79,308

1.c. Secondary Search Results

Older Adults Search Strategy #2

(aged[Mesh]) AND (depressive disorder[Mesh] OR depression[Mesh] OR depress*[Title/Abstract] OR dysthymi*[Title/Abstract]) AND (exercise[Title/Abstract] OR physical activity[Title/Abstract] OR weight training[Title/Abstract] OR weight lifting[Title/Abstract] OR resistance training[Title/Abstract] OR strength training[Title/Abstract] OR balance training[Title/Abstract] OR aerobic training[Title/Abstract] OR anaerobic training[Title/Abstract] OR yoga[Title/Abstract] OR tai chi[Title/Abstract] OR taiji[Title/Abstract] OR qigong[Title/Abstract] OR walk*[Title/Abstract] OR jog*[Title/Abstract] OR run*[Title/Abstract] OR swim*[Title/Abstract] OR danc*[Title/Abstract] OR cycl*[Title/Abstract])

Total Search Results = 8,113

Younger Adults Search Strategy #2

(middle aged[Mesh] OR young adult[Mesh]) AND (depressive disorder[Mesh] OR depression[Mesh] OR depress*[Title/Abstract] OR dysthymi*[Title/Abstract]) AND (exercise[Title/Abstract] OR physical activity[Title/Abstract] OR weight training[Title/Abstract] OR weight lifting[Title/Abstract] OR resistance training[Title/Abstract] OR strength training[Title/Abstract] OR balance training[Title/Abstract] OR aerobic training[Title/Abstract] OR anaerobic training[Title/Abstract] OR yoga[Title/Abstract] OR tai chi[Title/Abstract] OR taiji[Title/Abstract] OR qigong[Title/Abstract] OR walk*[Title/Abstract] OR jog*[Title/Abstract] OR run*[Title/Abstract] OR swim*[Title/Abstract] OR danc*[Title/Abstract] OR cycl*[Title/Abstract])

Total Search Results = 11,919

Children and Adolescents Search Strategy #2

(adolescent[Mesh] OR child[Mesh] OR infant[Mesh]) AND (depressive disorder[Mesh] OR depression[Mesh] OR depress*[Title/Abstract] OR dysthymi*[Title/Abstract]) AND (exercise[Title/Abstract] OR physical activity[Title/Abstract] OR weight training[Title/Abstract] OR weight lifting[Title/Abstract] OR resistance training[Title/Abstract] OR strength training[Title/Abstract] OR balance training[Title/Abstract] OR aerobic training[Title/Abstract] OR anaerobic training[Title/Abstract] OR yoga[Title/Abstract] OR tai chi[Title/Abstract] OR taiji[Title/Abstract] OR qigong[Title/Abstract] OR walk*[Title/Abstract] OR jog*[Title/Abstract] OR run*[Title/Abstract] OR swim*[Title/Abstract] OR danc*[Title/Abstract] OR cycl*[Title/Abstract])

Total Search Results = 3,319

2. Histogram of Social Support

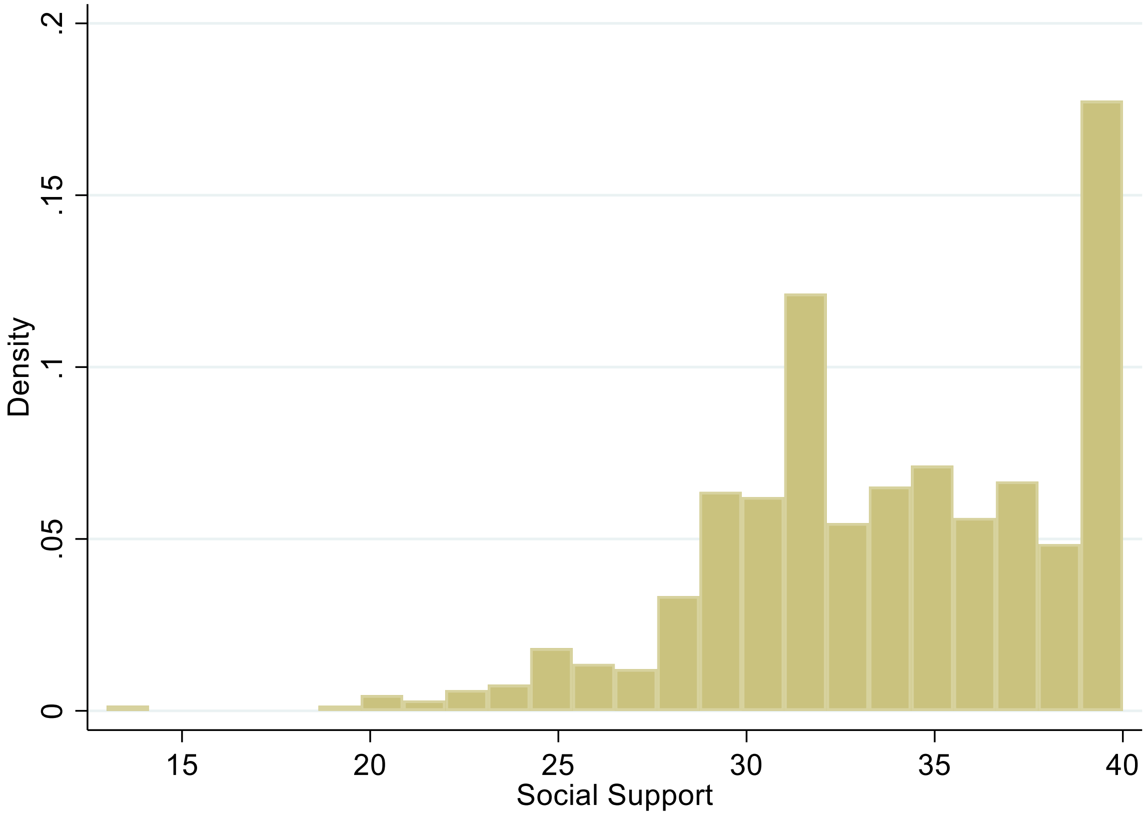


Figure E1. Histogram depicting the distribution of social support scores measured with the Social Provisions Scale - Short Form (SPS-10) in community-dwelling older adults aged 65-96 years (*n* = 586).

Appendix F: Tools for Chapters V and VI

1. Example of PubMed Search Strategy

aged, 80 and over[Mesh] OR ***frail elderly[Mesh]*** OR older[Title/Abstract] OR elderly[Title/Abstract] OR senior*[Title/Abstract] OR geriatric*[Title/Abstract]

AND

exercise[Title/Abstract] OR physical activity[Title/Abstract] OR weight training[Title/Abstract] OR weight lifting[Title/Abstract] OR resistance training[Title/Abstract] OR strength training[Title/Abstract] OR balance training[Title/Abstract] OR aerobic training[Title/Abstract] OR anaerobic training[Title/Abstract] OR yoga[Title/Abstract] OR tai chi[Title/Abstract] OR taiji[Title/Abstract] OR qigong[Title/Abstract] OR walk*[Title/Abstract] OR jog*[Title/Abstract] OR run*[Title/Abstract] OR swim*[Title/Abstract] OR danc*[Title/Abstract] OR cycl*[Title/Abstract]

AND

depressive disorder[Mesh] OR ***depression[Mesh]*** OR depress*[Title/Abstract] OR dysthymi*[Title/Abstract]

AND

randomized controlled trial[Publication Type] OR controlled trial[Title/Abstract] OR controlled study[Title/Abstract] OR controlled clinical trial[Title/Abstract] OR controlled clinical study[Title/Abstract] OR RCT[Title/Abstract] OR randomiz*[Title/Abstract] OR randomis*[Title/Abstract] OR randomly[Title/Abstract]

2. Data Extraction Form

Author(s): ____

Year: __________ Country: ______________

Publication Status:

☐ Published

☐ Unpublished

Treatment Group			Control Group		
M_{age}	SD_{age}	% Females	M_{age}	SD_{age}	% Females

Source of Participants:

☐ Community

☐ Residential

☐ Clinical

Depression at Baseline:

☐ No

☐ Yes

Depression Diagnosis:

☐ Cut-off: ____________________

☐ Clinical: ____________________

Inclusion and Inequity Criteria: ____

____

Cluster RCT Design:

☐ No

☐ Yes: ______ (Number of Clusters)

Intention-to-Treat Analysis:

☐ No

☐ Yes: ______________________

Potential Non-Exercise Components: ☐ No
☐ Yes: ________________________

Objective Fitness Measure(s): ____
____

Control Type: ☐ Wait-List
☐ Usual Care
☐ Attention-Control: ____________

Length of Exercise Intervention: __________ Weeks / Months

Type of Exercise: ☐ Aerobic
☐ Resistance
☐ Mind-Body
☐ Combination

Intensity of Exercise: ☐ Low ☐ Moderate ☐ High

____
HRmax / VO2max / 1Rmax / RPE

Frequency of Exercise (Per Week): __________

Duration of Exercise (Per Session): __________

Format of Exercise: ☐ Group
☐ Individual

Format of Supervision: ☐ Supervised
☐ Unsupervised: _______________

Outcome Data

Adherence to Exercise Treatment: ________________

Treatment Attrition (Dropout):

_________ (Pre-Treatment) - _________ (Post-Treatment) = _________ (Total Attrition)

Adverse Events: ____

____

____

____

Depression Effect Size Data

(1) Depression Measure:

Treatment Group					Control Group				
Pre-Test		Post-Test		*n*	Pre-Test		Post-Test		*n*
M	*SD*	*M*	*SD*		*M*	*SD*	*M*	*SD*	

Other Effect Size Data:	

(2) Depression Measure:

Treatment Group					Control Group				
Pre-Test		Post-Test		*n*	Pre-Test		Post-Test		*n*
M	*SD*	*M*	*SD*		*M*	*SD*	*M*	*SD*	

Other Effect Size Data:	

(3) Depression Measure:

Treatment Group					Control Group				
Pre-Test		Post-Test		*n*	Pre-Test		Post-Test		*n*
M	*SD*	*M*	*SD*		*M*	*SD*	*M*	*SD*	

Other Effect Size Data:	

Risk of Bias Assessment

Random Sequence Generation (Selection Bias): ☐ Low ☐ Moderate ☐ High

____

Allocation Concealment (Selection Bias): ☐ Low ☐ Moderate ☐ High

____

Blinding of Outcome Assessment (Detection Bias): ☐ Low ☐ Moderate ☐ High

____

Incomplete Outcome Data (Attrition Bias): ☐ Low ☐ Moderate ☐ High

____

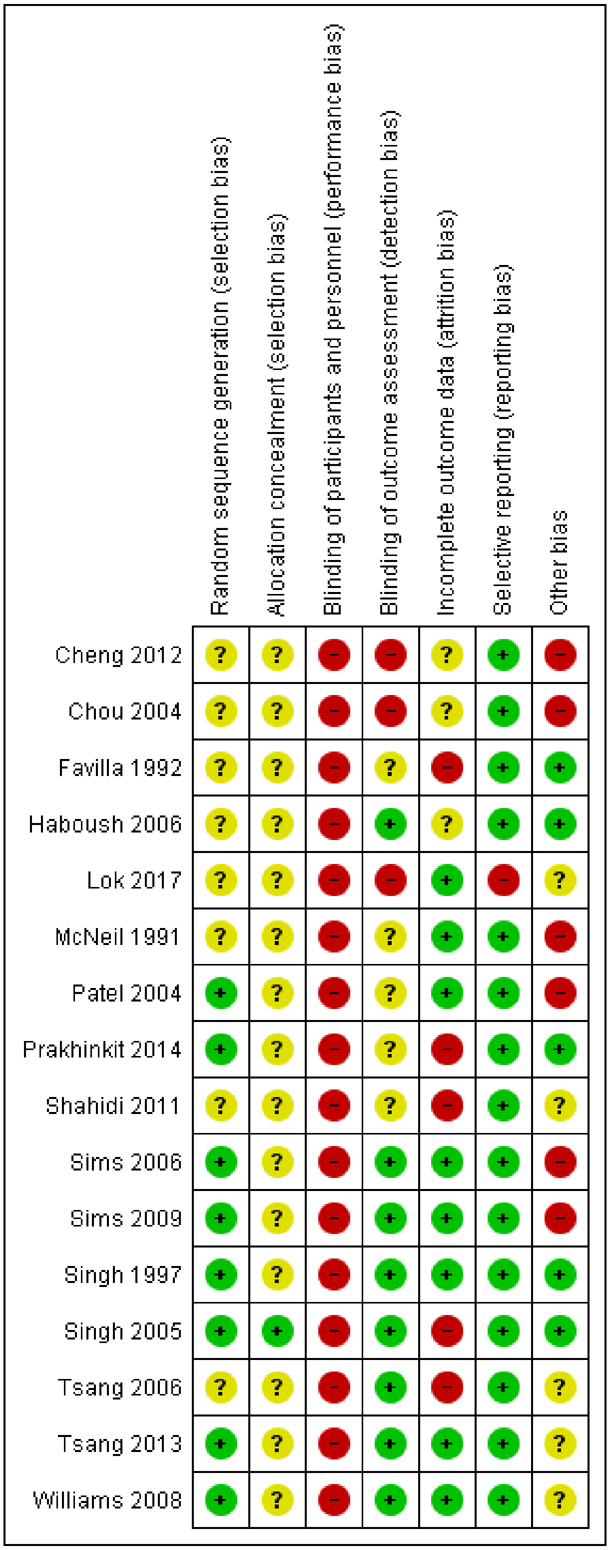
Selective Reporting (Reporting Bias): ☐ Low ☐ Moderate ☐ High

____

Other Bias: ☐ Low ☐ Moderate ☐ High

____

Appendix G: Supplementary Data for Chapter V



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Cheng 2012	?	?	−	−	?	+	−
Chou 2004	?	?	−	−	?	+	−
Favilla 1992	?	?	−	?	−	+	+
Haboush 2006	?	?	−	+	?	+	+
Lok 2017	?	?	−	−	+	−	?
McNeil 1991	?	?	−	?	+	+	−
Patel 2004	+	?	−	?	+	+	−
Prakhinkit 2014	+	?	−	?	−	+	+
Shahidi 2011	?	?	−	?	−	+	?
Sims 2006	+	?	−	+	+	+	−
Sims 2009	+	?	−	+	+	+	−
Singh 1997	+	?	−	+	+	+	+
Singh 2005	+	+	−	+	−	+	+
Tsang 2006	?	?	−	+	−	+	?
Tsang 2013	+	?	−	+	+	+	?
Williams 2008	+	?	−	+	+	+	?

