





L'ASSOCIATION CANADIENNE des MEDECINS et CHIRURGIENS BARIATRIQUE The CANADIAN ASSOCIATION of BARIATRIC PHYSICIANS and SURGEONS

Physical Activity in Obesity Management

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KEY MESSAGES FOR HEALTHCARE PROVIDERS

- Regular physical activity induces a wide range of health benefits in adults across all BMI categories, even in the absence of weight loss.
- Aerobic and resistance exercise can favour the maintenance or improvements in cardiorespiratory fitness, mobility, strength and muscle mass during weight management interventions. This can be important, as these outcomes are not targeted and sometimes are negatively affected by other therapies, such as caloric restriction, medications and bariatric surgery.

RECOMMENDATIONS

- 1. Aerobic physical activity (30–60 minutes of moderate to vigorous intensity most days of the week) can be considered for adults who want to:
 - a) Achieve small amounts of body weight and fat loss (Level 2a, Grade B);¹
 - b) Achieve reductions in abdominal visceral fat (Level 1a, Grade A)²⁻⁴ and ectopic fat such as liver and heart fat (Level 1a, Grade A),⁴ even in the absence of weight loss;
 - c) Favour weight maintenance after weight loss (Level 2a, Grade B); ^{1,5} $\,$
 - d) Favour the maintenance of fat-free mass during weight loss; (Level 2a, Grade B);⁶ and,
 - e) Increase cardiorespiratory fitness (Level 2a, Grade B)⁷ and mobility (Level 2a, Grade B).⁸
- 2. For adults living with overweight or obesity, resistance training may promote weight maintenance or modest increases in muscle mass or fat-free mass and mobility (Level 2a, Grade B).⁹

- 3. Increasing exercise intensity, including high-intensity interval training, can achieve greater increases in cardiorespiratory fitness and reduce the amount of time required to achieve similar benefits as from moderate-intensity aerobic activity (Level 2a, Grade B).^{7,10}
- 4. Regular physical activity, with and without weight loss, can improve many cardiometabolic risk factors in adults who have overweight or obesity, including:
 - a) Hyperglycemia and insulin sensitivity (Level 2b, Grade B) 7,11,12
 - b) High blood pressure (Level 1a, Grade B);^{13,14}
 - c) Dyslipidemia (Level 2a, Grade B).15,16
- Regular physical activity can improve health-related quality of life, mood disorders (i.e., depression, anxiety) and body image in adults with overweight or obesity (Level 2b, Grade B).^{17,18}

KEY MESSAGES FOR PEOPLE LIVING WITH OBESITY

• Weight loss should not be the sole outcome by which the success of physical activity therapy is judged.

Introduction

It is well documented via results of randomized control trials (RCTs) that regular physical activity is associated with a lower prevalence of cardiovascular risk factors (e.g., high blood pressure, LDL-cholesterol [LDL-C], triglycerides, glucose and low HDL-cholesterol ([HDL-C] levels) and a lower incidence of chronic disease (e.g., type 2 diabetes, cardiovascular disease, certain types of cancer).¹⁹ Increasing one's level of cardiorespiratory fitness is also associated with reduced risk of chronic disease and all-cause mortality, independent of body mass index (BMI),20 which could be partly explained by lower amounts of abdominal fat.²¹ The health benefits related to physical activity are partly associated with the dose of physical activity (i.e. type, duration, intensity and frequency).²² However, reduction of sedentary activity during the day can also produce health benefits, independently of levels of regular physical activity.23 To improve health, it is recommended that individuals perform a minimum of 30 minutes of moderate to vigorous intensity aerobic physical activity on most days of the week, (accumulating at least 150 minutes per week), engage in strength (resistance) activity at least two days per week,24 and reduce the amount of daily sedentary time.25

The objective of this chapter is to provide primary care providers and kinesiologists with up-to-date evidence regarding the efficacy of physical activity as a therapeutic approach for people living with obesity.

Body composition

Significant but modest long-term weight loss (about 2 kg) can be expected with exercise alone (e.g., aerobic and resistance) in male and female adults who have overweight or obesity. In general, diet interventions produce a greater weight loss (about 4 kg) compared to exercise alone, and when exercise is combined with diet, there is an additional increase in the amount of weight loss (about 6 kg).^{5,6,26,27} Weight loss interventions that incorporate exercise generally report either maintenance or gain in fat-free mass.^{1,6} In addition, physical activity therapy, with or without dietary changes, is associated with several health benefits. For example, regular physical activity can have a positive effect on cardiovascular risk factors; this occurs independently of significant weight loss.²⁰ Behavioural intervention incorporating exercise also reduces weight, fat mass, waist circumference and cardiometabolic risk factors in participants with Class II and III obesity.^{28–30} In older participants, exercise alone led to better physical function without significant weight loss, but when added to dietary changes, it attenuated the decrease in muscle and bone mass normally observed with diet

• Increasing physical activity can be an integral component of all obesity management strategies.

alone.³¹ The volume and intensity of physical activity affect the magnitude of health benefits that are associated with exercise.⁵

Regarding the long-term effects of physical activity, Washburn et al.⁶ stated that there is limited evidence in favour of one intervention modality (exercise, diet or combined) in order to prevent weight regain and/or maintain changes in cardiovascular risk factors over time. However, in the Look AHEAD (Action for Health in Diabetes) study, Pownall et al. (2015)³² monitored body composition changes in a subset of 1019 participants with overweight or obesity and type 2 diabetes over eight years. This RCT examined an intensive lifestyle intervention that included an increase of physical activity of up to 175 minutes per week and a reduction of caloric intake between 1200-1800 kcal/day. They observed a significant effect of the lifestyle intervention on changes in body composition after one year. In addition, weight, fat mass and lean mass were lower in the intervention group versus control (diabetes support and education) at all testing points during the eight-year follow-up. Overall, there seems consistent evidence from many large, relatively high-quality trials and meta-analyses that physical activity contributes to improvements in body composition and other indications of cardiometabolic health.

