THE IMPACT OF PHYSICAL ACTIVITY ON PHYSICAL FUNCTION OUTCOMES IN OLDER ADULTS AT RISK FOR DIABETES

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ABSTRACT

***Background*:** About 29 million US adults are living with diabetes, a condition that can lead to many negative health outcomes, including poor physical function. Physical activity has been shown to decrease the risk for diabetes and improve physical function in adults as they age. The purpose of this review was to evaluate if physical activity interventions improve the physical function of older adults at risk for diabetes and identify intervention characteristics that might impact results.

***Methods*:** The PubMed database was searched to identify publications of randomized clinical trials of physical activity interventions to impact physical function in older adults at risk for diabetes. Eligible studies included adults age ≥ 50 years with ≥ overweight, metabolic syndrome or pre-diabetes, and evaluated change in physical function (gait speed, strength, or the short performance physical battery test). The search was limited to English language articles, using the terms ‘physical activity’, ‘exercise’, ‘sedentary’, ‘physical function’, ‘gait speed’, ‘obesity’, ‘metabolic syndrome’, and ‘pre-diabetes’.

***Results*:** Of the 140 studies that were identified from PubMed, 8 met eligibility criteria. One additional study was identified through the reference lists of eligible studies. Eight of 9 studies found significant improvements in physical function outcomes in the PA intervention vs control group. Interventions that included both aerobic and resistance training together resulted in better improvements in physical function than just aerobic or resistance training alone.

Conclusion**:** Increasing physical activity levels in this population has shown to improve physical function, which can potentially lead to increased independence, decreased healthcare costs, and improvements in quality of life for these adults as they age. These results indicate important findings for the public health of older adults at risk for diabetes.

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DEFINITION OF ACRONYMS

AT – Aerobic Training

BMI – Body Mass Index

BP – Blood Pressure

CDC - Centers for Disease Control and Prevention

CVD - Cardiovascular Disease

DPP – Diabetes Prevention Program

MetS – Metabolic Syndrome

MVPA – Moderate-Vigorous Physical Activity

PA – Physical Activity

PPT – Physical Performance Test

RCT – Randomized Clinical Trial

RPE – Rating of Perceived Exertion

RT – Resistance Training

SPPB – Short Physical Performance Battery

WL – Weight-loss

1.0 INTRODUCTION

According to the Centers for Disease Control and Prevention (CDC), in 2016 there were more than 29 million US adults living with diabetes, with about 25% of cases being undiagnosed. About 95% of diabetes cases are due to Type II diabetes, which is primarily developed later in life among adults with overweight or obesity and/or low physical activity level, and about 5% due to Type I, which usually has juvenile onset which is unrelated to behavior.[1] Additionally, about 86 million US adults are living with prediabetes, a condition defined as having a blood glucose level that is too high to be considered normal but too low to be considered diabetes.[2] In 2013, diabetes was the seventh leading cause of death in the US, and remains the leading cause of kidney failure, lower-limb amputations, and adult-onset blindness.[1] Diabetes increases one's risk of heart disease and stroke, while prediabetes increases one's risk of diabetes and other chronic conditions.[1] Both prediabetes and diabetes also make it more likely for individuals to develop physical limitations or disability later in life.[3] The economic burden of diabetes is high, with over 20% of total healthcare spending on people with diabetes, even though they only represent 9.4% of the population. In 2012, the total cost of diabetes in the US was about $245 billion.[4] Due to both the economic and health burdens that diabetes imposes, it is important that interventions be developed for those most at-risk for this disease.

Risk factors for Type II diabetes and prediabetes include excess adiposity, over 45 years old, and/or being physically inactive.[1] Studies have focused on populations with these risk factors in order to decrease diabetes risk and promote healthy lifestyle change. For example, the Diabetes Prevention Program (DPP) and resulting translation studies have proved that decreasing body weight and increasing moderate physical activity to 150 minutes per week can effectively decrease the risk of diabetes in adults.[5,29] The 150 minute/week goal used in the DPP originated from recommendations in the 1996 Surgeon General's report on Physical Activity and Health[6], and remains the current guideline that is recommended by the American College of Sports Medicine, the American Diabetes Association, and the CDC.[7] More recently, strength training at least two days per week has also been added to this physical activity guideline for adults.[8]

To measure their effect on various outcomes, physical activity interventions can be administered and assessed in different ways. Conducting supervised exercise sessions is one way to ensure that participants are performing specific types of exercise at controlled intensities for certain amounts of time. This method creates a controlled environment that makes assessing activity more accurate and precise, even though it is more time-consuming and costly.[10] Physiological measures like peak oxygen intake and heart rate are often used to measure exercise intensity, as well as ratings of perceived exertion (RPE). Activity can also be measured objectively using devices like accelerometers. Accelerometers are devices worn on the body that can capture the intensity, duration, and frequency of free-living activity done throughout the day.[11] This method is not accurate in capturing all aspects of physical activity, but is a way to measure activity a participant might do on their own time.

Along with preventing chronic diseases such as diabetes, meeting the recommended physical activity guidelines may also help to improve physical function in adults. Older adults with obesity and/or diabetes are at an increased risk for developing functional disabilities, so preventing these conditions may help to maintain function in this population.[3,12] Physical function is an important aspect of overall health, especially during the aging process. It is necessary for maintaining independence and overall quality of life, and can also prevent institutionalization and additional healthcare costs.[13] Because of the association between physical activity and physical function, studies have been done to try and determine the type, duration, and frequency of exercise that is necessary to improve function in adult populations, including those at-risk for or with diabetes.