Figure G1. Risk of bias summary for studies included in the systematic review.

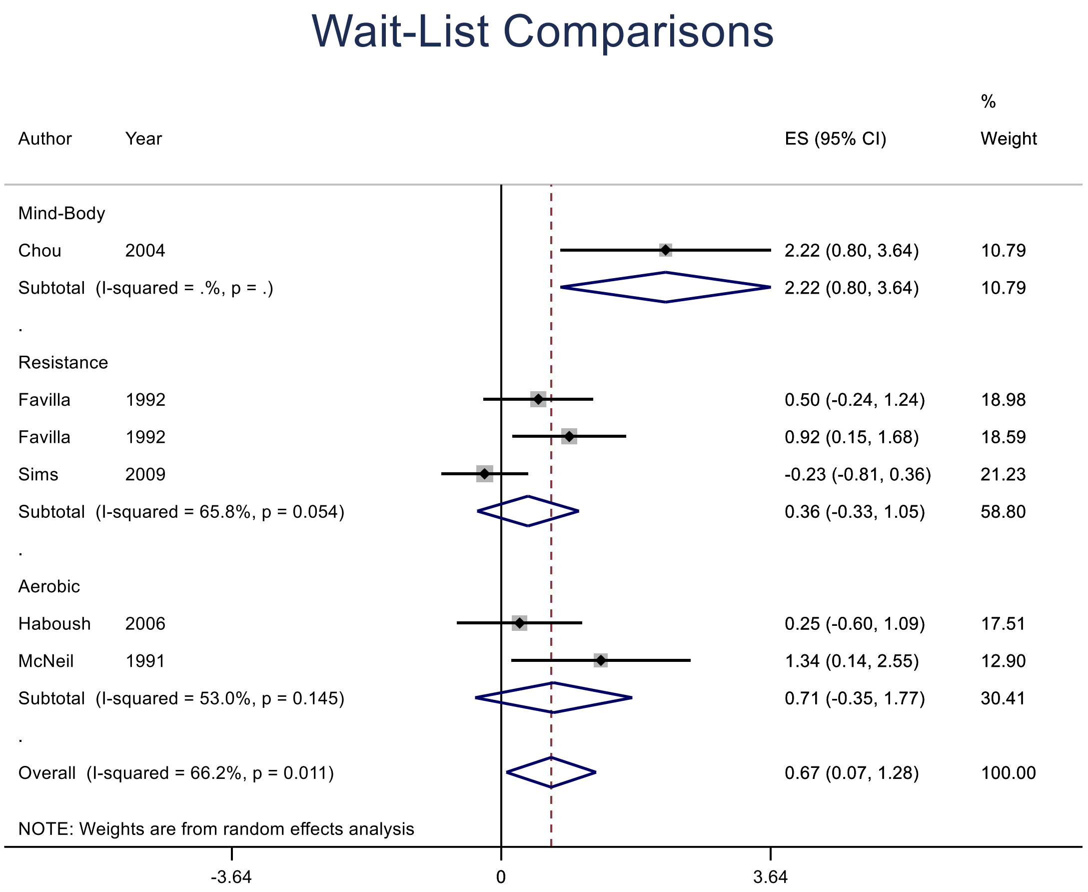


Figure G2. Random-effects meta-analysis for exercise versus wait-list on the depressive symptoms network. The squares represent the effect size estimate (Hedges' *g*) for each study. The diamonds represent the effect size estimates for subgroups and the overall effect. The horizontal lines represent the confidence intervals (*CI*). The vertical line represents the null hypothesis (Hedges' *g* = 0). Positive scores indicate a greater decrease in depressive symptom for the exercise group.

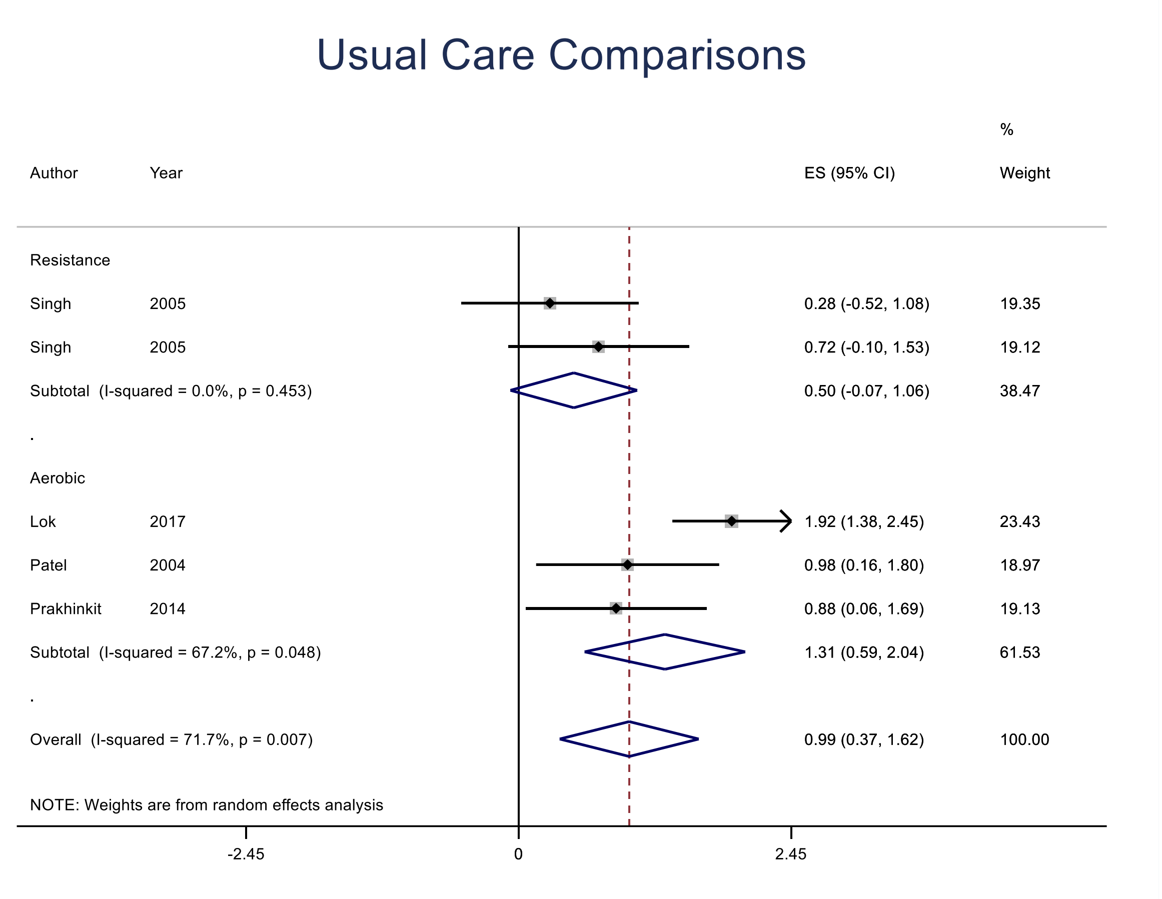


Figure G3. Random-effects meta-analysis for exercise versus usual care on the depressive symptoms network. The squares represent the effect size estimate (Hedges' *g*) for each study. The diamonds represent the effect size estimates for subgroups and the overall effect. The horizontal lines represent the confidence intervals (*CI*). The vertical line represents the null hypothesis (Hedges' *g* = 0). Positive scores indicate a greater decrease in depressive symptom for the exercise group.

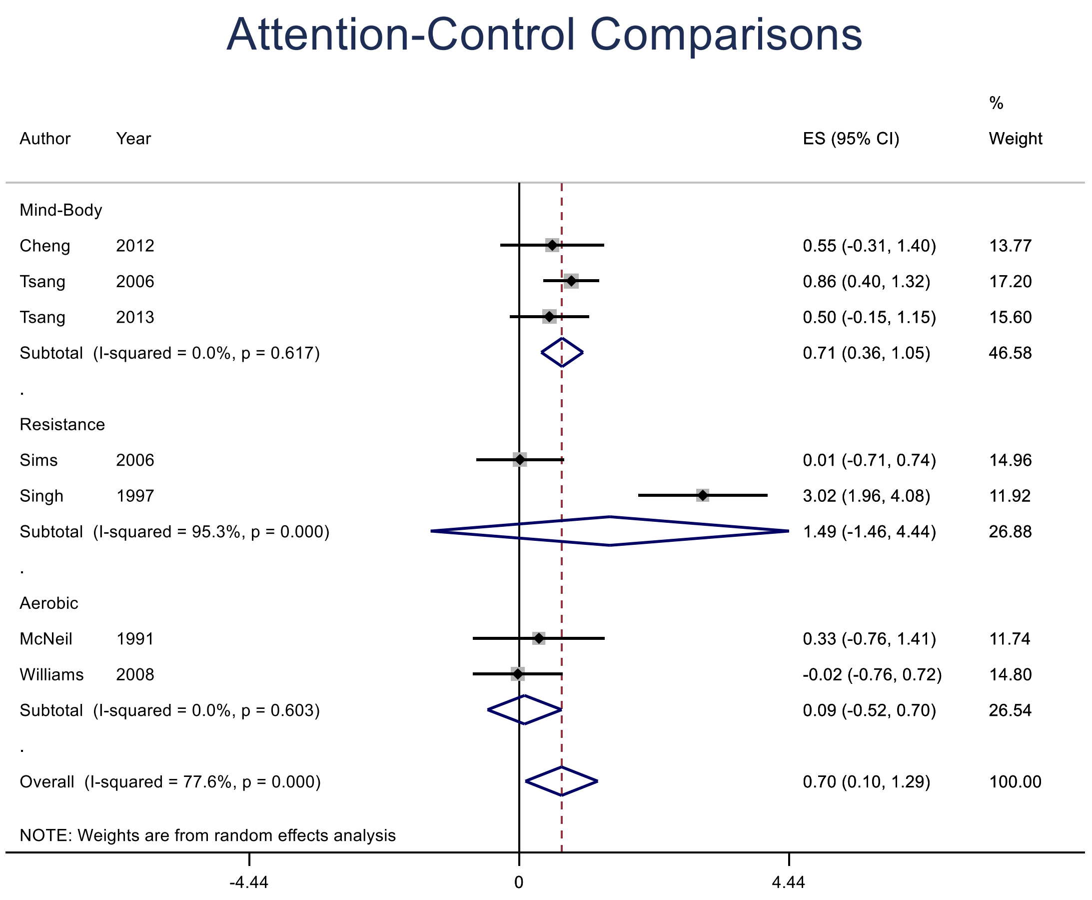
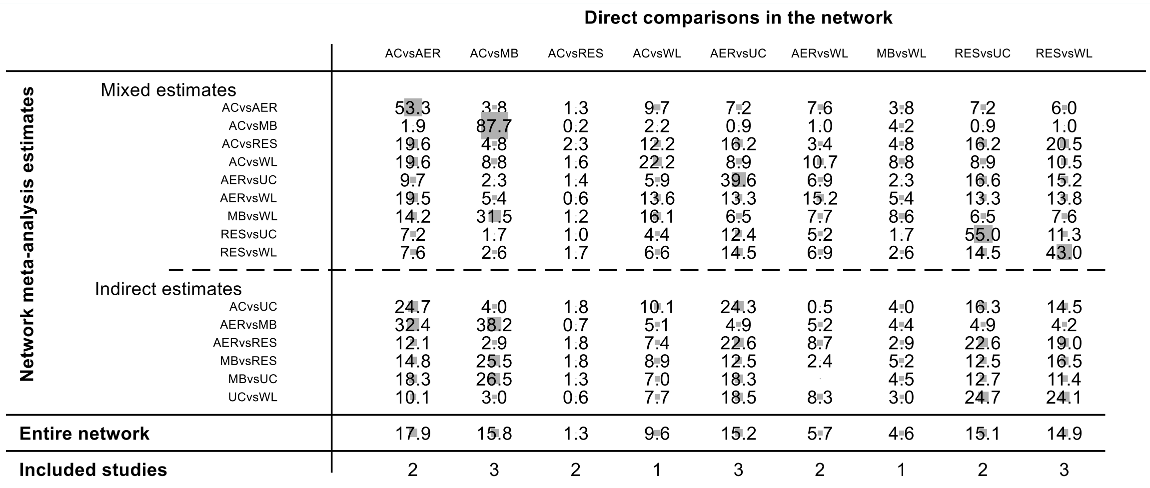


Figure G4. Random-effects meta-analysis for exercise versus attention-control on the depressive symptoms network. The squares represent the effect size estimate (Hedges' *g*) for each study. The diamonds represent the effect size estimates for subgroups and the overall effect. The horizontal lines represent the confidence intervals (*CI*). The vertical line represents the null hypothesis (Hedges' *g* = 0). Positive scores indicate a greater decrease in depressive symptom for the exercise group.