Brisk walking is the type of physical activity therapy that is most often recommended for the management of overweight or obesity in adults.³³ In this regard, Mabire et al.,¹ (2017) performed a systematic review and meta-analysis of 22 studies (n=1524; 81% female) to investigate the influence of age, sex and BMI on the effectiveness of brisk walking alone for managing obesity in adults. The intervention characteristics (average) were as follows: duration (46 minutes/session), intensity (73% maximum heart rate), frequency (four times/ week) and length (12 to 16 weeks), with an exercise compliance rate between 65% and 85%. Based on the pooled analysis, they found a statistically significant reduction in body weight (-2.13 Kg), BMI (-0.96 Kg/m²), waist circumference (WC) (-2.83 cm), fat mass (-2.59 Kg) and percent body fat (-1.38%), and no change in fat free mass. These results were in line with those reported in a Cochrane review on the effects of exercise alone in adults with overweight or obesity.5 In general, the magnitude of improvement in body composition indices was greater in participants under 50 years old. In addition, baseline BMI did not significantly influence the changes in body weight, waist circumference or body composition.

Body fat distribution

It is well documented that abdominal obesity, especially an excess of abdominal visceral fat, increases the risk for adverse health effects in individuals with overweight or obesity.³⁴ It is important to document the efficacy of exercise alone to reduce abdominal visceral fat considering the modest weight loss observed with lifestyle interventions. Based on multiple systematic reviews and meta-analyses performed since 2005, exercise alone is effective in reducing abdominal visceral fat.^{2,3,35,36} Reductions of abdominal visceral fat and total abdominal fat can also occur in the absence of weight loss or changes in WC.³⁵ Resistance training or its combination with aerobic training do not seem to have a significant impact on abdominal visceral fat reduction in comparison to control or aerobic training alone.^{2-4,37}

This is an unexpected finding which may in part be due to a smaller overall sample size in the meta-analyses of combined aerobic and resistance training, as well as the lower energy expenditure associated with resistance training compared to aerobic training. In general, aerobic training has the potential to result in reductions of abdominal visceral fat greater than 30 cm² and 40 cm² (on computerized tomography [CT] scan) in women and men, respectively. The higher reduction seen in men is mostly explained by the abdominal obesity phenotype of men.³ In regard to abdominal obesity, as measured by waist circumference, reductions are independent of exercise intensity. However, improvements in the cardiometabolic indices associated with abdominal visceral fat, as well as the increase of cardiorespiratory fitness in both women and men with abdominal obesity, seem to be intensity dependent (e.g., glucose tolerance).7 Finally, a recent meta-analysis on the effects of high-intensity interval training (HIIT) in adults with overweight or obesity showed that both cycling and running produce a significant reduction of total fat mass, abdominal fat mass and abdominal visceral fat in adults with overweight or obesity, with no difference between the sex.³⁸

Furthermore, sedentary individuals with high abdominal visceral fat are characterized by accumulation of fat at undesired sites (ectopic fat), such as the liver, the heart, the pancreas and the skeletal muscle. Ectopic fat plays an important role in the association between abdominal obesity and the increase in cardiovascular diseases risk.³⁴ In this regard, a meta-analysis showed that exercise alone could lead to a decrease in cardiac adiposity (e.g., epicardial and pericardial fat) and in intra-hepatic lipids, although the effect on the liver is greater when combined with dietary changes and with greater decrease in BMI or body weight.³⁹ In addition, aerobic training, and not resistance training, had an effect on reducing abdominal visceral fat and showed a trend toward reducing liver fat in adults with overweight or obesity and type 2 diabetes.^{4,40}

Therefore, there is quality evidence to recommend that regular aerobic exercise effectively reduces abdominal visceral fat. However, there is limited evidence concerning the effect of exercise alone on ectopic fat, but the available data suggest that exercise alone has the potential to decrease ectopic fat in the liver and the heart in adults with overweight or obesity.

Dose response considerations

Typical exercise prescriptions will include the following parameters: 1) type; 2) duration; 3) intensity; and 4) frequency. The volume of

physical activity is based on these four factors and is often defined as the total energy expenditure.

1) Type: We did not identify any study that randomly assigned participants to different aerobic exercise modalities, (e.g., walking versus cycling). However, there are several studies randomly assigning participants with obesity to resistance versus aerobic training. In one trial, 136 older men and women with abdominal obesity were randomly assigned to control, resistance, aerobic or combined aerobic and resistance training.⁸ Training took place over six months. The prescriptions were: three sessions of about 20 minutes in the resistance group; five sessions of 30 minutes in the aerobic group; and three sessions of 50 minutes in the combined aerobic and resistance training group. Fat mass was reduced by about 3 kg in both the aerobic and combined training group, whereas muscle mass increased by about 1 kg in the resistance and combined training group. The combined aerobic and resistance training group had the largest increase in insulin sensitivity and decrease in functional limitations. These findings are very similar to the ones from the Studies Targeting Risk Reduction Interventions through Defined Exercise-Aerobic Training and/ or Resistance Training (STRRIDE AT/RT) study.¹² In addition to the absence of a control group, one of the differences in this study was that the combined training group was asked to complete the totality of the prescription to the aerobic training (14 kcal/kg of body weight per week, or ~130 min/week) and resistance training (180 minutes per week).

2) Duration/volume: Previous guidelines on physical activity for obesity management^{41,42} have emphasized the effect of increasing the volume of physical activity. The studies that directly compare lesser to greater exercise volumes have typically achieved differences in volume by increasing exercise duration while keeping intensity, frequency and type of exercise consistent. While it seemed well-established that greater exercise volumes lead to greater weight loss,³⁶ some recent relatively large studies have not confirmed these findings. For example, Ross et al., (2015)⁷ randomly assigned 300 men and women with obesity to control, low-amount/low-intensity exercise (LALI), high-amount/low-intensity exercise (HALI), or highamount/high intensity exercise (HAHI). The high-amount groups were prescribed twice as much energy expenditure than the lowamount group. However, all three exercise groups showed a similar reduction in body weight and WC compared to control. There was, however, a dose-response relationship between exercise volume and improvements in cardiorespiratory fitness. Similarly, Church et al., (2007)¹³ randomly assigned 464 postmenopausal women with overweight or obesity and with elevated blood pressure to a control group or three exercise groups with increasing volume (i.e., prescribed energy expenditure of four vs. eight vs. 12 kcal per kilogram of body weight, per week). There was no difference in weight loss between groups, or in decreased WC compared to control. Here again, there was a dose-response relationship with greater exercise leading to greater improvements in cardiorespiratory fitness. It is interesting to note that the lower volume groups in these studies often performed less than 150 minutes per week^{7,13,36} and showed some benefits (e.g., cardiorespiratory fitness,13 or a decrease in waist circumference⁷).