There are several different aspects of physical function (i.e, balance, strength, ability to perform activities of daily living, and gait speed), and many measures for each. Some of the valid measures of function in older adults that have shown relationships with health outcomes include the Short Physical Performance Battery (SPPB), the Physical Performance Test (PPT), and the 4-meter walk. The SPPB focuses on lower extremity function through different balance, strength, and walking tests, resulting in an overall score between 0 and 12. Lower SPPB scores are associated with decreased function and declining overall health.[14] The PPT consists of several tasks (each having a score from 0-4) that simulate daily living to measure different levels of physical function in adults. Scores from each task are added to produce one total score, ranging from 0 to 36 (or 0 to 28 on the modified version). Lower PPT scores are also predictive of functional decline in older adults .[15] The 4-meter walk measures an individual's usual walking speed, which is highly correlated with overall health and physical function. These tests have been shown to predict functional decline, negative health outcomes, and even mortality, making them important outcomes in physical activity interventions.[14]

The current literature contains studies that have compared aerobic training, resistance training, or a combination of the two against a control group to determine its effects on physical function outcomes. These two types of exercise impact the body in different ways. Aerobic training utilizes the body's large muscles in a rhythmic pattern for a sustained period of time, while resistance training uses isolated muscle groups to work against an applied force.[7] There is much evidence that shows performing a combination of aerobic and resistance training can help to improve different aspects of fitness (i.e. cardiorespiratory factors, muscle strength, etc.), which can in turn lead to improved physical function.

Since physical function is extremely important to maintain as individuals age, interventions involving physical activity could be very beneficial for adults at risk for chronic diseases like diabetes that can increase risk of disability, leading to reduced physical function. The purpose of this literature review is to evaluate studies containing physical activity interventions to determine if they improved physical function in adults at risk for diabetes defined as being at least 50 years old and having overweight, obesity, metabolic syndrome, or prediabetes.

2.0 METHODS

A literature search was conducted using the PubMed search engine to identify publications from randomized clinical trials (RCT) of physical activity interventions to impact physical function in older adults with overweight, obesity, metabolic syndrome, or prediabetes. As seen in Figure 1, the initial search combined the following terms using the AND operator: 1) physical activity OR exercise OR sedentary; 2) physical function OR gait speed; and 3) obesity OR metabolic syndrome OR prediabetes. Although it was not restricted by date of publication, the search was limited to human subjects, English language, and adults ages 45 years and older. This yielded 183 potential articles.

Titles and abstracts were reviewed to evaluate the following inclusion and exclusion criteria. Studies were included if subjects were age 45 and older and overweight, obese, or classified as having metabolic syndrome or prediabetes, and the study included a physical activity intervention (any type), and certain physical function assessments. Specifically, studies were chosen if they included gait speed, strength, and/or the short performance physical battery (SPPB) test as a primary or secondary outcome. Studies were excluded if they focused on populations with other chronic diseases (osteoarthritis, cancer, chronic kidney disease, etc.), did not randomize participants to an intervention arm, at least one of which was a physical activity intervention, or did not have a longitudinal study-design. From this initial title and abstract review, 140 studiers were excluded.

After applying the inclusion and exclusion criteria, 43 full-text articles were evaluated to determine eligibility. A majority (n=35) of these were excluded based on lack of target outcomes (i.e. not gait speed, strength, and/or the SPPB) or using study designs other than a RCT. Finally, the reference lists of the eight selected articles were reviewed for studies that were not found through the PubMed search. One additional eligible article was identified. Thus, the final review consisted of nine studies.

3.0 RESULTS

Each study's objective, target population/inclusion criteria, exclusion criteria, location and setting, participant characteristics, and study design is presented in Table 1.

3.1 PARTICIPANT CHARACTERISTICS

Sample sizes ranged from 19 to 424 randomized participants. From the nine included studies, there were a total of 1,320 participants. The weighted average age of participants was 71.1 years old (calculation shown in Appendix). Both men and women were included in eight out of the nine studies, with one study including women only. Across the nine studies, female subjects were disproportionately represented (65.9%). Representation of white race was also slightly higher than in the US population (77.6% vs 73.3%).[27] The weighted average BMI of participants was 32.4 kg/m^2 (calculation shown in Appendix), which is in the class 1 obese range. It was common for participants to have several comorbid conditions, metabolic syndrome, and/or be taking medications for comorbid conditions.

3.2 STUDY CHARACTERISTICS

A majority of the studies (n=8) were conducted in locations across the United States, including Missouri, Pennsylvania, North Carolina, Alabama, Florida, Texas, New Mexico, California, and Washington. One study was conducted in Canada.[18] All nine studies were RCT's in which participants were randomized to either a physical activity intervention or a control group. The intervention arms performed their prescribed activity at moderate-to-vigorous intensity. Controls received either a health education intervention[16,19], a diet intervention[17,18,20,21], or continued with their usual diet and exercise behaviors.[22,23,24]

3.3 PHYSICAL ACTIVITY INTERVENTION

In most studies (n=7), participants performed all of their prescribed weekly physical activity by attending exercise sessions under supervision of study personnel.[16,18,19,21,22,23,24] Session frequency varied across studies from two to five times a week, and session length ranged from 20 to 90 minutes. In one study, participants did not attend exercise sessions, but rather performed prescribed physical activity on their own.[17] Only one study used both exercise sessions and prescribed on-own activity.[20]

Physical activity interventions varied by type of activity. In two studies[18,22], participants received: 1) aerobic training (AT), 2) resistance training (RT), or 3) a combination of aerobic and resistance training. Six studies used a combination of aerobic and resistance training as the sole exercise intervention[16,17,19,21,23,24], and one study compared aerobic and resistance training separately to a control group of no exercise.[20] All aerobic and resistance exercises were performed at moderate to vigorous intensity levels.

Each study's PA measurement, physical function outcomes, assessment time-points, completion rate, results, and study limitations are presented in Table 2.

3.4 PHYSICAL ACTIVITY ASSESSMENT

Seven studies did not measure physical activity as an outcome other than session participation[16,18,19,21,22,23,24]. This is likely due to the fact that for most of these studies, physical activity was increased through in-person supervised sessions. One study measured free-living physical activity via self-report and acceleromter[17], while another study measured both session participation and free-living physical activity via accelerometer.[20] Because PA levels were not specifically reported by most studies, this review focuses on primary analyses comparing intervention arms, rather than amount of physical activity performed.