Direct comparisons in the network

Network meta-analysis estimates	ACvsAER	ACvsMB	ACvsRES	ACvsWL	AERvsUC	AERvsWL	MBvsWL	RESvsUC	RESvsWL
Mixed estimates									
ACvsAER	53.3	3.8	1.3	9.7	7.2	7.6	3.8	7.2	6.0
ACvsMB	1.9	87.7	0.2	2.2	0.9	1.0	4.2	0.9	1.0
ACvsRES	19.6	4.8	2.3	12.2	16.2	3.4	4.8	16.2	20.5
ACvsWL	19.6	8.8	1.6	22.2	8.9	10.7	8.8	8.9	10.5
AERvsUC	9.7	2.3	1.4	5.9	39.6	6.9	2.3	16.6	15.2
AERvsWL	19.5	5.4	0.6	13.6	13.3	15.2	5.4	13.3	13.8
MBvsWL	14.2	31.5	1.2	16.1	6.5	7.7	8.6	6.5	7.6
RESvsUC	7.2	1.7	1.0	4.4	12.4	5.2	1.7	55.0	11.3
RESvsWL	7.6	2.6	1.7	6.6	14.5	6.9	2.6	14.5	43.0
Indirect estimates									
ACvsUC	24.7	4.0	1.8	10.1	24.3	0.5	4.0	16.3	14.5
AERvsMB	32.4	38.2	0.7	5.1	4.9	5.2	4.4	4.9	4.2
AERvsRES	12.1	2.9	1.8	7.4	22.6	8.7	2.9	22.6	19.0
MBvsRES	14.8	25.5	1.8	8.9	12.5	2.4	5.2	12.5	16.5
MBvsUC	18.3	26.5	1.3	7.0	18.3		4.5	12.7	11.4
UCvsWL	10.1	3.0	0.6	7.7	18.5	8.3	3.0	24.7	24.1
Entire network	17.9	15.8	1.3	9.6	15.2	5.7	4.6	15.1	14.9
Included studies	2	3	2	1	3	2	1	2	3

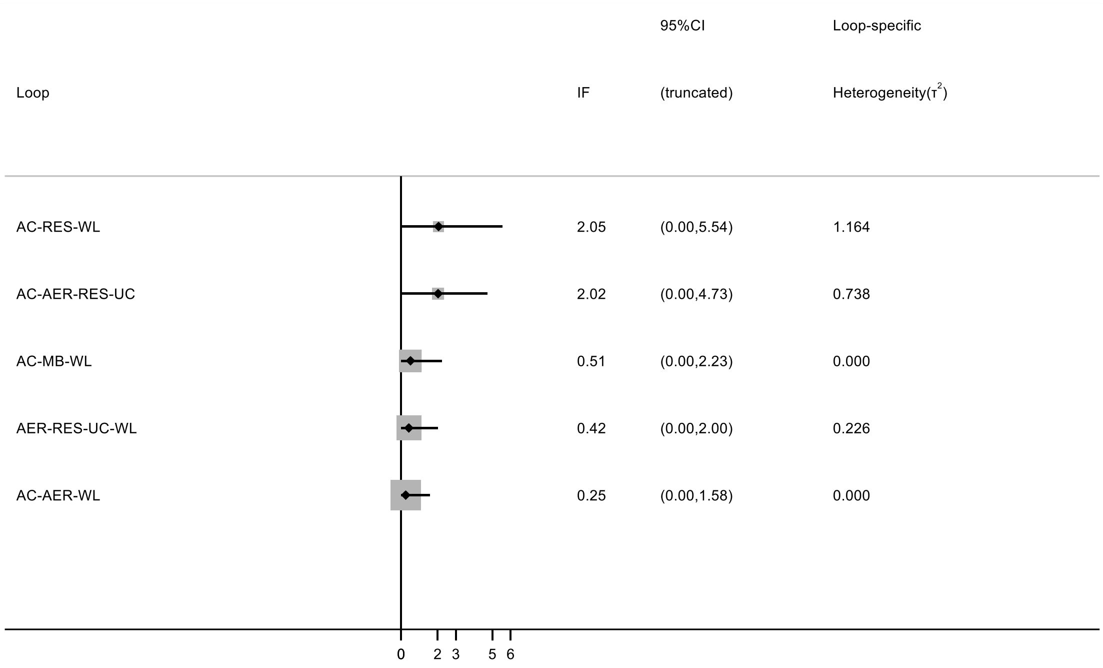
Figure G5. Contribution plots for the depressive symptoms network. Square size is proportional to the weight of each direct summary effect (horizontal axis) for the estimation of each network summary effect (vertical axis). AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

Table G1

Inconsistency test between direct and indirect comparisons for depressive symptoms

Side	***n***	**Direct**		**Indirect**		**Difference**		***p* > *Z***
		Coefficient	***SE***	**Coefficient**	***SE***	**Coefficient**	***SE***	
AER vs. WL	2	0.781	0.656	0.805	0.780	-0.023	1.019	.982
AER vs. UC	3	1.290	0.484	0.170	0.861	1.120	0.987	.257
RES vs. WL	3	0.379	0.487	1.372	0.726	-0.993	0.874	.256
RES vs. UC	2	0.498	0.605	1.618	0.779	-1.120	0.987	.257
MB vs. WL	1	2.217	1.040	0.651	0.706	1.566	1.257	.213
AC vs. WL	1	0.996	0.895	-0.016	0.575	1.012	1.064	.341
AC vs. AER	2	-0.154	0.612	-1.127	0.808	0.973	1.014	.337
AC vs. RES	2	-1.316	0.541	0.696	0.574	-2.012	0.789	.011
AC vs. MB	3	-0.644	0.473	-2.211	1.165	1.566	1.257	.213

Notes. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.



Loop	IF	95%CI (truncated)	Loop-specific Heterogeneity(τ^2)
AC-RES-WL	2.05	(0.00,5.54)	1.164
AC-AER-RES-UC	2.02	(0.00,4.73)	0.738
AC-MB-WL	0.51	(0.00,2.23)	0.000
AER-RES-UC-WL	0.42	(0.00,2.00)	0.226
AC-AER-WL	0.25	(0.00,1.58)	0.000

Figure G6. Inconsistency plot for the depressive symptoms network, assuming loop-specific heterogeneity estimates. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

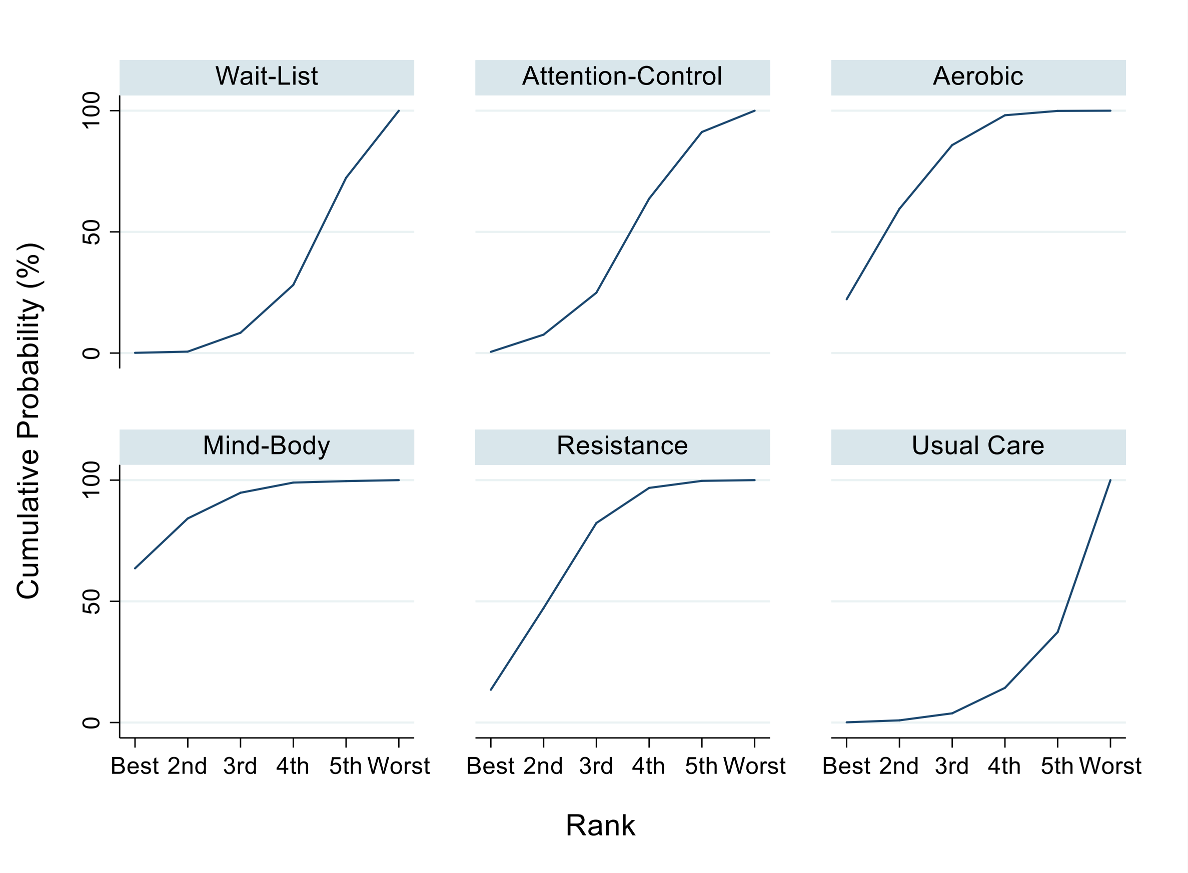


Figure G7. Plots of the surface under the cumulative ranking curves (SUCRA) for all comparisons in the depressive symptoms network.