It is unclear why these studies did not show a dose-response relationship when comparing different prescribed exercise volume on changes in body weight or WC. Studies did not suggest any compensatory decreases in daily physical activity or increases in energy intake with greater exercise volume. However, compliance to the exercise prescription within groups was highly variable. The volume of exercise actually completed was shown to be a strong predictor of the amount of weight loss in studies such as these. For example, a study cited from the previous edition of these guidelines,⁴³ which was updated with weight maintenance data,⁴⁴ suggested that the actual amount of physical activity completed predicted the amount of weight loss, whereas the amount prescribed did not. In one of the longest duration intervention studies comparing different exercise volumes, standard behaviour therapy was compared to high physical activity levels.45 Participants from both groups received identical instructions and training on reducing energy and fat intake, but one group was given the goal of participating in 1000 Kcal per week (or about 30 minutes per day) of physical activity, whereas the other had the goal of 2500 kcal per week. The interventions lasted 18 months, and participants were followed for an additional 12 months. There was no difference in weight loss after the first six months, but the difference reached significance after 12 and 18 months.⁴⁴ After the intervention, physical activity declined and the differences in weight loss between groups was no longer present, but once again, it was observed that those who maintained greater physical activity levels maintained greater weight loss.45

3) Intensity: In the years since the previous edition of these guidelines, a large amount of literature has compared moderate versus vigorous intensity exercise. Three of the studies described in the previous section on exercise volume also included comparisons of moderate versus vigorous intensity, matched for exercise volume. The vigorous intensity groups in these studies had relatively similar intensity prescriptions of 75% of peak oxygen consumption (VO_{2peak}) in the study by Ross et al., (2015),⁷ 65–80% VO_{2peak} in the study by Slentz et al. (2005)³⁶ and 70-85% of maximum heart rate in those by Jakicic et al., (2003, 2008).43,44 The moderate intensity exercise was prescribed as 50% VO_{2peak}, 40-55% VO_{2peak} and 50-65% of maximum heart rate in these studies, respectively. Greater exercise intensity necessitated less time to complete a given volume and led to greater improvements in cardiorespiratory fitness,^{7,46} but was not associated with statistically significant greater weight loss or changes in fat mass in these three studies.

Many of the recent studies examining the role of exercise intensity have utilized HIIT. There have been several systematic reviews and meta-analyses on this topic.^{10,38,47–51} There is evidence that HIIT reduces total and intra-abdominal fat,³⁸ but at this time there is no clear evidence that HIIT causes more fat loss compared to moderate intensity exercise.^{48,51} While some HIIT protocols require less time (and less volume), these HIIT protocols may not lead to as much fat loss when compared to moderate intensity protocols with greater volumes.^{48,51}

HIIT causes greater improvements in cardiorespiratory fitness¹⁰ and some indicators of cardiometabolic health^{47,49} compared to mod-

erate intensity exercise. A limitation of these meta-analyses was that most included studies had small sample sizes and training was often less than four months in duration. In one of the longest and largest studies examining HIIT training, Roy et al. (2018)⁵² allowed participants to choose between unsupervised HIIT three days per week or 30 minutes of daily moderate intensity exercise. Forty-two percent chose HIIT, but after one year there was no significant difference in weight or abdominal fat loss between interventions.

4) Frequency: Our search identified few studies directly comparing different exercise frequencies while keeping total exercise volume constant. In a study by Madjd et al. (2016),⁵³ 75 women with overweight and obesity were randomly allocated to high- versus low-frequency physical activity groups. Both groups were asked to follow the same dietary weight loss program and to exercise for 300 minutes per week, but either for 50 minutes/day, six days/ week (high frequency) or 100 minutes/day, three days/week (low frequency). Compared with the high frequency group, the low freguency group had a greater decrease in weight (9.6 kg vs. 7.8 kg) and a greater increase in daily steps. However, it was not clear if the greater number of steps was due to better compliance to the protocol or a greater number of steps outside of the prescribed session. As this is the only study identified by our search, these results should be confirmed before recommending a reduced frequency of exercise sessions. It should also be noted that, in recent years, a large body of literature is reporting short-term improvements in cardiometabolic risk factors (e.g., glucose and triglycerides) by breaking sedentary time with multiple frequent bouts of standing or light- to moderate-intensity walking (e.g., two to five minutes every 30 minutes).54,55 Additional long-term studies on the effects of breaking up sedentary time with frequent short bouts of activity are still required.

Cardiometabolic risk factors and chronic diseases

Several large longitudinal studies have consistently observed that greater physical activity (or cardiorespiratory fitness) were associated with reductions in all-cause mortality, cardiovascular diseases and metabolic diseases, such as type 2 diabetes.^{19,20} Our literature search did not identify any trials with the primary goal of examining the effects of exercise on mortality. This is likely due to the challenges of undertaking a study of sufficient duration and including a large sample size. In addition, most large trials having the incidence of chronic diseases as a primary outcome often include a combined diet and physical activity intervention. It would not be feasible in the present paper to examine the independent effects of physical activity on all cardiometabolic risk factors. Therefore, the following subsections will focus on components commonly associated with the metabolic syndrome, including hyperglycemia and insulin resistance, hypertension and dyslipidemia.