3.5 PHYSICAL FUNCTION OUTCOMES

Seven studies include at least one measure of physical function as a primary outcome[16,18,19,20,22,23,24], while two studies included a physical function measure as a secondary outcome.[17,21] Other primary outcomes included change in visceral adipose tissue[17], change in insulin sensitivity[18], and change in intrahepatic fat content[21]. Other secondary outcomes included cardiometabolic risk factors (glucose, lipids, insulin, blood pressure)[17,20,21], body composition[18,20,21,22,23,24], frailty[22,24], and quality of life[17,20,23,24]. A variety of physical function measures were used as primary and secondary outcomes, including both mobility and strength assessments. A test to measure gait speed (4-m walk, 400-m walk, or 6-minute walk test) was used in seven out of nine studies.[16,17,18,19,20,22,23] The SPPB was performed in three studies[16,17,19], the PPT was used in three studies,[22,23,24] and different strength tests (knee extensor strength, grip strength, bench press, or leg press) were done in five studies.[17,18,20,21,22]

3.6 INTERVENTION LENGTH

The duration of the interventions varied in length, lasting either 6 months[16,18,21,22,23], 12 months[17,19,24], or 18 months[20]. For the interventions lasting 6 months, assessments were done at baseline and 6 months. For the interventions lasting 12 months, assessments were done at baseline, 6 months, and 12 months. The intervention used by Rejeski et al. included an intensive phase (0-6 months), transition phase (7-12 months), and maintenance phase (13-18 months), and assessments were done at baseline, 6 months, and 18 months. The percentage of participants completing final assessments (at the end of intervention) ranged from 77.1% to 95% (Table 2).

3.7 STUDY FINDINGS

Seven out of the nine studies found clinically meaningful improvements in physical function in the PA arm compared to the control arm. In these seven studies, the PA intervention consisting of a combination of aerobic and resistance training resulted in the most significant improvements.[16,18,19,20,22,23,24] The remaining two studies found clinically meaningful improvements in cardiometabolic disease risk but not physical function in the PA arm(s) in their study results.[17,21]

4.0 DISCUSSION

This literature review evaluated RCTs of physical activity interventions to determine if they improved physical function in adults at risk for diabetes. Results of the included studies indicate that physical activity, especially combined aerobic and resistance training, may be associated with clinically relevant improvements in physical function and in older, obese adults.

Across the nine studies, improvements in physical function differed based on whether physical activity was supervised by study personnel or performed on the participant's own time. The seven studies that used only supervised exercise interventions resulted in statistically significant improvements in at least one physical function test between. In the supervised interventions, exercise physiologists, physical therapists, or other trained experts administered the frequency, duration, and intensity of different aerobic and/or resistance exercise to participants. In contrast, the two studies that relied on participants to perform physical activity on their own time, did not. This includes one study which used supervised exercise sessions at first and then transitioned to on-own PA.[20] The results for this study indicated a statistically significant, but not clinically meaningful, improvement in 400m walk time in the PA group compared to control; there were also no significant differences found in knee extensor strength between the PA group and control. The other study's PA intervention only had an activity goal related to increasing unsupervised physical activity.[17] In that intervention, activity was discussed in weekly educational sessions and tracked using accelerometers. While there were no statistically significant changes in any physical function measure between groups using this method, there was not enough information presented to determine the reasons for the lack of change in function. Improvements in function in the supervised groups could be due to the controlled environment in which they were doing activity. Although exercise sessions are not always attended, when attended it was guaranteed that participants were performing the exact activity for the exact duration and intensity prescribed. This kind of adherence cannot be assumed with a lifestyle intervention that relies on participants to follow exercise prescriptions.[26]

Physical function outcomes also differed by the type of physical activity performed in the intervention. Intervention arms consisted of aerobic training (AT), resistance training (RT), or combination groups that performed both AT and RT. In several of the reviewed studies, the participants performing AT and RT together during exercise sessions saw more improvements in physical function measures compared to AT alone[18,22], RT alone[18,22], or the control group[16,18,19,21,22,23,24]. Results from Manini et al. showed both a decline in gait speed but improvement in SPPB scores from the exercise group performing both AT and RT. The authors suggest that RT done in the intervention was similar to the movements done in the SPPB, making results somewhat bias.[19] These results coincide with current literature that shows combining AT and RT to be the most beneficial for improving health measures like physical function. Because the two types of activity impact different aspects of physical fitness, physical function can be improved in different ways as well.[25]

Across studies, improvements in physical function differed by the frequency and duration of exercise performed. Duration of activity was not consistent across intervention arms within studies. In two studies, the group doing both AT and RT was exercising for more minutes per week than the other intervention arms doing just AT or just RT (150 vs 60 mins/week[18] and 270 vs. 180 mins/week[22]). Other interventions comparing a combination group (AT and RT) to a control doing no activity had participants exercising at moderate intensity for 225 to 270 minutes per week[21,23,24], which is higher than the recommended guidelines for healthy adults, but in line with recommendations for weight control for overweight and obese adults[7,28]. Since the combination groups were exercising for more minutes per week than the other arms, it cannot be determined if the significant improvements were due to the effects of combining AT and RT or from exercising for longer periods of time. Physical function outcomes across the studies did not differ by intervention length. Significant improvements in function were found in 6-month interventions, 12-month interventions, and even the 18-month intervention.

The studies also differed in whether physical function was a primary or secondary outcome. The majority of studies had at least one physical function measure as a primary outcome[16,18,19, 22,23] [20,24]. When function was a primary outcome, clinically meaningful improvements in function were found in the PA arm(s) compared to the control arms. In the remaining studies, at least one physical function measure was a secondary outcome and the primary outcome was a measure of fat content.[17,21] These results showed marginal improvements in function, but reported clinically meaningful improvements in cardiometabolic risk factors like glucose, lipids, insulin, blood pressure, etc. for the PA group compared to control. Thus, it appears that the focus of the intervention impacts which outcomes are improved with clinically meaningful significance.