Table G2

Results of the network rank test for depressive symptoms

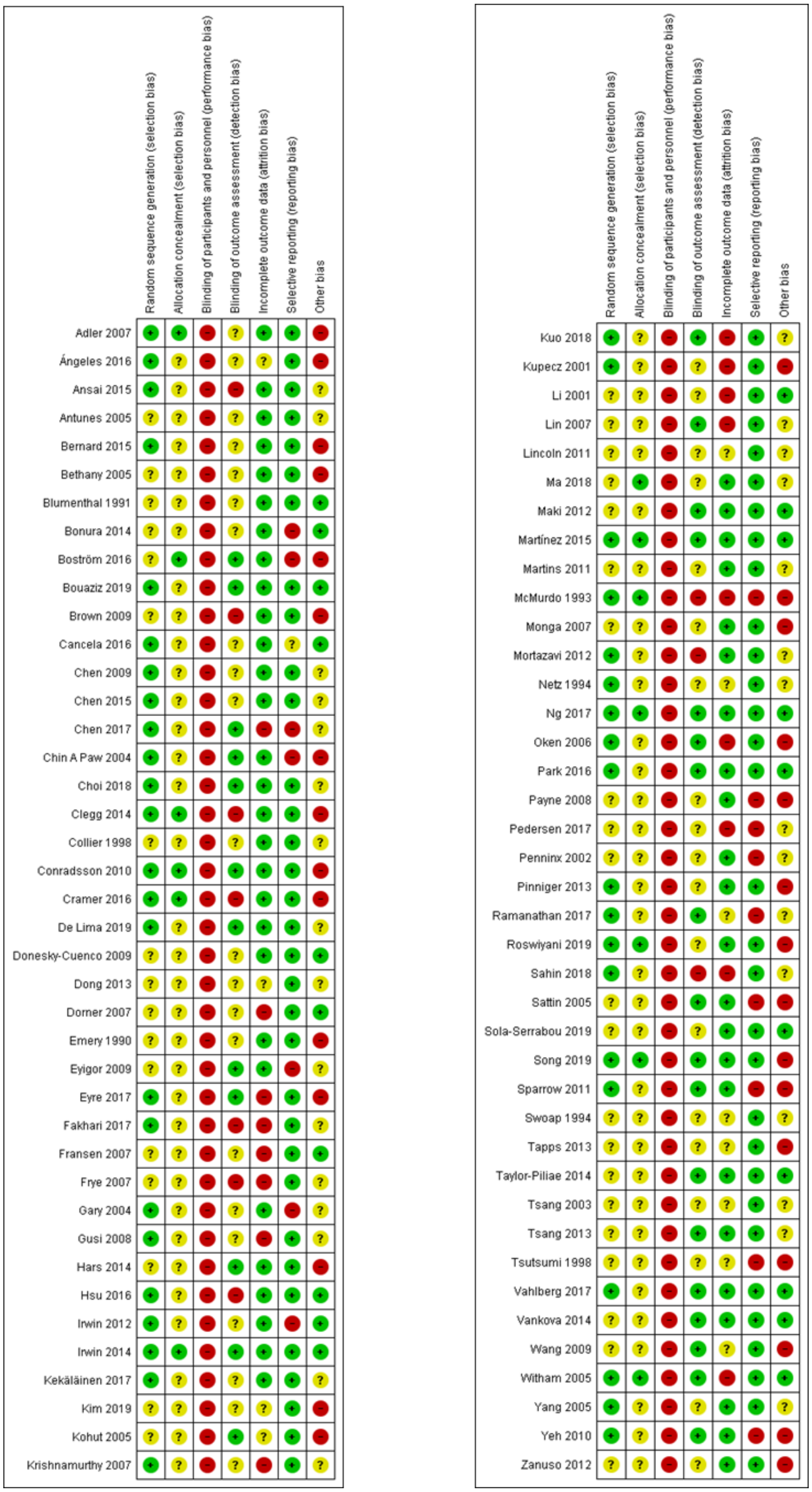
	Wait-List	**Attention-Control**	**Aerobic**	**Mind-Body**	**Resistance**	**Usual Care**
Best	0.1	0.5	22.2	63.6	13.5	0.1
2nd	0.5	7.1	37.3	20.6	33.7	0.8
3rd	7.8	17.3	26.3	10.6	35.1	2.9
4th	19.7	38.8	12.3	4.2	14.5	10.5
5th	44.2	27.5	1.8	0.6	2.9	23.0
Worst	27.7	8.8	0.1	0.4	0.3	62.7
Mean Rank	4.9	4.1	2.3	1.6	2.6	5.4
SUCRA	21.9	37.6	73.1	88.2	67.9	11.3

Table G3

Meta-regression for effect modifiers on depressive symptoms

Effect Modifier	***n***	**β**	***SE***	***t***	***p*-value**	**Lower 95% *CI***	**Upper 95% *CI***	**τ^2**	**Residual I^2**	**Adj. R^2**
Year	18	0.013	0.035	0.38	.710	-0.060	0.087	1.108	87.23%	-6.64%
Risk of bias	18	-0.561	0.289	-1.94	.070	-1.173	0.052	0.855	84.59%	17.77%
Adherence	8	0.039	0.071	0.56	.599	-0.134	0.213	2.008	87.17%	-14.85%
Age	17	-0.031	0.050	-0.62	.544	-0.137	0.075	0.912	80.44%	-5.18%
Gender	16	-0.018	0.017	-1.01	.331	-0.055	0.020	1.112	87.04%	-0.14%
Source of participants	18	-0.101	0.579	-0.17	.864	-1.327	1.125	1.123	87.59%	-8.09%
Publication status	18	0.677	0.714	0.95	.357	-0.836	2.190	1.040	86.80%	-0.08%
Intention-to-treat	18	-0.544	0.637	-0.86	.405	-1.894	0.805	1.059	86.86%	-1.91%
Cluster randomisation	18	-0.828	1.189	-0.70	.496	-3.348	1.693	1.080	87.32%	-3.93%
Length of program	18	-0.094	0.079	-1.18	.255	-0.261	0.074	0.987	84.77%	5.01%
Format of exercise	18	-0.006	0.622	-0.01	.992	-1.325	1.313	1.122	87.61%	-7.93%
Intensity of exercise	8	-0.261	0.257	-1.02	.349	-0.890	0.368	1.294	84.81%	-0.03%
Frequency of exercise	18	0.181	0.362	0.50	.623	-0.586	0.949	1.098	86.76%	-5.69%
Duration of exercise	17	0.005	0.019	0.25	.807	-0.036	0.046	1.196	86.86%	-7.56%

Appendix H: Supplementary Data for Chapter VI



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Adler 2007	+	+	−	?	+	+	−
Ángeles 2016	+	?	−	?	?	+	−
Ansai 2015	+	?	−	−	+	+	?
Antunes 2005	?	?	−	?	+	+	?
Bernard 2015	+	?	−	?	+	+	−
Bethany 2005	?	?	−	?	+	+	−
Blumenthal 1991	?	?	−	?	+	+	+
Bonura 2014	?	?	−	?	+	−	+
Boström 2016	?	+	−	+	+	−	−
Bouaziz 2019	+	?	−	+	+	+	+
Brown 2009	?	?	−	−	+	+	−
Cancela 2016	+	?	−	?	+	?	+
Chen 2009	+	?	−	?	+	+	?
Chen 2015	+	?	−	?	+	+	?
Chen 2017	+	?	−	+	−	−	?
Chin A Paw 2004	+	?	−	+	+	−	−
Choi 2018	+	?	−	+	+	+	?
Clegg 2014	+	+	−	−	+	+	−
Collier 1998	?	?	−	?	+	+	?
Conradsson 2010	+	+	−	+	+	+	−
Cramer 2016	+	+	−	−	+	+	−
De Lima 2019	+	?	−	+	+	+	?
Donesky-Cuenco 2009	?	?	−	?	+	+	+
Dong 2013	?	?	−	?	?	+	?
Dorner 2007	?	?	−	?	−	+	+
Emery 1990	?	?	−	?	+	+	−
Eyigor 2009	?	?	−	+	+	−	?
Eyre 2017	+	?	−	+	−	+	−
Fakhari 2017	+	?	−	−	−	+	?
Fransen 2007	?	?	−	?	−	+	+
Frye 2007	?	?	−	−	−	+	?
Gary 2004	+	?	−	?	+	−	?
Gusi 2008	+	?	−	?	−	+	?
Hars 2014	?	?	−	+	+	+	−
Hsu 2016	+	?	−	−	+	+	+
Irwin 2012	+	?	−	?	+	−	+
Irwin 2014	+	+	−	+	+	+	+
Kekäläinen 2017	+	?	−	?	+	+	?
Kim 2019	?	?	−	?	?	+	−
Kohut 2005	?	?	−	+	?	+	−
Krishnamurthy 2007	+	?	−	?	−	+	?

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Kuo 2018	+	?	−	+	−	+	?
Kupecz 2001	+	?	−	?	−	+	−
Li 2001	?	?	−	?	−	+	+
Lin 2007	?	?	−	+	−	+	?
Lincoln 2011	?	?	−	?	?	+	?
Ma 2018	?	+	−	?	+	+	?
Maki 2012	?	?	−	+	+	+	+
Martínez 2015	+	+	−	+	+	+	+
Martins 2011	?	?	−	?	+	+	?
McMurdo 1993	+	+	−	−	−	−	−
Monga 2007	?	?	−	?	+	+	−
Mortazavi 2012	+	?	−	−	+	+	?
Netz 1994	+	?	−	?	?	+	?
Ng 2017	+	+	−	+	+	+	+
Oken 2006	+	?	−	+	−	+	−
Park 2016	+	?	−	+	+	+	+
Payne 2008	?	?	−	?	+	−	−
Pedersen 2017	?	?	−	?	−	−	?
Penninx 2002	?	?	−	?	+	−	?
Pinniger 2013	+	?	−	?	+	+	−
Ramanathan 2017	+	?	−	+	?	−	?
Roswiyani 2019	+	+	−	?	+	+	−
Sahin 2018	+	?	−	−	−	+	?
Sattin 2005	?	?	−	+	+	−	−
Sola-Serrabou 2019	?	?	−	?	+	+	+
Song 2019	+	+	−	+	+	+	−
Sparrow 2011	+	?	−	+	+	−	−
Swoap 1994	?	?	−	?	?	+	?
Tapps 2013	?	?	−	?	?	+	−
Taylor-Piliae 2014	?	?	−	+	+	+	+
Tsang 2003	?	?	−	?	?	+	?
Tsang 2013	?	?	−	+	+	+	?
Tsutsumi 1998	?	?	−	?	?	−	−
Vahlberg 2017	+	?	−	+	+	+	+
Vankova 2014	?	?	−	+	+	+	+
Wang 2009	?	?	−	+	?	+	−
Witham 2005	+	+	−	+	−	+	+
Yang 2005	+	?	−	?	+	+	?
Yeh 2010	+	?	−	+	+	−	−
Zanuso 2012	?	?	−	?	+	+	−

Figure H1. Risk of bias summary.

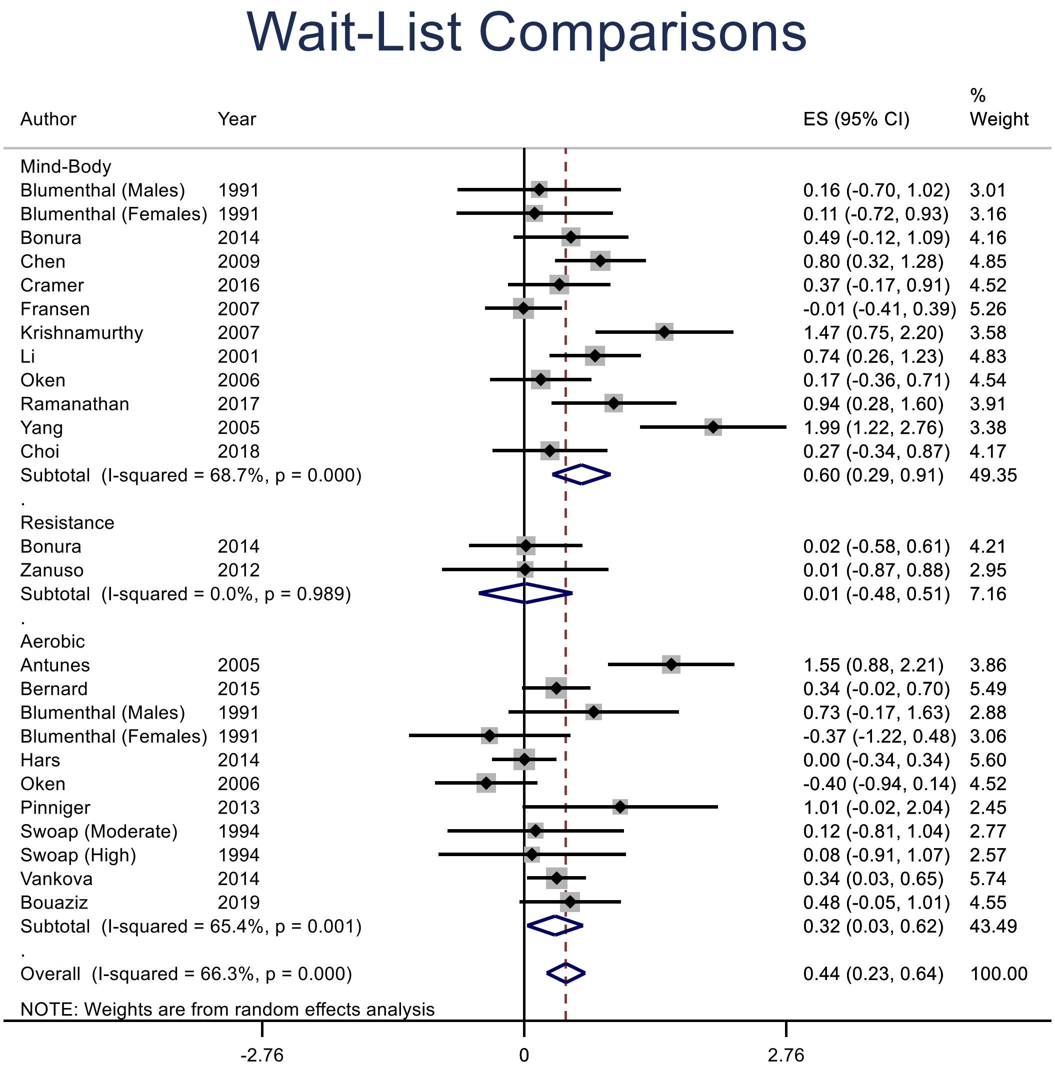


Figure H2. Random-effects meta-analysis for exercise versus wait-list on the depressive symptoms network. The squares represent the effect size estimate (Hedges' *g*) for each study. The diamonds represent the effect size estimates for subgroups and the overall effect. The horizontal lines represent the confidence intervals (*CI*). The vertical line represents the null hypothesis (Hedges' *g* = 0). Positive scores indicate a greater decrease in depressive symptom for the exercise group.