Glycemia: Meta-analyses have consistently shown improvements in glycated hemoglobin following structured/supervised aerobic and/or resistance exercise training in people with type 2 diabetes,⁵⁶ even in the absence of weight loss.⁵⁷ In people who do not have diabetes, improvements in postprandial glucose and especially insulin sensitivity can occur with exercise training of sufficient volume and intensity, but improvements in fasting glucose are not typically observed in the absence of large weight loss.^{7,11,12} Some of the largest and longest-duration trials have been performed for the prevention and management of type 2 diabetes in people with impaired glucose tolerance. For example, trials such as the Diabetes Prevention Program,⁵⁸ the Finnish Diabetes Prevention Study,⁵⁹ the Indian Diabetes Prevention Program⁶⁰ and the Da Qing Impaired Glucose Tolerance and Diabetes Study.⁶¹ The large majority of participants in these studies had a BMI above 25 kg/m². With the exception of the Da Qing study, which included an exercise-only group (39% reduction in incidence of diabetes), other studies examined a combined diet and physical activity interventions and found 38–58% reduction in the incidence of diabetes.

The Look AHEAD study was the largest RCT to date evaluating the efficacy of intensive lifestyle intervention in adults with overweight or obesity and with type 2 diabetes.^{62,63} The intensive lifestyle intervention group targeted at least 175 minutes/week of unsupervised physical activity and a \geq 7% weight loss, while the diabetes support and education group received usual care. The intensive lifestyle intervention group did not achieve significant reductions in the rate of cardiovascular events. However, they achieved significant weight loss which was maintained below the standard education group for up to 10 years, and improved cardiorespiratory fitness and glycemic control with fewer medications. They also achieved decreased rates of sleep apnea, severe diabetic chronic kidney disease and retinopathy, depression, sexual dysfunction and urinary incontinence. They also had better physical mobility maintenance and guality of life. All of these outcomes were achieved with lower overall healthcare costs.64

Blood pressure. Several meta-analyses have examined the effects of supervised exercise on blood pressure without excluding normal-weight participants (for example Lemes et al., 2018).¹⁴ They suggest that exercise reduces systolic blood pressure (-5 mmHg) and diastolic pressure (-3 mmHg). People with preexisting hypertension also show similar or larger improvements in blood pressure are not consistently observed, especially with smaller exercise volumes.¹³ Improvements have been shown following both HIIT⁶⁵ and resistance training.⁶⁶

Blood lipids and lipoproteins: Meta-analyses, including those that have limited studies to those with participants with overweight or obesity, have shown that exercise improves many lipid and lipoprotein risk factors, including reducing total cholesterol and triglycerides,^{15,16} and sometimes HDL-C.¹⁴ One of these meta-analyses showed a tendency toward improvements in HDL-C but results were heterogeneous.¹⁵ However, an effect of exercise on LDL-C is less likely.¹⁵ For example, the Oslo Diet and Exercise Study was a one-year trial randomizing 219 healthy participants (mean BMI = 29 kg/m²) to exercise or no exercise, dietary advice or no advice, in a 2x2 factorial design.⁶⁷ Exercise did not lower LDL-C although it increased HDL-C and ApoA-I and decreased ApoB.⁶⁷ It is possible that greater exercise volumes or intensities

are required to improve LDL-C and HDL-C. The Studies Targeting Risk Reduction Interventions through Defined Exercise-Aerobic Training and/or Resistance Training (STRRIDE AT/RT) trial compared walking approximately 12 miles per week at a moderate intensity, 12 miles per week at a high intensity (i.e., greater speed) and 20 miles per week at a high intensity. Improvements in LDL-C, HDL-C (and most other studied lipid parameters) tended to improve with increasing intensity or distance (volume), and often the only significant difference compared to control was in the high-volume high intensity group.^{36,68} Although not limited to participants who had overweight or obesity, a meta-analysis also supported the effects of walking⁶⁹ and perhaps resistance training^{70,71} on lipid/lipoproteins. Improvements are also seen in meta-analyses examining men⁷² and women⁷³ separately.

Physical fitness indices and mobility

Increases in physical fitness are among the most consistently documented effects of regular physical activity. Increases in cardiorespiratory fitness are proportional to the volume^{7,13} and intensity^{7,10,46} of exercise. In addition to being associated with reduced mortality, cardiorespiratory fitness is associated with improved mobility and ability to take part in many activities, including activities of daily living. For example, greater cardiorespiratory fitness can make activities such as stair climbing feel easier. Resistance training is often aimed at increasing strength, which can also improve independence and activities of daily living. Such improvements have most often been documented in people who initially had mobility impairments, including older people with obesity, as well as people with Class II or III obesity. For example, in the Lifestyle Interventions and Independence for Elders (LIFE) study,⁷⁴ 1,635 sedentary men and women aged 70 to 89 years were randomly assigned to a moderate-intensity physical activity or health education program for 24 months. Major mobility disability was defined as the inability to walk for 400 meters, which was observed in 30% of the physical activity group and 35% of the health education group. In participants with Class II or III obesity, major mobility disability developed in 36% of the physical activity group versus 46% in the health education group. Resistance training also improved functional limitations in older adults with obesity; adding resistance training to aerobic training led to additional benefits.8 A meta-analysis of 14 trials⁷⁵ comparing energy restriction alone to energy restriction combined with physical activity suggested that the addition of aerobic and resistance training improved cardiovascular fitness and muscle strength, and increased fat mass loss and preserved lean body mass.