Improvements in function may also have differed based on the study's target population. For example, most interventions with a target population of obese, sedentary, and frail older adults resulted in significant improvements in physical function outcomes.[16,19,22,23,24] Since these subjects were not exercising and had low function to begin with, they may have benefitted from physical activity more than those who were already active and functional. Other target populations included older adults who were obese, sedentary, and/or had greater cardiometabolic risks.[17,18,20,21] Some improvements in the physical function outcomes were not considered clinically significant in these studies.[17,18,20]

Physical function outcomes across the studies did not differ by sample size or completion rate. Both small and large sample sizes (ranging from 19 to 424 subjects) found significant functional improvements, and all studies had relatively high completion rates. They ranged from 77.1% to 95% completion, the lowest being at the end of the 18-month intervention. Seven of nine studies used intent-to-treat (ITT) analysis, while two studies did not mention using ITT analysis, but had high completion rates (93.6% and 94.7%).[19,21]

When comparing participant characteristics across studies, some were found to be relatively homogeneous. A large proportion of subjects were white, female, and well-educated. Participants were also healthy enough and physically able to participate in a physical activity intervention, indicating that results may not apply to all older individuals who are unable to exercise. Although this limits the generalizability to populations who are not white, female, well-educated, or able to exercise, it validates the findings that physical activity can improve physical function in this particular group of adults.

This review shows that participating in an intervention with a supervised PA component that includes both aerobic and resistance training can improve aspects of physical function including gait speed, balance, strength, and ability to perform activities of daily living. However, the durability of such improvements may be dependent on whether PA is maintained following such interventions. While none of the studies evaluated whether results were sustained after the PA intervention, some included a "maintenance phase" in the interventions[17,19,20]. In one study, both a decrease in PA levels and a decline in gait speed were observed at the end of the maintenance phase.[19] Another study with over 80% PA session attendance at 18-months resulted in both weight maintenance and physical function maintenance at 18-months.[20] Therefore, this could imply that maintaining physical activity levels at the conclusion of an intervention could be important for maintaining outcomes like weight and physical function. Future research is needed to assess the sustainability of interventions with supervised aerobic and resistance training. If the physical activity performed under these conditions can be maintained and incorporated into individuals' daily routines and environments, outcomes like physical function could potentially be improved.

5.0 CONCLUSION

Increasing physical activity levels could have important public health significance for aging adults at risk for diabetes. Based on the results of these studies, prescribing supervised physical activity could be a potential therapy for older adults with excess adiposity, metabolic syndrome, or pre-diabetes to help improve function. If physical function can be improved and maintained through physical activity, adults at risk for diabetes could potentially better manage their own health, keep their independence, and improve their overall quality of life as they age.

APPENDIX A: FIGURE AND TABLES

Keywords searched in PubMed: (physical activity[Title/Abstract] OR exercise[Title/Abstract] OR sedentary[Title/Abstract]) AND (physical function[Title/abstract] OR gait speed[Title/Abstract]) AND (obesity[Title/Abstract] OR metabolic syndrome[TitleAbstract] OR prediabetes[Title/Abstract])