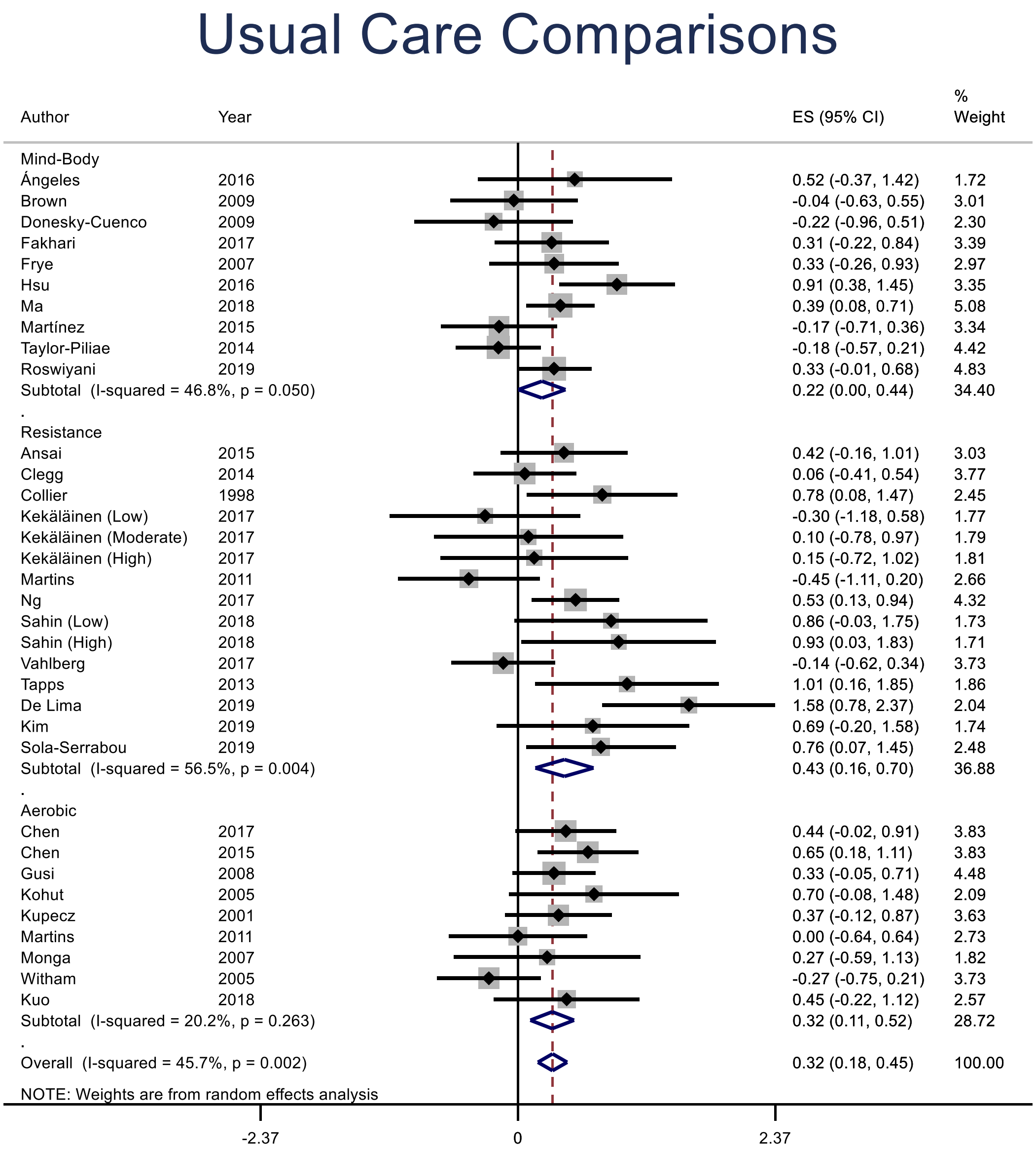


Figure H3. Random-effects meta-analysis for exercise versus usual care on the depressive symptoms network. The squares represent the effect size estimate (Hedges' *g*) for each study. The diamonds represent the effect size estimates for subgroups and the overall effect. The horizontal lines represent the confidence intervals (*CI*). The vertical line represents the null hypothesis (Hedges' *g* = 0). Positive scores indicate a greater decrease in depressive symptom for the exercise group.

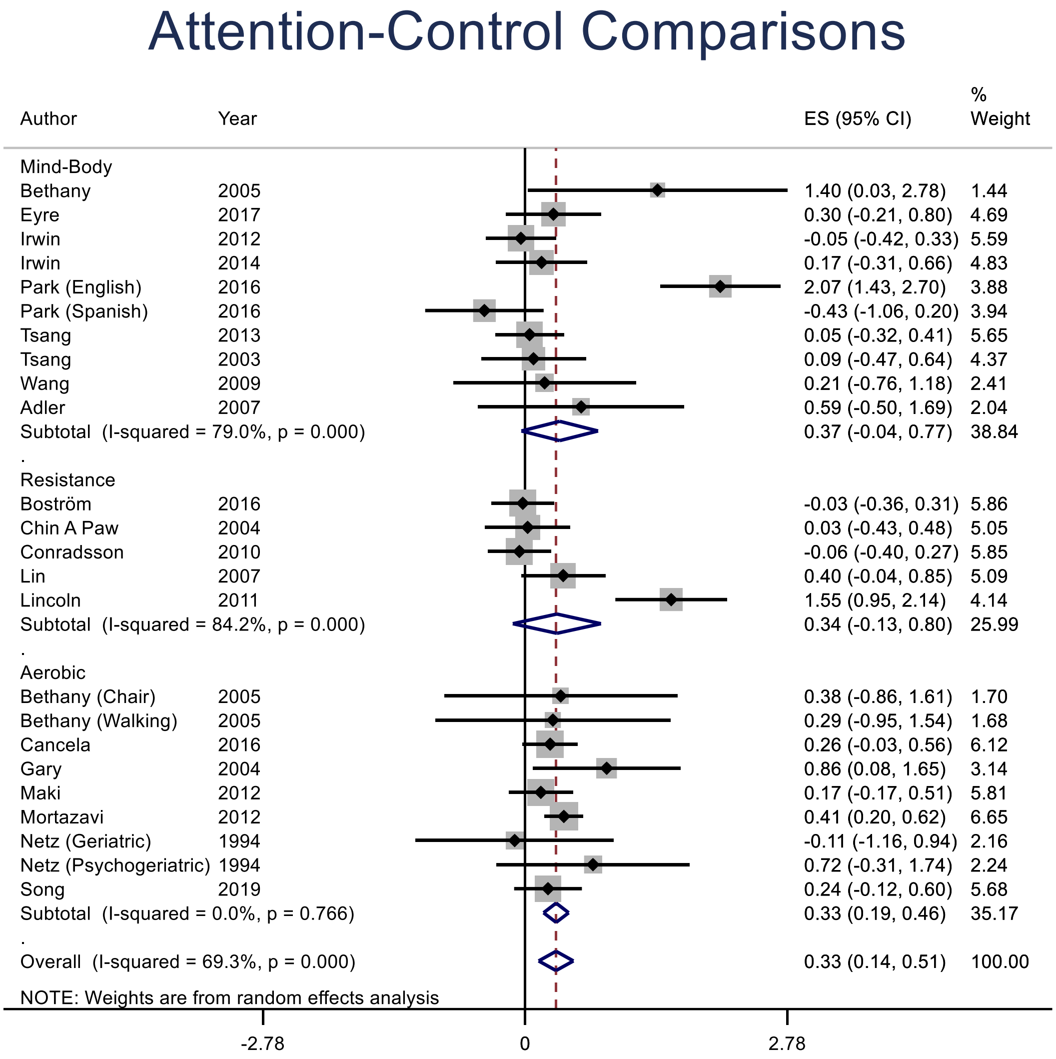


Figure H4. Random-effects meta-analysis for exercise versus attention-control on the depressive symptoms network. The squares represent the effect size estimate (Hedges' *g*) for each study. The diamonds represent the effect size estimates for subgroups and the overall effect. The horizontal lines represent the confidence intervals (*CI*). The vertical line represents the null hypothesis (Hedges' *g* = 0). Positive scores indicate a greater decrease in depressive symptom for the exercise group.

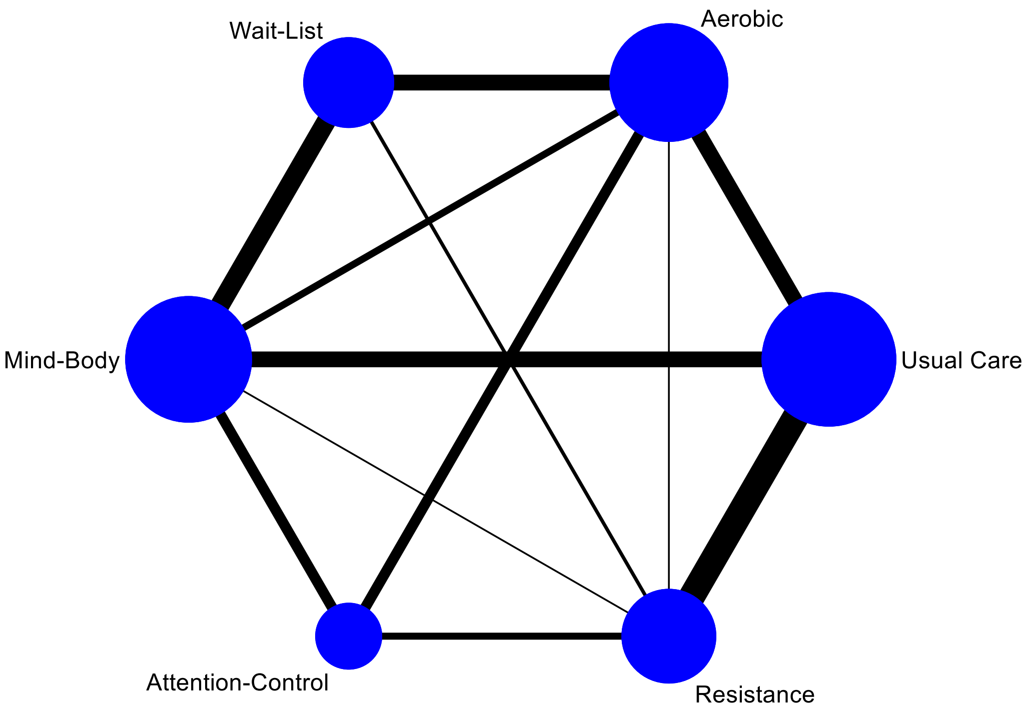
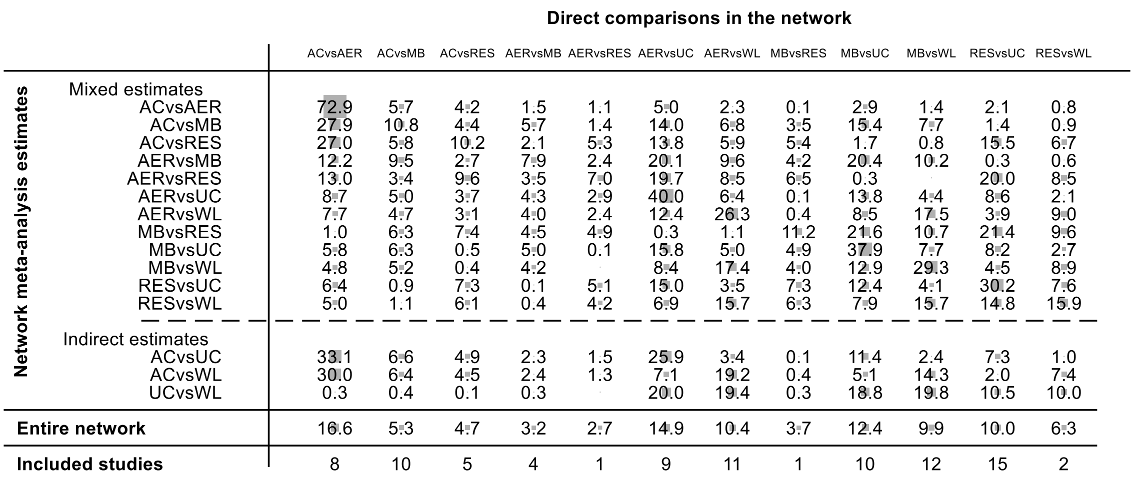