Quality of life and mental health

Individuals with overweight or obesity are at an increased risk of developing depression, based on a systematic review and meta-analysis of longitudinal studies.⁷⁶ It is documented that physical activity can be used to prevent, or as a therapy to treat, mood disorders (i.e., depression, anxiety), and to improve quality of life and body image in non-clinical and clinical populations.¹⁸ However, the efficacy of physical activity to improve mood disorders in adults with overweight or obesity is less conclusive. In fact, Baker et al., (2016)¹⁷ reported, based on a systematic review, no significant changes in mental health outcomes and quality of life following exercise intervention in postmenopausal women with overweight or obesity. In addition, Baillot et al. (2018)¹⁸ recently reported the results of a systematic review and meta-analysis on the effects of physical activity on quality of life, depression, anxiety and body image in adults (male and female) with obesity. Twenty-two studies (16 RCTs, one controlled clinical trial and five before-and-after studies (n=2510; > 75% female) met their inclusion criteria. In general, the parameters of the exercise prescription were the following: type (50% aerobic, 14% resistance, 23% combination and 9% comparison between aerobic vs. resistance training), session duration (12 to 90 min), frequency (two to five sessions/ week) and intensity (light to moderate) for a duration >16 weeks; most were supervised (73%). Results of the meta-analysis of RCTs revealed no significant effect of exercise for physical or mental domains of quality of life or for depression. The few RCTs for anxiety (n=2) and body image (n=1) reported no significant effects of exercise intervention. In contrast, all the controlled clinical trials and before-and-after studies (n=5) reported significant improvements in many quality of life domains (e.g., psychosocial and physical functioning, self-esteem, public distress), and one controlled clinical trial showed an improvement in body consciousness and mental representation. Considering the lack of quality studies available, the authors concluded that we must be careful before drawing conclusions that physical activity therapy is not effective to improve mood disorders, quality of life and/or body image in adults with overweight or obesity. In fact, since the publication of this systematic review, Fanning et al., (2018)⁷⁷ randomized 249 (71.1% female) older adults (66.9 years) with obesity (BMI = 34.4 kg/m²) associated with cardiovascular disease or the metabolic syndrome to three different interventions. The interventions were: dietary weight loss or dietary weight loss in combination with aerobic training or dietary weight loss in combination with resistance training. The intervention included a six-month intensive phase and 12-month follow-up. The results suggested that both combined interventions including exercise were superior to dietary changes alone to improve physical function indicators, such as greater walking and climbing self-efficacy, as well as health-related quality of life scores for general physical functioning.

Therefore, overall, there is little evidence to recommend that physical activity therapy alone may improve quality of life, mood disorders, or body image in adults with overweight or obesity.

Risk-benefit ratio of increasing physical activity

It is important to consider that physical activity can be associated with an increased risk of injury in some studies, but not all.^{78,79} In the study by Janney and Jakicic (2010)⁷⁹ which included data from 397 participants from two separate trials, walking was prescribed as the primary mode of exercise for 150, 200, or 300 minutes/ week. Participants included men and women with BMI ranging from 25 to 40 kg/m². While there was no increased risk of inju-

ry compared to control, a substantial proportion of participants (46%) reported some injury or illness. Only 7% of the injuries were associated with exercise alone. A higher BMI was associated with increased odds of injury over time, as well as being injured earlier during the intervention.⁷⁹ However, in a study by Goodpaster et al. (2010)²⁸ with 130 participants who had a BMI above 35 kg/m², delaying physical activity by six months during diet-induced weight loss did not reduce the risk of adverse events compared to those who started the diet and physical activity intervention simultaneously. In the Diabetes Prevention Program,⁸⁰ the researchers randomized 3234 participants to placebo, metformin or a lifestyle intervention (which included physical activity). There was an increased incidence of musculoskeletal symptoms (number of events/100 person-year) in the lifestyle intervention group compared to placebo and metformin (24%, 21% and 20%, respectively).

Strategies to reduce the risk of injury could include gradual progression in the intensity, duration and frequency of exercise, as some trials reported a greater increased risk of adverse events with increasing volume and/or intensity.⁷ Proper footwear and equipment fitting (if relevant) may also help reduce injuries. Many exercise studies also utilize the expertise of exercise professionals (e.g., kinesiologists or exercise specialists) to guide and supervise exercise sessions.^{63,81}

Conclusion

Adults with overweight or obesity should consider increasing physical activity as an integral component of all obesity management strategies. Physical activity offers a wide range of health benefits that are partly independent of weight loss. Sedentary individuals should progress to 30–60 minutes or more of moderate to vigorous intensity aerobic physical activity (e.g., walking, biking) on most days of the week (i.e., aim to accumulate 150 minutes or more per week), engage in strength (resistance) activity at least two days per week, and reduce the amount of daily sedentary time for body weight control and/or health benefits.

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The summary of the Canadian Adult Obesity Clinical Practice Guideline is published in the *Canadian Medical Association Journal*, and contains information on the full methodology, management of authors' competing interests, a brief overview of all recommendations and other details. More detailed guideline chapters are published on the Obesity Canada website at www.obesitycanada.ca/guidelines.

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References

- Mabire L, Mani R, Liu L, Mulligan H, Baxter D. The influence of age, sex and body mass index on the effectiveness of brisk walking for obesity management in adults: A systematic review and meta-analysis. J Phys Act Heal. 2017;14(5):389-407. doi:10.1123/jpah.2016-0064
- Ismail I, Keating SE, Baker MK, Johnson NA. A systematic review and meta-analysis of the effect of aerobic vs. resistance exercise training on visceral fat. Obes Rev. 2012;13(1):68-91. doi:10.1111/j.1467-789X.2011.00931.x
- Vissers D, Hens W, Taeymans J, Baeyens JP, Poortmans J, Van Gaal L. The Effect of Exercise on Visceral Adipose Tissue in Overweight Adults: A Systematic Review and Meta-Analysis. PLoS One. 2013;8(2). doi:10.1371/journal.pone.0056415
- Sabag A, Way KL, Keating SE, et al. Exercise and ectopic fat in type 2 diabetes: A systematic review and meta-analysis. Diabetes Metab. 2017;43(3):195-210. doi:10.1016/j.diabet.2016.12.006
- Shaw K, Gennat H, O'Rourke P, Del Mar C. Exercise for overweight or obesity. Cochrane Database Syst Rev. 2006;(4):4-5. doi:10.1002/14651858.CD003817.pub3
- Washburn RA, Szabo AN, Lambourne K, et al. Does the method of weight loss effect long-term changes in weight, body composition or chronic disease risk factors in overweight or obese adults? A systematic review. PLoS One. 2014;9(10). doi:10.1371/journal.pone.0109849
- Ross R, Stotz PJ, Lam M. Effects of exercise amount and intensity on abdominal obesity and glucose tolerance in obese adults: A randomized trial. Ann Intern Med. 2015;162(5):325-334. doi:10.7326/M14-1189
- Davidson LE, Hudson R, Kilpatrick K, et al. Effects of exercise modality on insulin resistance and functional limitation in older adults: a randomized controlled trial. Arch Intern Med. 2009;169(2):122-131. doi:10.1007/s12170-009-0037-4
- Mann S, Jimenez A, Steele J, Domone S, Wade M, Beedie C. Programming and supervision of resistance training leads to positive effects on strength and body composition: Results from two randomised trials of community fitness programmes. BMC Public Health. 2018;18(1):420. doi:10.1186/s12889-018-5289-9
- Hwang CL, Wu YT, Chou CH. Effect of aerobic interval training on exercise capacity and metabolic risk factors in people with cardiometabolic disorders: a meta-analysis. J Cardiopulm Rehabil Prev. 2011;31(6):378-385. doi:10.1097/ hcr.0b013e31822f16cb
- Frank LL, Sorensen BE, Yasui Y, et al. Effects of exercise on metabolic risk variables in overweight postmenopausal women: A randomized clinical trial. Obes Res. 2005;13(3):615-625. doi:10.1038/oby.2005.66
- 12. AbouAssi H, Slentz CA, Mikus CR, et al. The effects of aerobic, resistance, and combination training on insulin sensitivity and secretion in overweight adults from STRRIDE AT/RT: A randomized trial. J Appl Physiol. 2015;118(12):1474-1482. doi:10.1152/japplphysiol.00509.2014
- Church T, Earnest C, Skinner J, Blair S. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. JAMA. 2007;297(19):2081-2091. doi:10.1016/S1134-2072(07)71883-2