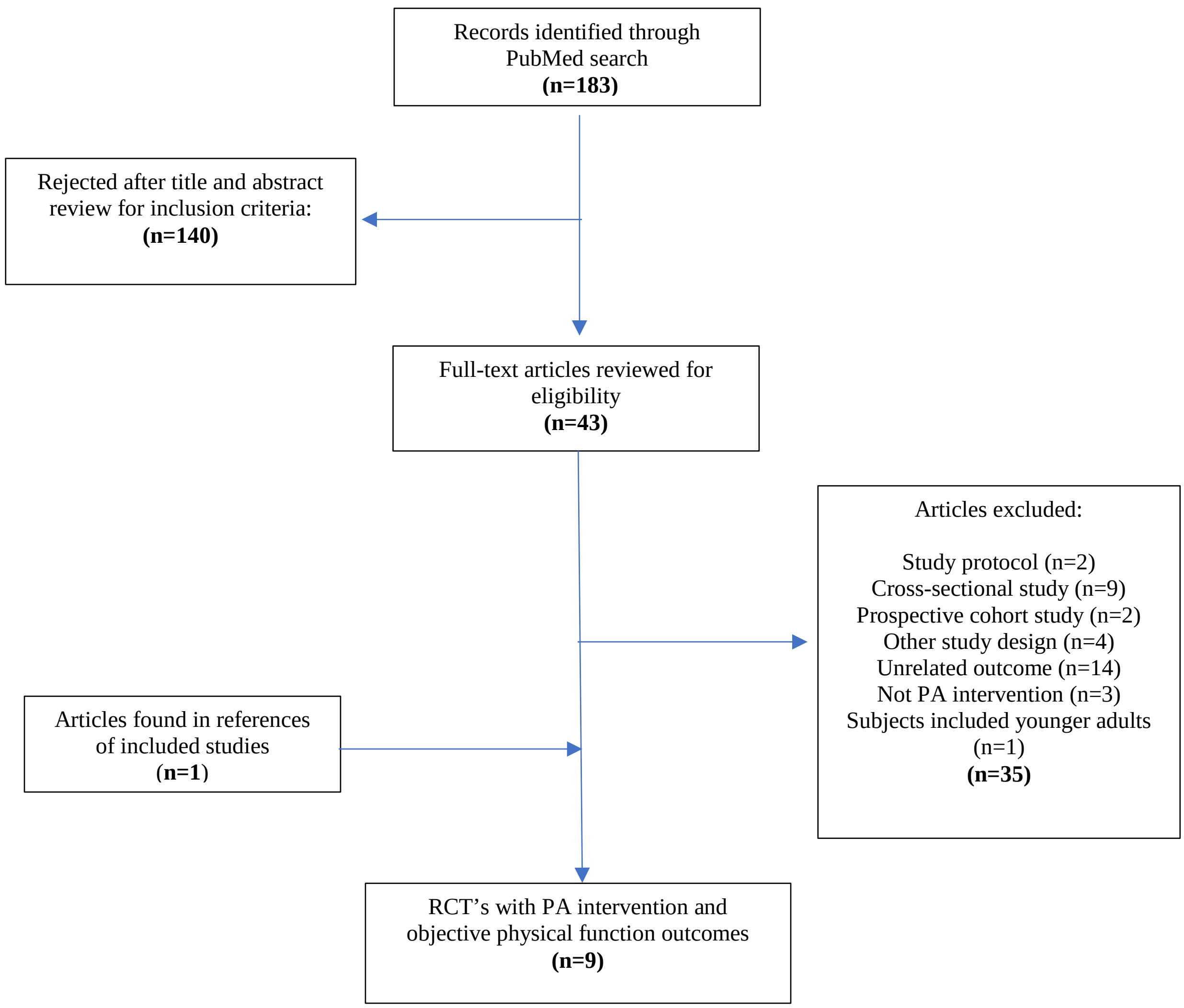

Figure 1. Literature Search Strategy

Table 1. Study Characteristics

Author, year	Objective	Target Population/ Inclusion criteria	Exclusion criteria	Location/ setting	N screened, n (%) enrolled	Participant characteristics	Study design/Arms
Anton et al., 2011[16]	To examine the effects of a lifestyle-based weight loss plus exercise intervention involving both aerobic and resistance exercise	- Obese older women with moderate physical limitations - Age 55-79 years - BMI ≥28 kg/m2 - Sedentary lifestyle (<20 min/week of aerobic exercise) - Mild to moderate impairment on SPPB (scores 4–10)	- Weight >136.1 kg - Weight loss >4.5 kg in the past 6 months - Hx of weight loss surgery - Hospitalization within past 6 months - Significant underlying disease (CHD, respiratory or GI conditions, cancer, etc. within 5 years) - Fasting blood glucose >110 mg/dL - Resting blood pressure >160/90 mmHg - Bone, muscle, or joint conditions that would prevent walking	University of Florida's Aging and Rehabilitation Research Center	N=412 screened, n=34 (8.3%) enrolled	- Mean age 63.7 ± 6.7 yrs - 53% African American - 47% Caucasian	- Single-blinded RCT - Educational control group - Weight loss (WL) + exercise intervention: weekly walking goal of 150 mins - 3 exercise sessions/week : 2 15-minute bouts of walking during each session, then were guided through a set of 5 lower-body exercises (wide leg squat, standing leg curl, knee extension, side hip raise, and toe stand) during a 15-minute strength training routine - Lighter-intensity exercise gradually increased over the first 2–3 weeks of the intervention
Ard et al., 2016[17]	To compare the effects of a change in diet composition alone or combined with weight loss with an exercise only control intervention on functional status and quality of life	- Adults at risk for cardio-metabolic disease - Men and women - At least 65 years old; - BMI of 30–40 kg/m^2 - Taking at least 1 medication for control of lipids, blood pressure, or blood glucose	- Involved in other weight loss methods (pharmacotherapy) - Ongoing treatment for cancer, uncontrolled depression, etc. - Limitations in ability to engage in the prescribed interventions	The greater Birmingham, Alabama, metropolitan area	N=807 screened, n=164 (20.3%) enrolled	- Mean age 70.3 ± 4.7 yrs - 62.2% female - 23.8% African American - 88.6% on BP meds -67.7% on lipid meds - 20.4% on glucose meds	- RCT - Exercise only control - Exercise + Diet Quality + Weight Maintenance - Exercise + Diet Quality + Weight Loss - AT= gradually increase weekly mins of MVPA until 90–150 mins of MVPA each week is reached (could be any type of cardio exercise); - RT= use of resistance bands and 2 full sets of exercise prescriptions, with a goal of completing 2 resistance training sessions each week; 1 of the 2 sessions was completed during the 30 mins of each group session devoted to exercise

Table 1 Continued

Author, year	Objective	Target Population/ Inclusion criteria	Exclusion criteria	Location/ setting	N screened, n (%) enrolled	Participant characteristics	Study design/Arms
Davidson et al., 2009[18]	To investigate the independent and combined effects of resistance and aerobic exercise on insulin resistance and functional limitations	- Abdominally obese older men and women - 60 to 80 years old - Non-smokers - Waist circumference of at least 102 cm in men and at least 88 cm in women - Stable weight (±2 kg) for 6 months before study entry	- Hx of CVD, stroke, diabetes mellitus, or condition preventing them from exercising - Currently dieting or intended to diet - Already engaging in 2 or more planned exercise sessions/week	Queen's University in Ontario, Canada	N=1876 screened, n=136 (7.2%) enrolled	- Mean age 67.6 ± 5 yrs - 98.5% white - 33.1% on BP meds - 19.1% on lipid-lowering meds - 58.1% women	- Single-center RCT - Non-exercise control - Resistance training (RT) - Aerobic training (AT) - Combined exercise (RT+AT) - **RT**= 3x/week, 1 set of 9 exercises to fatigue: chest press, shoulder raise, shoulder flexion, leg extension, leg flexion, triceps extension, biceps curl, abdominal crunches, modified push-ups (~ 20 mins/session) - **AT**= 5x/week, 30 min of moderate-intensity treadmill walking (measured heart rate to ensure 60%-75% V˙ O2 peak range obtained from GXT) - **Combined**= RT + AT (~50 mins/session)
Manini et al., 2010[19]	To determine whether obese and non-obese older adults have similar changes in mobility function due to increased levels of moderate intensity physical activity.	- Obese older adults at risk for disability - Age 70-89 yrs - Sedentary (<20 min per week in physical activity) - SPPB score ≤9 - Able to walk 400 meters within 15 min	- Congestive heart failure - Clinically significant aortic stenosis - Hx of MI - Use of a cardiac defibrillator - Uncontrolled angina - Lung disease requiring steroids - Use of supplemental oxygen - Severe arthritis - Cancer requiring treatment in the past 3 years - Parkinson's disease/ serious neurological disorders - Renal disease requiring dialysis	4 clinical sites: Wake Forest University School of Medicine in Winston Salem, NC, the University of Pittsburgh in Pittsburgh, PA, the Cooper Institute in Dallas, TX, and Stanford University School of Medicine in Palo Alto, CA.	N=3141 screened, n=424 (13.5%) enrolled	- Mean age 76.6 ± 4 yrs - 70% women - 26.9% non-white - 69.6% hypertensive	- RCT - "Successful aging" (SA) control= received basic health education about PA, included stretching - Physical activity group - Weeks 1-8: 3 PA sessions/week, about 40-60 mins/session - Goal to walk 150 mins at mod intensity at least 5x/week - Strength exercises: standing chair squats, toe stands, leg curl, knee extensions and side hip raises with ankle weights - Intensity: walking at RPE of 13 and perform strength training at RPE of 15-16
Rejeski et al., 2017[20]	To examine the long-term effects of exercise modality during weight loss on body composition and physical function	- Men and women - 60–79 years old - Who engaged in <60 min/wk mod PA - BMI 28-42 kg/m^2 - Limitations with mobility - CVD or diagnosis of MetS	- Severe heart disease - Severe systematic disease - Hx of MI or CVD procedure in the past 3 months - Blood glucose ≥ 140 mg/dL - Type I diabetes - Insulin-dependent Type II diabetes - Severe psychiatric condition	Three YMCAs in Forsyth County, NC.	N=2057 screened, n=249 (12.1%) enrolled	- Mean age 66.8 ± 4.7 yrs - 71.1% women - 32.1% African American - 84.3% MetS - 26.1% CVD - mean (SD) BMI 33.8 (3.6) kg/m2 - 74.2% hypertensive	- Single-blinded RCT - Weight loss (WL) only control - WL + aerobic training (AT) - WL + resistance training (RT) - AT= walking on an indoor cushioned track at the YMCA 4x/week, goal of 45 min/session with a walking intensity of 12–14 RPE - RT= 4x/week, RPE of 15–18 for each RT exercise with sessions shaped to 45 minutes, three sets of 10–12 repetitions on 8 machines