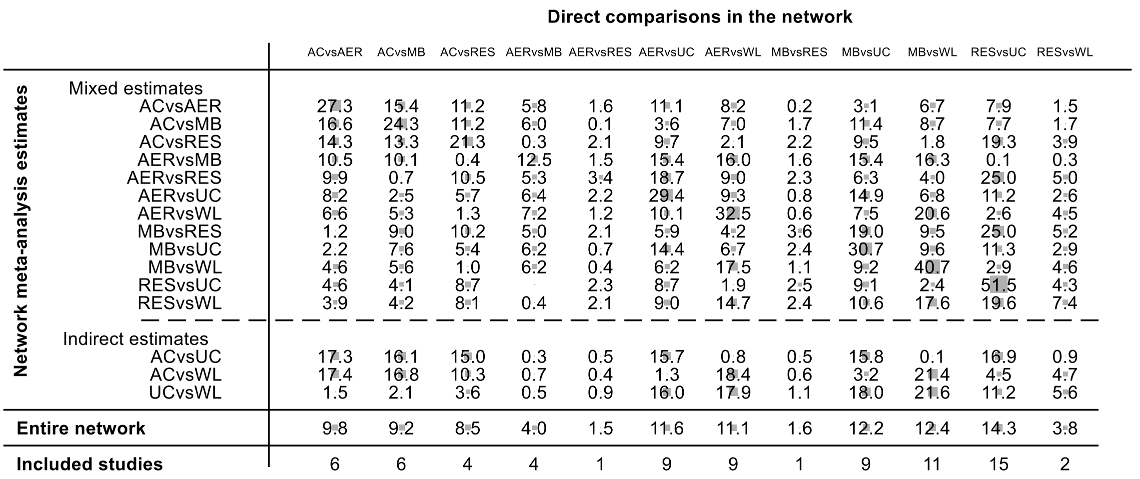
Figure H5. Network plot of comparisons for attrition. Line width is proportional to the number of pairwise effect size estimates and node size is proportional to the number of participants.



Direct comparisons in the network

Network meta-analysis estimates

	ACvsAER	ACvsMB	ACvsRES	AERvsMB	AERvsRES	AERvsUC	AERvsWL	MBvsRES	MBvsUC	MBvsWL	RESvsUC	RESvsWL
Mixed estimates												
ACvsAER	72.9	5.7	4.2	1.5	1.1	5.0	2.3	0.1	2.9	1.4	2.1	0.8
ACvsMB	27.9	10.8	4.4	5.7	1.4	14.0	6.8	3.5	15.4	7.7	1.4	0.9
ACvsRES	27.0	5.8	10.2	2.1	5.3	13.8	5.9	5.4	1.7	0.8	15.5	6.7
AERvsMB	12.2	9.5	2.7	7.9	2.4	20.1	9.6	4.2	20.4	10.2	0.3	0.6
AERvsRES	13.0	3.4	9.6	3.5	7.0	19.7	8.5	6.5	0.3		20.0	8.5
AERvsUC	8.7	5.0	3.7	4.3	2.9	40.0	6.4	0.1	13.8	4.4	8.6	2.1
AERvsWL	7.7	4.7	3.1	4.0	2.4	12.4	26.3	0.4	8.5	17.5	3.9	9.0
MBvsRES	1.0	6.3	7.4	4.5	4.9	0.3	1.1	11.2	21.6	10.7	21.4	9.6
MBvsUC	5.8	6.3	0.5	5.0	0.1	15.8	5.0	4.9	37.9	7.7	8.2	2.7
MBvsWL	4.8	5.2	0.4	4.2		8.4	17.4	4.0	12.9	29.3	4.5	8.9
RESvsUC	6.4	0.9	7.3	0.1	5.1	15.0	3.5	7.3	12.4	4.1	30.2	7.6
RESvsWL	5.0	1.1	6.1	0.4	4.2	6.9	15.7	6.3	7.9	15.7	14.8	15.9
Indirect estimates												
ACvsUC	33.1	6.6	4.9	2.3	1.5	25.9	3.4	0.1	11.4	2.4	7.3	1.0
ACvsWL	30.0	6.4	4.5	2.4	1.3	7.1	19.2	0.4	5.1	14.3	2.0	7.4
UCvsWL	0.3	0.4	0.1	0.3		20.0	19.4	0.3	18.8	19.8	10.5	10.0
Entire network	16.6	5.3	4.7	3.2	2.7	14.9	10.4	3.7	12.4	9.9	10.0	6.3
Included studies	8	10	5	4	1	9	11	1	10	12	15	2



Direct comparisons in the network

Network meta-analysis estimates

	ACvsAER	ACvsMB	ACvsRES	AERvsMB	AERvsRES	AERvsUC	AERvsWL	MBvsRES	MBvsUC	MBvsWL	RESvsUC	RESvsWL
Mixed estimates												
ACvsAER	27.3	15.4	11.2	5.8	1.6	11.1	8.2	0.2	3.1	6.7	7.9	1.5
ACvsMB	16.6	24.3	11.2	6.0	0.1	3.6	7.0	1.7	11.4	8.7	7.7	1.7
ACvsRES	14.3	13.3	21.3	0.3	2.1	9.7	2.1	2.2	9.5	1.8	19.3	3.9
AERvsMB	10.5	10.1	0.4	12.5	1.5	15.4	16.0	1.6	15.4	16.3	0.1	0.3
AERvsRES	9.9	0.7	10.5	5.3	3.4	18.7	9.0	2.3	6.3	4.0	25.0	5.0
AERvsUC	8.2	2.5	5.7	6.4	2.2	29.4	9.3	0.8	14.9	6.8	11.2	2.6
AERvsWL	6.6	5.3	1.3	7.2	1.2	10.1	32.5	0.6	7.5	20.6	2.6	4.5
MBvsRES	1.2	9.0	10.2	5.0	2.1	5.9	4.2	3.6	19.0	9.5	25.0	5.2
MBvsUC	2.2	7.6	5.4	6.2	0.7	14.4	6.7	2.4	30.7	9.6	11.3	2.9
MBvsWL	4.6	5.6	1.0	6.2	0.4	6.2	17.5	1.1	9.2	40.7	2.9	4.6
RESvsUC	4.6	4.1	8.7		2.3	8.7	1.9	2.5	9.1	2.4	51.5	4.3
RESvsWL	3.9	4.2	8.1	0.4	2.1	9.0	14.7	2.4	10.6	17.6	19.6	7.4
Indirect estimates												
ACvsUC	17.3	16.1	15.0	0.3	0.5	15.7	0.8	0.5	15.8	0.1	16.9	0.9
ACvsWL	17.4	16.8	10.3	0.7	0.4	1.3	18.4	0.6	3.2	21.4	4.5	4.7
UCvsWL	1.5	2.1	3.6	0.5	0.9	16.0	17.9	1.1	18.0	21.6	11.2	5.6
Entire network	9.8	9.2	8.5	4.0	1.5	11.6	11.1	1.6	12.2	12.4	14.3	3.8
Included studies	6	6	4	4	1	9	9	1	9	11	15	2

Figure H6. Contribution plots for the depressive symptoms (upper) and attrition (lower) networks. Square size is proportional to the weight of each direct summary effect (horizontal axis) for the estimation of each network summary effect (vertical axis). AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

Table H1

Inconsistency test between direct and indirect comparisons for depressive symptoms

Side	***n***	**Direct**		**Indirect**		**Difference**		***p* > *Z***
		Coefficient	***SE***	**Coefficient**	***SE***	**Coefficient**	***SE***	
AER vs. WL	11	0.283	0.152	0.596	0.213	-0.313	0.262	.232
AER vs. RES	1	0.471	0.496	-0.111	0.152	0.583	0.519	.261
AER vs. MB	4	-0.423	0.257	-0.032	0.136	-0.392	0.291	.177
AER vs. UC	9	0.314	0.165	0.227	0.180	0.086	0.244	.723
RES vs. WL	2	0.012	0.369	0.553	0.179	-0.541	0.411	.188
RES vs. UC	15	0.420	0.139	0.116	0.225	0.303	0.264	.251
MB vs. WL	12	0.575	0.143	0.332	0.228	0.243	0.269	.365
MB vs. RES	1	0.466	0.471	0.015	0.148	0.451	0.494	.361
MB vs. UC	10	0.218	0.152	0.620	0.175	-0.402	0.231	.082
AC vs. AER	8	-0.334	0.176	-0.202	0.186	-0.132	0.256	.606
AC vs. RES	5	-0.323	0.206	-0.344	0.198	0.021	0.286	.942
AC vs. MB	10	-0.363	0.163	-0.424	0.189	0.061	0.249	.808

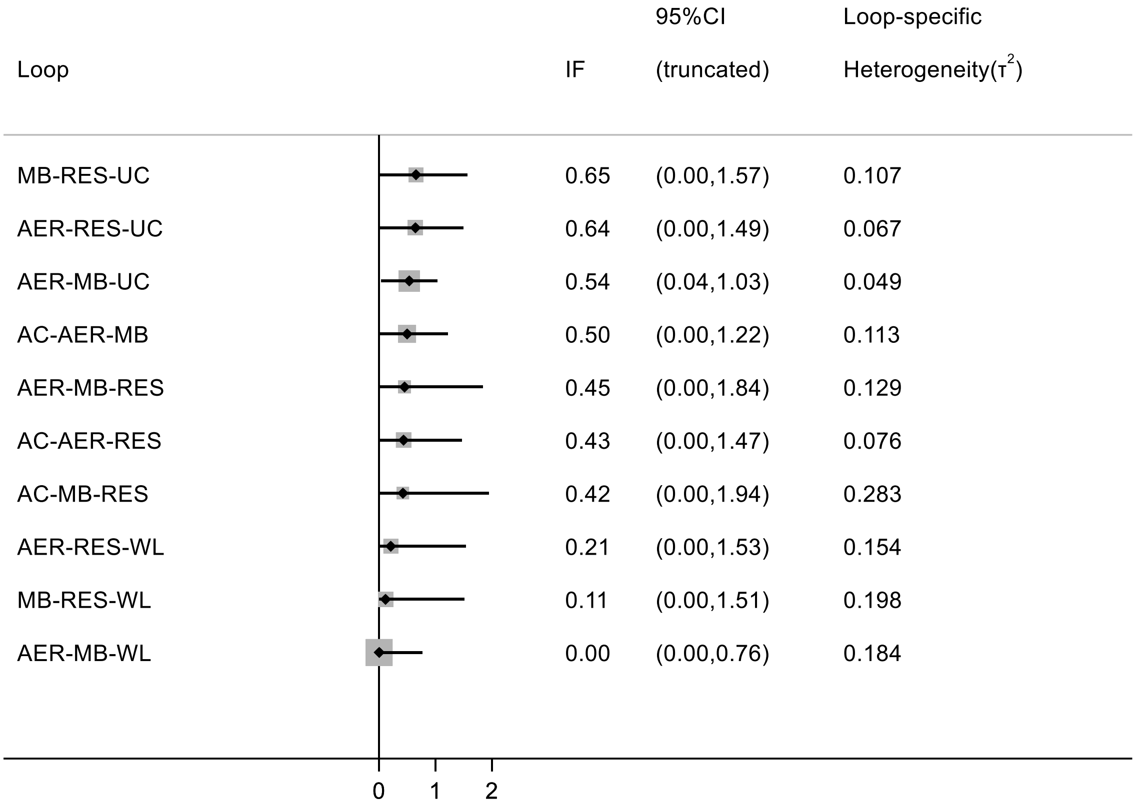
Notes. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

Table H2

Inconsistency test between direct and indirect comparisons for attrition

Side	***n***	**Direct**		**Indirect**		**Difference**		***p > Z***
		Coefficient	***SE***	**Coefficient**	***SE***	**Coefficient**	***SE***	
AER vs. WL	9	-0.074	0.465	0.059	0.625	-0.133	0.780	.865
AER vs. RES	1	0.044	1.445	-0.361	0.427	0.405	1.507	.788
AER vs. MB	4	0.062	0.705	-0.046	0.419	0.108	0.820	.895
AER vs. UC	9	-0.017	0.455	0.169	0.522	-0.186	0.692	.788
RES vs. WL	2	0.052	1.011	0.368	0.518	-0.315	1.136	.781
RES vs. UC	15	0.512	0.358	-0.030	0.671	0.542	0.761	.476
MB vs. WL	11	0.060	0.411	-0.205	0.694	0.265	0.807	.743
MB vs. RES	1	0.000	1.396	-0.340	0.427	0.340	1.460	.816
MB vs. UC	9	-0.059	0.443	0.275	0.521	-0.334	0.684	.626
AC vs. AER	6	-0.099	0.535	0.161	0.592	-0.260	0.799	.745
AC vs. RES	4	-0.064	0.634	-0.524	0.589	0.460	0.865	.595
AC vs. MB	6	-0.157	0.564	0.110	0.561	-0.267	0.795	.737

Notes. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.