- Lemes ÍR, Turi-Lynch BC, Cavero-Redondo I, Linares SN, Monteiro HL. Aerobic training reduces blood pressure and waist circumference and increases HDL-c in metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials. J Am Soc Hypertens. 2018;12(8):580-588. doi:10.1016/j.jash.2018.06.007
- Kelley GA, Kelley KS, Vu Tran Z. Aerobic exercise, lipids and lipoproteins in overweight and obese adults: A meta-analysis of randomized controlled trials. Int J Obes. 2005;29(8):881-893. doi:10.1038/sj.ijo.0802959
- Kuhle CL, Steffen MW, Anderson PJ, Murad MH. Effect of exercise on anthropometric measures and serum lipids in older individuals: A systematic review and meta-analysis. BMJ Open. 2014;4(6):e005283. doi:10.1136/bmjopen-2014-005283
- Baker A, Sirois-Leclerc H, Tulloch H. The Impact of Long-Term Physical Activity Interventions for Overweight/Obese Postmenopausal Women on Adiposity Indicators, Physical Capacity, and Mental Health Outcomes: A Systematic Review. J Obes. 2016. doi:10.1155/2016/6169890
- Baillot A, Saunders S, Brunet J, Romain AJ, Trottier A, Bernard P. A systematic review and meta-analysis of the effect of exercise on psychosocial outcomes in adults with obesity: A call for more research. Ment Health Phys Act. 2018;14:1-10. doi:10.1016/j.mhpa.2017.12.004
- Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. Cmaj. 2006;174(6):801-809.
- 20. Pedersen B. Body mass index ☐ independent effect of fitness and physical activity for all ☐ cause mortality. Scand J Med Sci Sports. 2007;17(3):196-204.
- Janssen I, Katzmarzyk PT, Ross R, et al. Fitness alters the associations of BMI and waist circumference with total and abdominal fat. Obes Res. 2004;12(3):525-537. doi:10.1038/oby.2004.60
- Haskell WL, Lee IM, Pate RR, et al. "ACSM/AHA Recommendations." Circulation. 2007;116(9):1081-1093. doi:10.1161/CIRCULATIONAHA.107.185649
- de Rezende LFM, Rey-López JP, Matsudo VKR, do Carmo Luiz O. Sedentary behaviors and psychological outcomes among older adults: A systematic review. BMC Public Health. 2014;14(1):333. doi:10.6063/motricidade.12223
- Tremblay MS, Warburton DER, Janssen I, et al. New Canadian physical activity guidelines. Appl Physiol Nutr Metab. 2011;36(1):36-46. doi:10.1139/H11-009
- Hamilton MT, Healy GN, Dunstan DW, Zderic TW, Owen N. Too Little Exercise and the Need for New Recommendations on Sedentary Behavior. Curr Cardiovasc Risk Rep. 2008;2(4):292-298. doi:10.1007/s12170-008-0054-8.Too
- Miller WC, Koceja DM, Hamilton EJ. A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. Int J Obes. 1997;21(10):941-947. doi:10.1038/sj.ijo.0800499
- Borek AJ, Abraham C, Greaves CJ, Tarrant M. Group-based diet and physical activity weight-loss interventions: A systematic review and meta-analysis of randomised controlled trials. Appl Psychol Heal Well-Being. 2018;10(1):62-86. doi:10.1111/aphw.12121
- Goodpaster BH, DeLany JP, Otto AD, et al. Effects of diet and physical activity interventions on weight loss and cardiometabolic risk factors in severely obese adults: A randomized trial. JAMA - J Am Med Assoc. 2010;304(16):1795-1802. doi:10.1001/jama.2010.1505
- Hassan Y, Head V, Jacob D, Bachmann MO, Diu S, Ford J. Lifestyle interventions for weight loss in adults with severe obesity: a systematic review. Clin Obes. 2016;6(6):395-403.