Table 1 Continued

Author, year	Objective	Target Population/ Inclusion criteria	Exclusion criteria	Location/ setting	N screened, n (%) enrolled	Participant characteristics	Study design/Arms
Shah et al., 2009[21]	To determine the effect of diet-induced weight loss and diet induced weight loss in conjunction with exercise training on IHF content and associated metabolic abnormalities	- Obese older adults - BMI≥30 kg/m2 - 65–82 years old - Sedentary lifestyle (no regular exercise more than twice a week) - Stable body weight (± 2 kg) over the past year -No changes in meds for at least 6 months	- Diabetes - Current smoking history - Anemia - Severe cardiopulmonary disease - Renal disease - Visual, hearing, or cognitive impairments - History of malignant neoplasm - Recent use of corticosteroid or sex-steroid compounds agents	Washington University School of Medicine, St Louis, MO	N=? screened, n=19 enrolled	- Mean age 68.6±1.2 yrs - 72% female	- RCT (stratified by sex) - Diet therapy (D) - Diet and exercise training (D+ET) - ET= sessions 3x/week, ~90 min: 15 min of flexibility exercises, 30 min of aerobic exercise, 30 min of strength training, and 15 min of balance. - ET Intensity: initially ~70% of peak heart rate, gradually increased over several weeks to ~85% of peak heart rate. - Weight lifting sessions: 1–2 sets at a resistance of ~65% of 1-rep max, with 8–12 reps - Exercise volume was gradually increased to 2–3 sets at ~80% of 1-rep max, with 6–8 reps
Villareal et al., 2017[22]	To test whether weight loss plus resistance exercise would improve physical function more than weight loss plus aerobic exercise or weight loss plus combined aerobic and resistance exercise.	- Obese older adults who were inactive - 65 years of age or older - BMI ≥30 kg/m^2 - Sedentary (regular exercise <1 hour per week) - Stable body weight and stable med use for past 6 months - Mild to moderate frailty	- Severe cardiopulmonary disease (recent MI, unstable angina, etc.) - Musculoskeletal/ neuromuscular conditions impairing exercise - Cognitive impairments - Taking drugs that affect bone metabolism	University of New Mexico School of Medicine and New Mexico Veterans Affairs Health Care System	N=258 screened, n=160 (62%) enrolled	-Mean age 70 ± 4 yrs - 64.3% women - 88% white - average BMI of 36.3 - Average of 3±2 chronic conditions	-RCT - Control: neither a weight-management (WM) nor an exercise intervention - Aerobic training (AT)= WM + AT - Resistance training (RT)= WM + RT - Combo group= WM+RT+AT - AT= ~ 60 min session (10 mins flexibility, 40 mins of aerobic exercises and 10 minutes of balance) - AT exercises: walking, stationary cycling, stair climbing - AT intensity: ~ 65% of peak heart rate, gradually increased to 70-85 - RT= 3x/week; ~60 min sessions (10 mins of flexibility, 40 mins of resistance exercises and 10 minutes of balance) -RT exercises: 9 upper-body and lower-body exercises using weight-lifting machines - RT Intensity: initial sessions were 1 to 2 sets of 8-12 reps at 65% of the 1-rep max, increased progressively to 2-3 sets at ~85% of the 1-rep max - Combo group= AT+RT (75 to 90 minutes long)