Loop	IF	95%CI (truncated)	Loop-specific Heterogeneity(τ^2)
MB-RES-UC	0.65	(0.00,1.57)	0.107
AER-RES-UC	0.64	(0.00,1.49)	0.067
AER-MB-UC	0.54	(0.04,1.03)	0.049
AC-AER-MB	0.50	(0.00,1.22)	0.113
AER-MB-RES	0.45	(0.00,1.84)	0.129
AC-AER-RES	0.43	(0.00,1.47)	0.076
AC-MB-RES	0.42	(0.00,1.94)	0.283
AER-RES-WL	0.21	(0.00,1.53)	0.154
MB-RES-WL	0.11	(0.00,1.51)	0.198
AER-MB-WL	0.00	(0.00,0.76)	0.184

Figure H7. Inconsistency plot for the depressive symptoms network, assuming loop-specific heterogeneity estimates. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

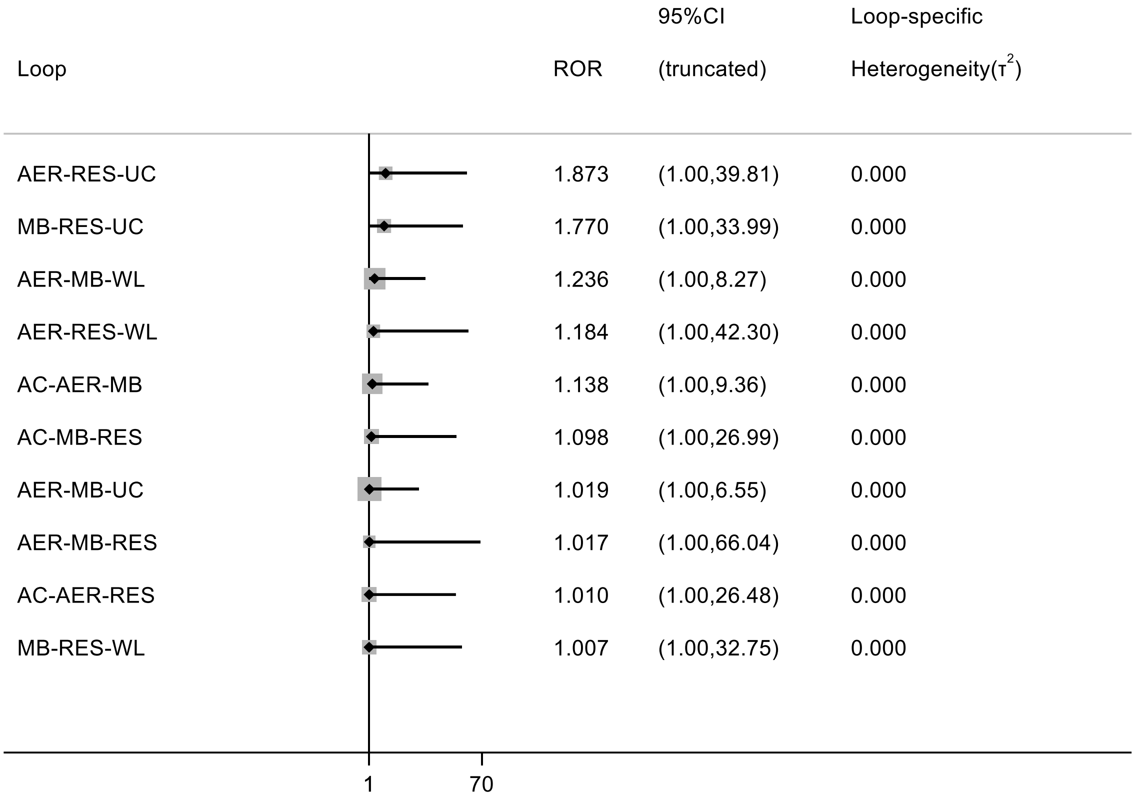


Figure H8. Inconsistency plots for the attrition network, assuming loop-specific heterogeneity estimates. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

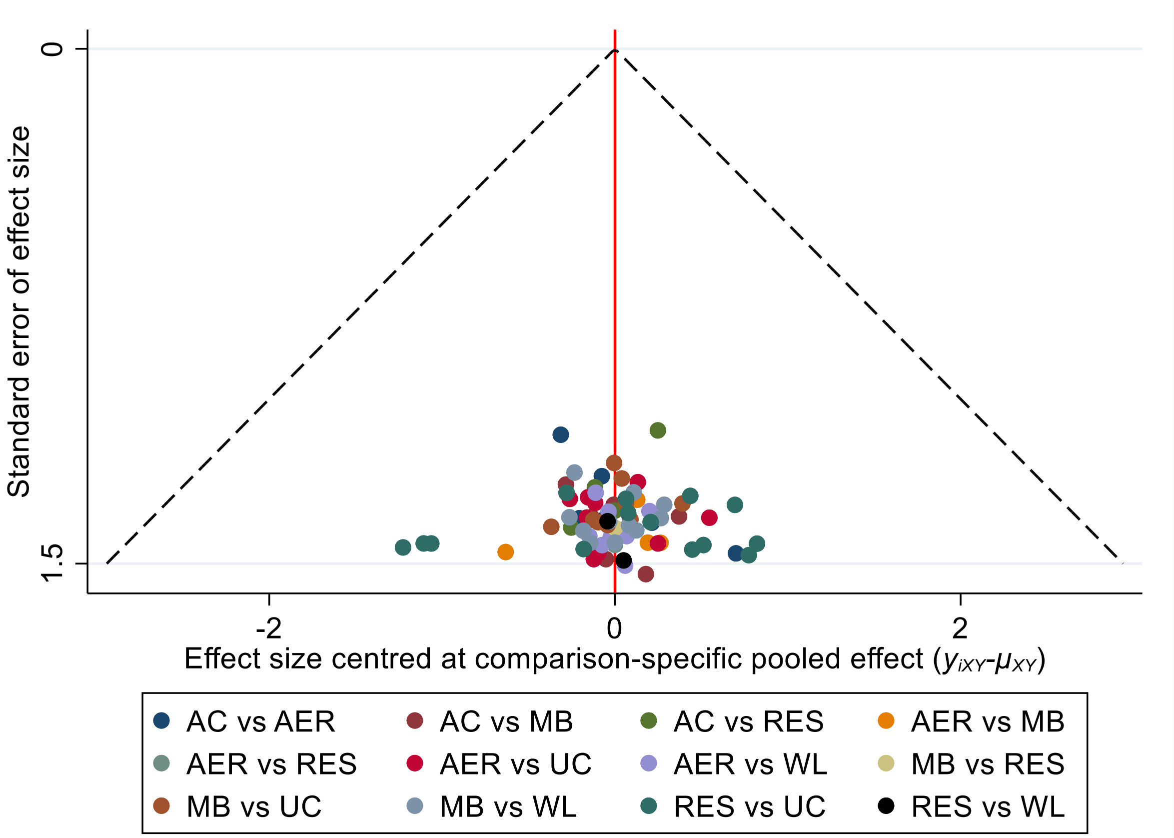


Figure H9. Comparison-adjusted funnel plots for the attrition networks. The red line represents the null hypothesis that independent effect size estimates are not different to comparison-specific pooled estimates. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

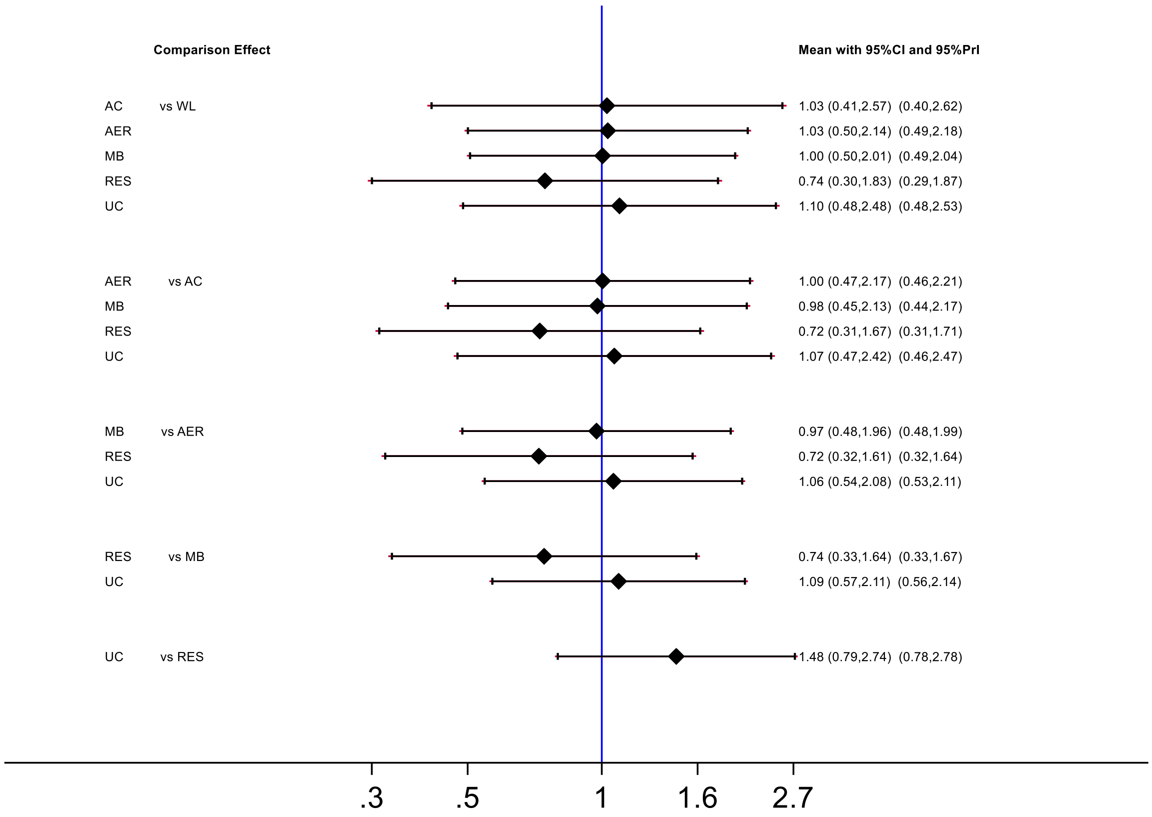


Figure H10. Predictive interval plot for the attrition network. Black diamonds represent the difference in the effect size estimate (odds ratio). Narrow horizontal lines represent the confidence intervals (*CI*) and the wider horizontal lines represent the prediction intervals (*PrI*). The blue vertical line represents the null hypothesis (odds ratio = 1). Odds ratios lower than 1 indicate a lower attrition in the comparison (left) group. AC = attention-control; AER = aerobic; MB = mind-body; RES = resistance; UC = usual care; WL = wait-list.

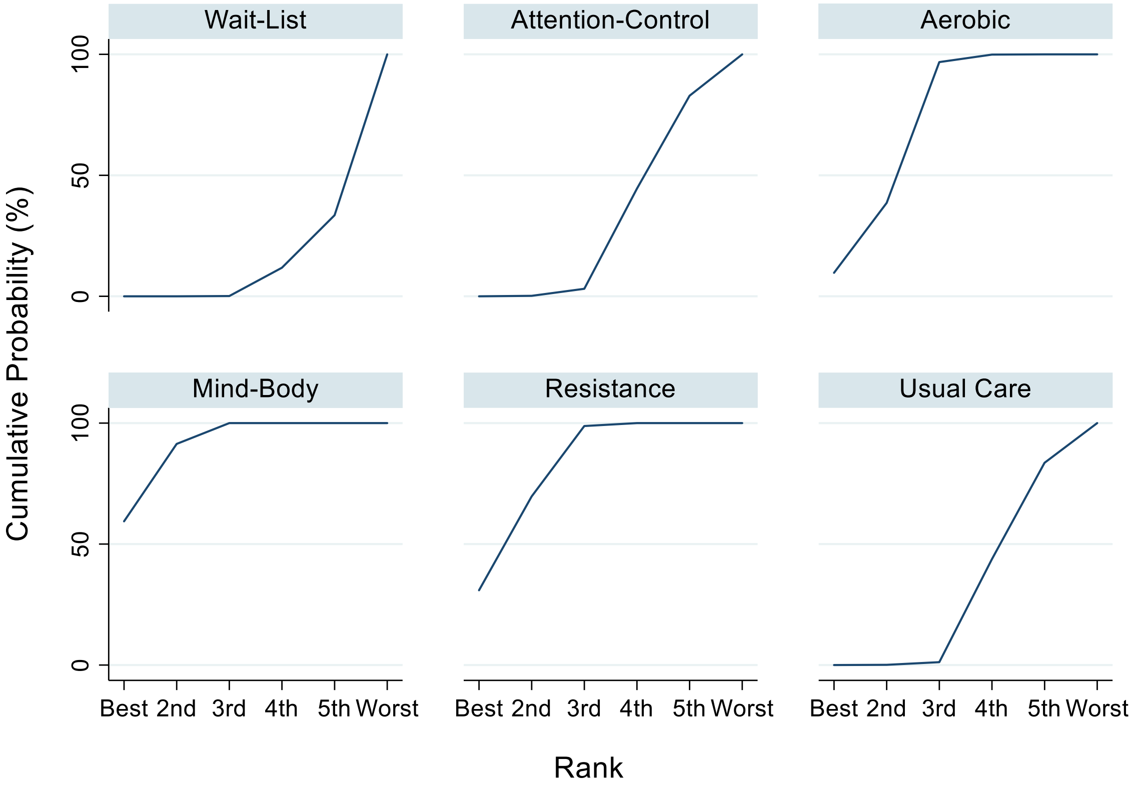


Figure H11. Plots of the surface under the cumulative ranking curves (SUCRA) for all comparisons in the depressive symptoms network.