- Baillot A, Romain AJ, Boisvert-Vigneault K, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: A systematic review and meta-analysis. PLoS One. 2015;10(4). doi:10.1371/ journal.pone.0119017
- Batsis JA, Gill LE, Masutani RK, et al. Weight Loss Interventions in Older Adults with Obesity: A Systematic Review of Randomized Controlled Trials Since 2005. J Am Geriatr Soc. 2017;65(2):257-268. doi:10.1111/jgs.14514
- Pownall HJ, Bray GA, Wagenknecht LE, et al. Changes in body composition over 8 years in a randomized trial of a lifestyle intervention: The look AHEAD study. Obesity. 2015;23(3):565-572. doi:10.1002/oby.21005
- Watson KB, Frederick GM, Harris CD, Carlson SA, Fulton JE. U.S. Adults' Participation in Specific Activities: Behavioral Risk Factor Surveillance System--2011. J Phys Act Health. 2015;12(Suppl 1):S3-S10. doi:10.1123/jpah.2013-0521
- 34. Després JP, Lemieux I, Bergeron J, et al. Abdominal Obesity and the Metabolic Syndrome: Contribution to global cardiometabolic risk. Arterioscler Thromb Vasc Biol. 2008;28(6):1039-1049. doi:10.1161/ATVBAHA.107.159228
- Kay SJ, Fiatarone Singh MA. The influence of physical activity on abdominal fat: A systematic review of the literature. Obes Rev. 2006;7(2):183-200. doi:10.1111/j.1467-789X.2006.00250.x
- Slentz CA, Aiken LB, Houmard JA, et al. Inactivity, exercise, and visceral fat. STRRIDE: A randomized, controlled study of exercise intensity and amount. J Appl Physiol. 2005;99(4):1613-1618. doi:10.1152/japplphysiol.00124.2005
- Bateman LA, Slentz CA, Willis LH, et al. Comparison of aerobic versus resistance exercise training effects on metabolic syndrome (from the Studies of a Targeted Risk Reduction Intervention Through Defined Exercise - STRRIDE-AT/RT). Am J Cardiol. 2011;108(6):838-844. doi:10.1016/j.amjcard.2011.04.037
- Maillard F, Pereira B, Boisseau N. Effect of High-Intensity Interval Training on Total, Abdominal and Visceral Fat Mass: A Meta-Analysis. Sport Med. 2018;48(2):269-288. doi:10.1007/s40279-017-0807-y
- Hens W, Taeymans J, Cornelis J, Gielen J, Van Gaal L, Vissers D. The effect of lifestyle interventions on excess ectopic fat deposition measured by noninvasive techniques in overweight and obese adults: A systematic review and meta-analysis. J Phys Act Heal. 2016;13(6):671-694. doi:10.1123/jpah.2015-0560
- Keating SE, Hackett DA, George J, Johnson NA. Exercise and non-alcoholic fatty liver disease: A systematic review and meta-analysis. J Hepatol. 2012;57(1):157-166. doi:10.1016/j.jhep.2012.02.023
- Lau DCW, Douketis JD, Morrison KM, Hramiak IM, Sharma AM, Ur E. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]. Can Med Assoc J. 2007;176(8):S1-S13. doi:10.1503/cmaj.061409
- 42. Colberg SR, Sigal RJ, Fernhall B, et al. Exercise and type 2 diabetes: The American College of Sports Medicine and the American Diabetes Association: Joint position statement. Diabetes Care. 2010;33(12):e147-e167. doi:10.2337/dc10-9990
- Jakicic JM, Marcus BH, Gallagher KI, Napolitano M, Lang W. Effect of Exercise Duration and Intensity on Weight Loss in Overweight, Sedentary Women: A Randomized Trial. J Am Med Assoc. 2003;290(10):1323-1330. doi:10.1001/jama.290.10.1323
- Jakicic JM, Marcus BH, Lang W, Janney C. Effect of exercise on 24-month weight loss maintenance in overweight women. Arch Intern Med. 2008;168(14):1550-1559. doi:10.1001/archinte.168.19.2162
- Tate DF, Jeffery RW, Sherwood NE, Wing RR. Long-term weight losses associated with prescription of higher physical activity goals. Are higher levels of physical activity protective against weight regain? Am J Clin Nutr. 2007;85(4):954-959. doi:10.1093/ajcn/85.4.954
- Slentz CA, Houmard JA, Johnson JL, et al. Inactivity, exercise training and detraining, and plasma lipoproteins. STRRIDE: A randomized, controlled study of exercise intensity and amount. J Appl Physiol. 2007;103(2):432-442. doi:10.1152/japplphysiol.01314.2006
- Jelleyman C, Yates T, O'Donovan G, et al. The effects of high-intensity interval training on glucose regulation and insulin resistance: A meta-analysis. Obes Rev. 2015;16(11):942-961. doi:10.1111/obr.12317