Table 1 Continued

Author, year	Objective	Target Population/ Inclusion criteria	Exclusion criteria	Location/ setting	N screened, n (%) enrolled	Participant characteristics	Study design/Arms
Villareal et al., 2006[23]	To test whether weight loss and exercise training improves physical function and ameliorate frailty while preserving fat-free mass.	- Frail obese older adults - BMI≥30 - Age 65 years and older - Men and women - Sedentary (did not participate in regular exercise more than 2x/ week) - Stable body weight (±2 kg) over the past year - Mild to moderate frailty	- Severe cardiopulmonary disease - Musculoskeletal or neuromuscular impairments that preclude exercise - Visual, hearing, or cognitive impairments - Hx of malignant neoplasms - Recent use of corticosteroid agents or sex-steroid compounds	Washington University School of Medicine, St Louis, MO	N=40 screened, n=27 (67.5%) enrolled	- Mean age 70.25±5 yrs - 66.7% women - 85.2% white - Average BMI of 38.75±5.2 kg/m^2	- RCT - No treatment control: continued with usual diet and activities - Diet + exercise program - Exercise program: 3x/week, ~90 min/session (15 min flexibility exercises, 30 min of endurance exercise, 30 min of strength training, 15 min balance)
Villareal et al., 2011[24]	To evaluate the independent and combined effects of weight loss and exercise on physical function, body composition, bone and muscle metabolism, and quality of life	- 65 years or older - BMI≥30 - Sedentary lifestyle - Stable body weight over the past year - Stable meds for the past 6 months - Mild-to-moderate frailty	- Severe cardiopulmonary disease - Musculoskeletal or neuromuscular impairments -Visual, hearing, or cognitive impairments - Hx of cancer - Receiving drugs that affect bone health and metabolism - Current smokers	Washington University School of Medicine	N=234 screened, n=107 (45.7%) enrolled	- Mean age 69.8±4 yrs - 63% women - 85% white - Average BMI of 37 ± 4 kg/m^2 - Average of 2.1(±1) chronic conditions	- RCT - Control group=neither diet nor exercise intervention - Diet group (weight-management) - Exercise training (ET) group - Diet + exercise group - ET= 3x/week, ~90 mins of aerobic exercises (walking, stationary cycling, stair climbing), resistance training, flexibility and balance. - Intensity: 65% of peak heart rate and gradually increased to 70-85% of peak heart rate - 1 or 2 sets of ~ 65% resistance of their one-rep max, with 8-12 reps of each exercise - Gradually increased to 2-3 sets at a resistance of ~80% of their one-rep max, with 6-8 reps of each exercise

Table 2. Study Measures, Outcomes, and Results

Author, year	PA measure/key independent variables	PF measure(s)/ dependent variable(s)	Timepoints for outcome(s) measured (ref=baseline)	N (%) completed follow-up	Results of primary/secondary outcomes	Study Limitations
Anton et al., 2011[16]	- Exercise session attendance - Self-report of mod-vig physical activity (min/week)	- 400-meter walk test (walk at usual pace, time was recorded) - SPPB: a 4-meter walk, repeated chair stands, and 3 standing balance tests (scored from 0 to 12)	- 24-week intervention - 6-month assessment	N=32 (94.12%) at 6-month assessment	- Walking speed of participants in the WL+E group significantly increased compared to the control group (mean [SE] = 0.16 [0.03] m/s vs 0.02 [0.03] m/s; P = 0.016; mean difference = 0.14; 95% confidence interval [CI] 0.04, 0.24) - Scores on the SPPB improved in both the WL+E and control groups (mean change [SE] in WL+E group = 1.82 [0.36]; P= 0.001; mean change in the control group = 0.8 [0.29]; P= 0.05; mean difference = 1.02; 95% CI: 0.16, 1.88; P= 0.02)	- The sample size was relatively small, and the study was not adequately powered to detect differences between African American and Caucasian women in response to the intervention. - Body composition was not directly measured; unable to determine the proportion of fat versus fat-free weight lost. - Participants completed just over two-thirds of the center-based exercise sessions (mean attendance = 70%)
Ard et al., 2016[17]	- Mean counts/day from an Actigraph Actitrainer accelerometer worn 7 days per time point - 3 24-hour dietary recalls	- The UAB LifeSpace Assessment - 6-minute walk test - Short Physical Performance Battery (SPPB) - Hand grip and knee extension strength - Chair sit and reach test.	- 12-month behavioral intervention - Assessments at 6-months and 12-months	- N=148 participants (90.2%) had measured weight at 12-months - N=133 (81.1%) had MRI scans at 12-months	-No statistically significant within-group or between-group changes in the SPPB total score for any of the groups. - At 12 months, isometric knee extension strength, hand grip, 6-minute walk, and chair sit and reach showed no differences overall by treatment assignment.	- Study was conducted by trained clinicians with specific expertise in behavioral interventions for lifestyle modification - Outcomes achieved with this intervention in a different setting or with different providers may not be similar - The population of participants had high levels of physical function at baseline.
Davidson et al., 2009[18]	-Graded exercise test: measured relationship between heart rate and oxygen consumption for aerobic exercise -Energy expenditure determined by multiplying oxygen consumption by 5.04 kcal/L.	- 30-second chair stand: the number of times the subject stood up from a chair - 2-minute step: number of steps in place in 2 minutes -8-ft up-and-go: time needed to get out of a chair, walk 2.4 m, and return to seated position - Seated arm curl - Functional limitation: determined by averaging the difference between scores obtained before and after the intervention for all 4 tests	- 6-month intervention - 6-month assessment	N=117 (86%) completed their assignment	- Functional limitation improved significantly in all exercise groups independent of the test - Improvement within the combined exercise group was greater than that in the aerobic exercise group (0.52 [0.10] vs −0.01 [0.10] standard units, z score [P=.003]), but not the resistance exercise group. -No difference in the improvement in functional limitation in the resistance exercise group compared to the aerobic exercise group independent of the test	- Relatively homogeneous sample of white men and women - Study was conducted in ideal circumstances - "Motivated" sample and supervised during all exercise sessions -Participants were encouraged to strictly follow their individualized diet plans