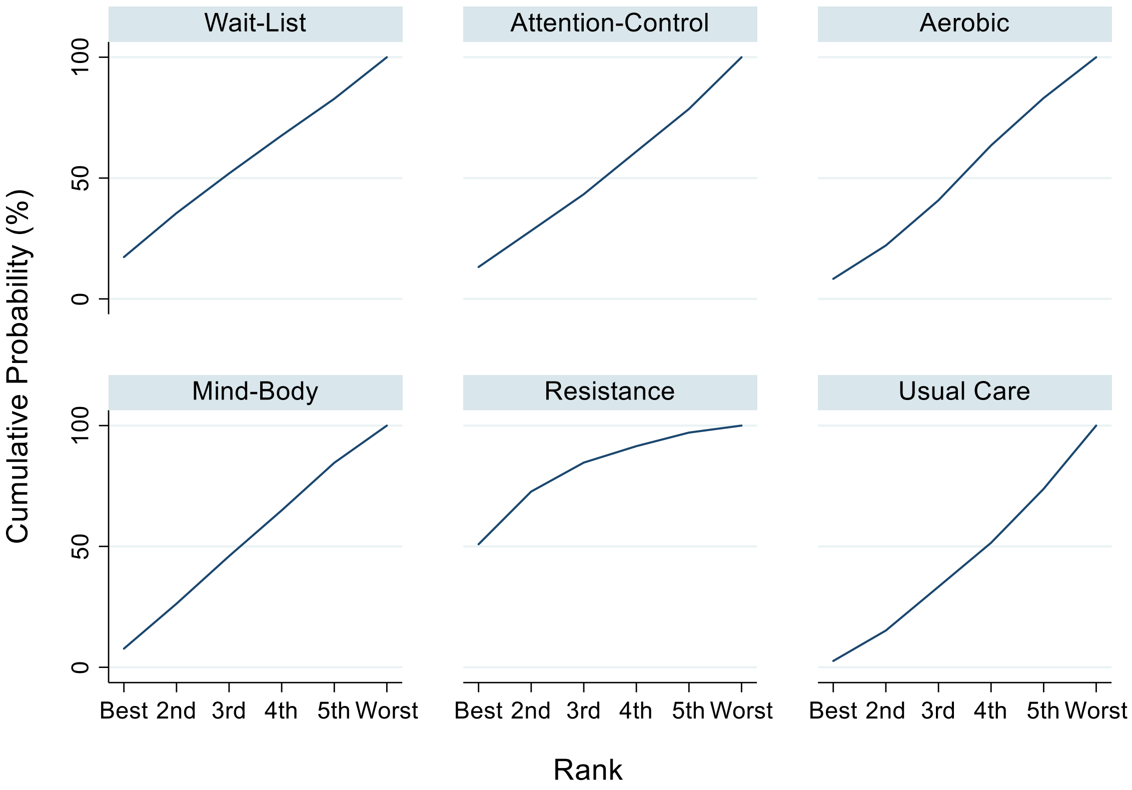


Figure H12. Plots of the surface under the cumulative ranking curves (SUCRA) for all comparisons in the attrition network.

Table H3

Results of the network rank test for depressive symptoms

	Wait-List	**Attention-Control**	**Aerobic**	**Mind-Body**	**Resistance**	**Usual Care**
Best	0.0	0.0	9.7	59.4	30.9	0.0
2nd	0.0	0.2	28.9	32.0	38.8	0.1
3rd	0.1	2.9	58.2	8.6	29.1	1.1
4th	11.7	41.4	3.1	0.0	1.2	42.6
5th	21.7	38.4	0.1	0.0	0.0	39.8
Worst	66.5	17.1	0.0	0.0	0.0	16.4
Mean Rank	5.5	4.7	2.5	1.5	2.0	4.7
SUCRA	9.1	26.1	69.0	90.2	79.9	25.7

Table H4

Results of the network rank test for attrition

	Wait-List	**Attention-Control**	**Aerobic**	**Mind-Body**	**Resistance**	**Usual Care**
Best	17.3	13.2	8.3	7.7	50.9	2.6
2nd	18.2	15.0	13.8	18.6	21.8	12.6
3rd	16.4	15.1	18.7	19.7	12.0	18.1
4th	15.7	17.7	22.7	18.9	6.8	18.2
5th	15.2	17.6	19.6	19.7	5.6	22.3
Worst	17.2	21.4	16.9	15.4	2.9	26.2
Mean Rank	3.4	3.8	3.8	3.7	2.0	4.2
SUCRA	51.0	44.9	43.6	45.9	79.4	35.3

Table H5

Summary of GRADE assessment for the certainty in attrition estimates

Comparison Effect	**Number of Participants**	**Number of Direct Comparisons**	**Nature of Evidence**	**Certainty**	**Reason for Downgrading**
Aerobic vs. wait-list	347 vs. 351	9	Mixed	Moderate	Imprecision[a]
Aerobic vs. usual care	351 vs. 364	9	Mixed	Very low	Risk of bias[b], inconsistency[c], imprecision[a]
Aerobic vs. attention-control	445 vs. 487	6	Mixed	Moderate	Imprecision[a]
Resistance vs. wait-list	45 vs. 46	2	Mixed	Low	Imprecision[ad]
Resistance vs. usual care	370 vs. 354	15	Mixed	Moderate	Imprecision[a]
Resistance vs. attention-control	290 vs. 292	4	Mixed	Low	Risk of bias[e], imprecision[b]
Mind-body vs. wait-list	398 vs. 383	11	Mixed	Moderate	Imprecision[a]
Mind-body vs. usual care	374 vs. 364	9	Mixed	Very low	Risk of bias[f], inconsistency[c], imprecision[a]
Mind-body vs. attention-control	233 vs. 200	6	Mixed	Moderate	Imprecision[a]
Aerobic vs. resistance	24 vs. 23	1	Mixed	Low	Imprecision[ad]
Aerobic vs. mind-body	90 vs. 83	4	Mixed	Moderate	Imprecision[a]
Resistance vs. mind-body	33 vs. 33	1	Mixed	Low	Imprecision[ad]

[a] Confidence intervals include values favouring either treatment.

[b] Potential attrition bias due to high number of studies with incomplete outcome data.

[c] Evidence of inconsistency in the network.

[d] Small sample size.

[e] Potential risk of bias due to high number of studies with low adherence.

Table H6

Meta-regression for effect modifiers on depressive symptoms for aerobic exercise

Effect Modifier	***n***	**β**	***SE***	***t***	***p*-value**	**Lower 95% *CI***	**Upper 95% *CI***	**τ^2**	**Residual I^2**	**Adj. R^2**
Year	29	0.006	0.012	0.53	.601	-0.018	0.030	0.152	70.44%	-5.96%
Risk of bias	29	-0.046	0.142	-0.32	.749	-0.337	0.245	0.151	70.24%	-5.48%
Adherence	17	0.008	0.008	1.05	.311	-0.008	0.024	0.089	61.04%	-11.56%
Age	29	-0.001	0.017	-0.08	.939	-0.036	0.033	0.152	70.40%	-6.23%
Gender	27	-0.006	0.003	-1.94	.063	-0.012	0.000	0.134	71.44%	6.40%
Source of participants	29	-0.022	0.154	0.14	.887	-0.293	0.337	0.150	69.45%	-5.07%
Publication status	29	-0.064	0.364	-0.18	.861	-0.812	0.683	0.152	70.21%	-6.28%
Intention-to-treat	29	-0.255	0.213	-1.20	.242	-0.692	0.182	0.137	69.41%	3.85%
Cluster randomisation	29	0.460	0.325	1.42	.168	-0.207	1.127	0.131	66.68%	8.72%
Length of program	29	0.003	0.006	0.47	.640	-0.010	0.016	0.153	74.25%	-6.79%
Format of exercise	27	-0.109	0.212	-0.51	.612	-0.546	0.328	0.098	63.81%	-9.20%
Intensity of exercise	18	0.231	0.118	1.95	.069	-0.020	0.482	0.163	61.41%	23.66%
Frequency of exercise	29	-0.017	0.074	-0.22	.825	-0.169	0.136	0.155	70.21%	-8.29%
Duration of exercise	29	0.001	0.005	0.24	.811	-0.010	0.012	0.154	70.41%	-7.97%

Table H7

Meta-regression for effect modifiers on depressive symptoms for resistance exercise

Effect Modifier	***n***	**β**	***SE***	***t***	***p*-value**	**Lower 95% *CI***	**Upper 95% *CI***	**τ^2**	**Residual I^2**	**Adj. R^2**
Year	22	0.033	0.026	1.29	.213	-0.021	0.087	0.279	71.98%	4.30%
Risk of bias	22	0.066	0.172	0.38	.706	-0.293	0.425	0.308	73.13%	-5.56%
Adherence	9	0.009	0.011	0.86	.416	-0.016	0.035	0.007	18.09%	-0.63%
Age	22	0.013	0.023	0.59	.561	-0.034	0.060	0.308	74.23%	-5.71%
Gender	18	0.008	0.008	0.92	.373	-0.010	0.025	0.198	68.81%	-4.42%
Source of participants	22	0.214	0.287	0.75	.465	-0.385	0.813	0.305	74.15%	-4.83%
Publication status	22	0.611	0.670	0.91	.373	-0.787	2.009	0.292	73.04%	-0.28%
Intention-to-treat	22	0.157	0.282	-0.56	.584	-0.744	0.431	0.313	74.27%	-7.31%
Cluster randomisation	22	0.171	0.442	-0.39	.702	-1.093	0.750	0.315	74.18%	-8.03%
Length of program	22	-0.004	0.017	-0.27	.793	-0.039	0.030	0.311	74.25%	-6.79%
Format of exercise	16	-0.402	0.337	-1.19	.253	-1.125	0.321	0.111	57.20%	7.49%
Intensity of exercise	12	-0.254	0.161	-1.58	.145	-0.613	0.104	0.285	74.74%	18.66%
Frequency of exercise	22	0.001	0.048	-0.02	.986	-0.101	0.100	0.316	74.31%	-8.37%
Duration of exercise	21	0.001	0.010	0.14	.888	-0.019	0.022	0.315	73.80%	-7.82%

Table H8

Meta-regression for effect modifiers on depressive symptoms for mind-body exercise

Effect Modifier	***n***	**β**	***SE***	***t***	***p*-value**	**Lower 95% *CI***	**Upper 95% *CI***	**τ^2**	**Residual I^2**	**Adj. R^2**
Year	32	-0.007	0.018	-0.38	.709	-0.044	0.030	0.350	77.52%	-3.48%
Risk of bias	32	-0.198	0.138	-1.43	.162	-0.479	0.084	0.315	75.67%	6.69%
Adherence	21	0.001	0.010	-0.14	.887	-0.022	0.020	0.345	78.41%	-7.40%
Age	32	-0.029	0.026	-1.11	.275	-0.082	0.024	0.342	77.17%	-1.37%
Gender	32	-0.002	0.006	-0.38	.710	-0.014	0.010	0.354	77.65%	-4.68%
Source of participants	31	0.133	0.206	0.65	.523	-0.288	0.554	0.363	78.30%	-4.21%
Publication status	32	-0.905	0.492	-1.84	.076	-1.910	0.100	0.318	76.63%	5.88%
Intention-to-treat	32	-0.211	0.246	-0.86	.398	-0.715	0.292	0.341	77.04%	-1.05%
Cluster randomisation	32	0.182	0.415	0.44	.663	-0.665	1.030	0.315	77.33%	-4.04%
Length of program	32	0.030	0.018	1.68	.104	-0.007	0.067	0.311	75.00%	8.03%
Format of exercise	32							0.338	76.93%	
Intensity of exercise	6	0.176	0.179	0.98	.383	-0.322	0.673	0.000	0.00%	0.00%
Frequency of exercise	32	0.201	0.113	1.77	.086	-0.030	0.432	0.303	75.43%	10.14%
Duration of exercise	32	-0.003	0.006	-0.43	.668	-0.015	0.010	0.350	77.53%	-3.69%