- Keating SE, Johnson NA, Mielke GI, Coombes JS. A systematic review and meta-analysis of interval training versus moderate-intensity continuous training on body adiposity. Obes Rev. 2017;18(8):943-964. doi:10.1111/obr.12536
- Batacan RB, Duncan MJ, Dalbo VJ, Tucker PS, Fenning AS. Effects of high-intensity interval training on cardiometabolic health: A systematic review and meta-analysis of intervention studies. Br J Sports Med. 2017;51(6):494-503. doi:10.1136/bjsports-2015-095841
- Türk Y, Theel W, Kasteleyn MJ, et al. High intensity training in obesity: a Meta-analysis. Obes Sci Pract. 2017;3(3):258-271. doi:10.1002/osp4.109
- Wewege M, van den Berg R, Ward RE, Keech A. The effects of high-intensity interval training vs. moderate-intensity continuous training on body composition in overweight and obese adults: a systematic review and meta-analysis. Obes Rev. 2017;18(6):635-646. doi:10.1111/obr.12532
- Roy M, Williams SM, Brown RC, et al. High-Intensity Interval Training in the Real World: Outcomes from a 12-Month Intervention in Overweight Adults. Med Sci Sports Exerc. 2018;50(9):1818-1826. doi:10.1249/MSS.000000000001642
- Madjd A, Taylor MA, Neek LS, et al. Effect of weekly physical activity frequency on weight loss in healthy overweight and obese women attending a weight loss program: A randomized controlled trial. Am J Clin Nutr. 2016;104(5):1202-1208. doi:10.3945/ajcn.116.136408
- Henson J, Davies MJ, Bodicoat DH, et al. Breaking Up Prolonged Sitting with Standing or Walking Attenuates the Postprandial Metabolic Response in Postmenopausal Women: A Randomized Acute Study. Diabetes Care. 2016;39(1):130-138. doi:10.2337/dc15-1240
- Dunstan DW, Kingwell BA, Larsen R, et al. Breaking up prolonged sitting reduces es postprandial glucose and insulin responses. Diabetes Care. 2012;35(5):976-983. doi:10.2337/dc11-1931
- Umpierre D, Ribeiro PA, Kramer CK, et al. Physical Activity Advice Only or Structured With HbA 1c Levels in Type 2 Diabetes. A Systematic Review and Meta-analysis. JAMA. 2011;305(17):1790-1799.
- Boulé NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: A meta-analysis of controlled clinical trials. J Am Med Assoc. 2001;286(10):1218-1227. doi:10.1001/ jama.286.10.1218
- Knowler W, Barrett-Connor E, Fowler S, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393-403.
- Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001;344(18):1343-1350. doi:10.1056/NEJM200105033441801
- Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia. 2006;49(2):289-297. doi:10.1007/ s00125-005-0097-z
- Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: The Da Qing IGT and diabetes study. Diabetes Care. 1997;20(4):537-544. doi:10.2337/diacare.20.4.537
- Jakicic JM, Egan CM, Fabricatore AN, et al. Four-year change in cardiorespiratory fitnessandinfluenceonglycemiccontrol in adults with type 2 diabetes in a randomized trial: The look AHEAD trial. Diabetes Care. 2013;36(5):1297-1303. doi:10.2337/dc12-0712
- 63. Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. N Engl J Med. 2013;369(2):145-154.
- 64. Pi-Sunyer X. The look AHEAD trial: a review and discussion of its outcomes. Curr Nutr Rep. 2014;3(4):387-391. doi:10.1007/s13668-014-0099-x.The
- Costa EC, Hay JL, Kehler DS, et al. Effects of High-Intensity Interval Training Versus Moderate- Intensity Continuous Training On Blood Pressure in Adults with Pre- to Established Hypertension : A Systematic Review and Meta-Analysis of Randomized Trials. Sport Med. 2018;48(9):2127-2142. doi:10.1007/s40279-018-0944-y

- Ashton RE, Tew GA, Aning JJ, Gilbert SE, Lewis L, Saxton JM. Effects of shortterm, medium-term and long-term resistance exercise training on cardiometabolic health outcomes in adults: systematic review with meta-analysis. Br J Sport Med bjsports. 2017.
- Holme I, Høstmark AT, Anderssen SA. ApoB but not LDL-cholesterol is reduced by exercise training in overweight healthy men. Results from the 1-year randomized Oslo Diet and Exercise Study. J Intern Med. 2007;262(2):235-243. doi:10.1111/j.1365-2796.2007.01806.x
- Kraus WE, Houmard JA, Duscha BD, et al. Effects of the amount and intensity of exercise on plasma lipoproteins. N Engl J Med. 2002;347(19):1483-1492. doi:10.1056/NEJMoa020194
- Gondim OS, de Camargo VTN, Gutierrez FA, de Oliveira Martins, P. F Passos MEP, Momesso CM, Cury-Boaventura MF. Benefits of Regular Exercise on Inflammatory and Cardiovascular Risk Markers in Normal Weight, Overweight and Obese Adults. PLoS One. 2015;10(10). doi:10.1371/journal.pone.0140596
- Correa CS, Teixeira BC, Bittencourt A, Reischak-Oliveira Á. Effects of strength training on blood lipoprotein concentrations in postmenopausal women. J Vasc Bras. 2014;13(4):312-317.
- Kelley GA, Kelley KS. Meditative Movement Therapies and Health- Related Quality-of-Life in Adults : A Systematic Review of Meta-Analyses. PLoS One. 2015;10(6). doi:10.1371/journal.pone.0129181
- Martens RJ, van der Berg JD, Stehouwer CD, et al. Amount and pattern of physical activity and sedentary behavior are associated with kidney function and kidney damage : The Maastricht Study. PLoS One. 2018;13(4).
- Kelley GA, Kelley KS, Tran Z V. Aerobic exercise and lipids and lipoproteins in women: a meta-analysis of randomized controlled trials. J women's Heal. 2004;13(10):1148-1164.
- Kritchevsky SB, Lovato L, Handing EP, et al. Exercise 's Effect on Mobility Disability in Older Adults With and Without Obesity : The LIFE Study Randomized Clinical Trial. Obesity. 2017;25(7):1199-1205. doi:10.1002/oby.21860
- Miller CT, Fraser SF, Levinger I, et al. The Effects of Exercise Training in Addition to Energy Restriction on Functional Capacities and Body Composition in Obese Adults during Weight Loss : A Systematic Review. PLoS One. 2013;8(11). doi:10.1371/journal.pone.0081692
- Luppino FS, de Wit LM, Bouvy PF, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry. 2010;67(3):220-229.
- Fanning J, Walkup MP, Ambrosius WT, Brawley, L. R., Ip EH, Marsh AP, Rejeski WJ. Change in health-related quality of life and social cognitive outcomes in obese, older adults in a randomized controlled weight loss trial: Does physical activity behavior matter? J Behav Med. 2019;41(3):299-308. doi:10.1007/ s10865-017-9903-6.Change
- Campbell K, Foster-Schubert K, Xiao L, et al. Injuries in sedentary individuals enrolled in a 12-month, randomized, controlled, exercise trial. J Phys Act Heal. 2014;9(2):198-207.
- Janney CA, Jakicic JM. The influence of exercise and BMI on injuries and illnesses in overweight and obese individuals : a randomized control trial. Int J Behav Nutr Phys Act. 2010;7(1):1.
- Herman WH, Hoerger TJ, Brandle M, et al. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. Ann Intern Med. 2009;142(5):323-332.
- Aubertin-Leheudre M, Lord C, Khalil A, Dionne JJ. Effect of 6 months of exercise and isoflavone supplementation on clinical cardiovascular risk factors in obese postmenopausal women: a randomized, double-blind study. Menopause. 2007;14(4):624-629. doi:10.1097/gme.0b013e31802e426b