Table 2 Continued

Author, year	PA measure/key independent variables	PF measure(s)/ dependent variable(s)	Timepoints for outcome(s) measured (ref=baseline)	N (%) completed follow-up	Results of primary/secondary outcomes	Study Limitations
Manini et al., 2010[19]	- Frequency of MVPA per week - Walking and RPE recorded at each center-based session - CHAMPS physical activity questionnaire (weekly frequency and duration of various physical activities over the prior 4-week period) to account for activity outside the clinic	- 400-meter walk test (walked at usual pace on 20-meter course, time recorded) - SPPB for physical function	- ~1.2 year intervention - Assessments at 6-months and 12-months	N=397 (93.6%) completed 12-month follow-up	- Obese subjects in both the PA and SA group had a decline in gait speed - SPPB scores improved in obese individuals with the PA group having an adjusted difference with the SA group of 0.98 at 6 months ($p < 0.001$) and 0.66 at 12 months ($p = 0.042$)	- The study was not statistically powered to detect differences among obese and non-obese individuals - Potential misinterpretation while performing subgroup analyses in a clinical trial not designed to investigate the effects PA by obesity status
Rejeski et al., 2017[20]	- Mean counts/day from an NL-2000 accelerometer worn for 7 days per time point (5 days week/>10 hrs required) - RT was captured by self-report	- 400-m walk test (walk as quickly as possible; time recorded); - Knee extensor strength	- 18-month intervention - 6-month and 18-month assessments	N=229 (77.1%) for 18-month assessment	-WL + AT and WL + RT resulted in greater improvement in 400-m walk time than WL only (mean difference 16.9 seconds $p < .0001$) at 18-months -There was no difference in knee extensor strength between WL + RT and WL + AT at both 6 and 18-months (mean difference −3.6 Nm, $p = .07$)	-The study sample included people with either CVD and/or MetS and were not powered to examine potential differences between these 2 subgroups on the outcomes of interest -Strength testing was restricted to knee extensor strength - Difference in 400-m walk time of 16.9 seconds may have marginal clinical significance
Shah et al., 2009[21]	- Aerobic training: percent of VO2peak - Strength training: percentage of 1-RM at which the participant trained	-VO2 peak was assessed during graded treadmill walking -1-RM for upper body exercises (biceps curl, bench press and seated row) -1-RM for lower body exercises (knee extension, knee flexion and leg press) -Total body strength was calculated as the sum of all 1-RM values	- 6-month intervention - 6-month assessment	N=18 (95%) completed 6-month assessment	- Absolute VO2peak and muscle strength increased significantly in the D + E group (VO2peak: 9 ± 2%; strength: 18 ± 3%) but not in the D group (VO2peak: −0 ± 1%; strength: 3 ± 6%).	- Small sample size

Table 2 Continued

Author, year	PA measure/key independent variables	PF measure(s)/ dependent variable(s)	Timepoints for outcome(s) measured (ref=baseline)	N (%) completed follow-up	Results of primary/secondary outcomes	Study Limitations
Villareal et al., 2017[22]	- Exercise session attendance	- Change in score on the Physical Performance Test from baseline to 6 months - Strength, balance, gait speed, and one-repetition maximum	- 26-week intervention - 6-month assessment - Physical Performance Test also repeated at 3 months	N=141 (88%) completed the study	- Scores on PPT increased more in the combo group than in aerobic or resistance groups: a change of 5.5±0.4 points versus a change of 3.9±0.4 points and a change of 3.9±0.4 points respectively (all P<0.001). - Gait speed increased more in the combination group: 68.8 to 80.9 m/min (14% increase) than in the aerobic group: 74.6 to 82.7 m/min (9% increase) [P<0.001]. - Total one-rep max strength increased in the resistance group (19% increase) and in the combination group (18% increase), whereas it was maintained in the aerobic group	- Participants in our study were physically able to participate in a lifestyle program so may not be fully representative of the general obese older adult population - The sample was not large enough to analyze differences according to sex - Most of the participants were women, white, and well educated
Villareal et al., 2006[23]	- Aerobic training: percent of VO2peak - Strength training: percentage of 1-RM at which the participant trained	- Modified PPT: 7 standardized tasks that are timed - Peak oxygen consumption was assessed during graded treadmill walking - Functional Status Questionnaire: self-report of ability to perform ADLs - Strength, balance, and gait, was performed	- 6-month intervention - Assessment at 26 weeks	N=24 (88.9%) completed assessment at 26 weeks	- All tests improved in treated subjects compared to control subjects - Physical Performance Test score (2.6±2.5 vs 0.1±1.0; p=.001) - Peak oxygen consumption (1.7±1.6 vs 0.3±1.1 mL/min per kilogram; p=.02) -Functional Status Questionnaire score (2.9±3.7 vs −0.2±3.9; p=.02) - Treatment also improved strength, walking speed, obstacle course, 1-leg limb stance time, and health survey physical subscale scores (all p=05).	- Sample size was small - A combined intervention of weight loss and exercise were assessed, which does not allow for assessment of the independent effects of each therapy - The duration of the study was only 6 months
Villareal et al., 2011[24]	- Percentage of exercise sessions successfully completed (70% or more of the exercises performed) - Aerobic training: percent of VO2peak - Strength training: percentage of 1-RM at which the participant trained	- Change from baseline modified Physical Performance Test score - Strength, balance, and gait speed	- 52-week study -Assessments at 6-months and 12-months	N= 93 (87%) at 12-months	- PPT: increase of 5.4±2.4 points in the diet–exercise group (a 21% change from baseline), as compared with increases of 3.4±2.4 points in the diet group (a 12% change) and 4.0±2.5 points in the exercise group (a 15% change). - Gait speed: increase in the diet–exercise group (an increase of 16.9±42.3 seconds, representing a 23% change from baseline) and in the exercise group (an increase of 8.2±15.5 seconds, representing a 14% change). - The total one-rep max increased in the diet–exercise group (35% change from baseline) and in the exercise group (34% change), whereas it was maintained in the diet group (a 3% change)	- Study was not powered to determine differences in the outcomes between sexes -Since volunteers were selected, results may not apply to the general obese, older adult population - Sample size was small, mostly women, white, well educated, and older (70±4 years) with mild-to-moderate frailty - Results cannot be generalized to markedly obese older persons with severe frailty

APPENDIX B: CALCULATIONS

Weighted average age:

$$\frac{(136)(67.6) + (107)(69.8) + (249)(66.8) + (164)(70.3) + (34)(63.7) + (424)(76.6) + (160)(70) + (19)(68.6) + (27)(70.3)}{1320}$$

= 71.1 years

Weighted average BMI:

$$\frac{(136)(30.1) + (107)(37) + (249)(33.8) + (164)(32.5) + (34)(36.8) + (424)(31.0) + (160)(36.3) + (19)(35.5) + (27)(38.8)}{1320}$$

= 32.4 kg/m^2

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