



Weight control and physical exercise in people with multiple sclerosis: Current knowledge and future perspectives



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ABSTRACT

There is extensive data supporting a high prevalence of both overweight and obesity status in people with multiple sclerosis, and increases in body mass index has been associated with an increased risk of multiple sclerosis. Body composition may influence the course, treatment and management of multiple sclerosis. One proposed strategy for managing overweight and obesity status and associated secondary effects in people with multiple sclerosis involves increasing the levels of physical activity. In fact, increased levels of physical activity affect various physiological (endurance capacity, strength, balance) and biological processes (fat oxidation, insulin sensitivity, anti-inflammation, neurotrophic factors) which are known to be dysfunctional in multiple sclerosis and which may worsen with increases in obesity. When designing personalized exercise programs it should be kept in mind that current exercise recommendations for people with multiple sclerosis should exceed energy expenditure recommendations to efficiently counteract weight gain. Therefore, it is necessary to consider body composition as a primary endpoint in experimental studies. In addition, designing guidelines for weight control or weight loss in people MS is needed. The most comprehensive weight management guidelines are outlined in the American College of Sports Medicine Position Statement, which recommends between 150–250 min per week of moderate-intensity physical activity for preventing weight gain, and between 225–420 min per week of moderate-intensity physical activity for weight loss. These recommendations seem applicable for people with multiple sclerosis.

1. Introduction

Multiple sclerosis (MS) is an autoimmune and demyelination disease of the central nervous system (CNS) ^{1,2} MS often occurs in people at early and middle-ages of adulthood ^{2,3} but MS is also a lifespan disease that effects children and older adults. To date, there is no definitive treatment for MS, therefore, different strategies are available for managing the disease and its course over time. One of the reasons for the diversification of MS therapy and management strategies may be associated with the varied comorbid conditions that complicate intervention delivery for therapists and medical practitioners. ^{2,4} Indeed, MS is associated with a range of comorbid conditions, including diabetes, cardiovascular disease and overweight/obesity ^{2,5–7} These conditions can accelerate the rate of disease progression and can influence the

efficacy of disease-modifying drugs and rehabilitation.

Overweight and obesity represent common comorbid conditions in MS and might be associated with excessive rates of physical inactivity and sedentary behavior ^{7,8} An epidemiological study that investigated obesity and overweight as two important comorbidities in MS, reported that among an international sample of people with MS (pwMS) (2399 participants), 22.5% were overweight, 19.4% were obese. Moreover, overweight and obese pwMS reported more comorbidities associated with weight gain that included diabetes, high blood pressure and even depression ⁷ Another study investigated prevalence of overweight, obesity in veterans with MS and reported prevalence rates of 28% and 42.8% for overweight status in women and men, respectively, while the prevalence of obesity was 25% and 21.2% among women and men with MS ⁸ These and other studies ^{7–12} strongly demonstrate the prevalence

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of excess weight status in pwMS and these findings may be an important variable in the development and management of MS.

Recent observational studies have further reported that obesity, especially childhood obesity, is associated with an increased risk of MS^{9,11,12} In addition, high levels of obesity have been observed in MS onset in adults, and has been associated with a faster rate of disability progression^{13,14} For instance, a large study that investigated “association between comorbidity and clinical characteristics of MS” using the North American Research Committee on Multiple Sclerosis (NARCOMS) data reported that over 50% of the participants were obese or overweight at MS onset.¹³ Moreover, when the relationship between progressions of MS disability (measured by expanded disability status scale, EDSS) with body mass index (BMI) in 150 participants during 5 years was examined,¹⁴ logistic regression analysis observed that BMI at baseline is an important predictor of disability progression. In other words, the odds of having at least 1 unit increase in EDSS was 8 times greater in patients who were obese vs. normal weight.

Obesity and overweight status are common health-related factors in pwMS and might exert effects through comorbid conditions. Excessive weight gain is associated with increased insulin resistance, blood lipid issues, risk of heart attack, low-grade systemic inflammation, depression and other related risk factors (Table 1)^{8,11,15,16} Therefore, excessive weight gain may explain many of the detrimental MS effects (Table 1). For instance, a recent study reported that increased fat mass appears to be an important cardiovascular risk factor in pwMS¹⁷ The convergence of obesity and related pathologies can create a complex and challenging health problem for people who have the disease (i.e., MS)^{8,11} This supports the importance of identifying strategies for controlling and reducing body weight as important for both individuals at risk of developing MS and individuals with the condition.

Various strategies are available to reduce and control body weight; one of the most utilized and effective of these strategies is regular physical activity¹⁸ Currently, evidence supports that exercise is well tolerated in pwMS and is feasible. Moreover, it has been reported that exercise has many benefits for pwMS that include, improvement in CNS structure and function, physical fitness and disease modification^{2,6,19} In this paper, we will discuss research findings on exercise, physical activity and weight status in MS, and then focus on putative secondary benefits of exercise-induced weight loss for further examination in focal research. We will then provide a further recommendation for weight loss in patients with MS based on existing evidence and the American College of Sports Medicine (ACSM) guidelines. Finally, we will provide a section outlining future research directions.

Table 1

A general overview of MS and weight gain effect on immunological factors, adipokines, CNS characteristics, and markers associated with CVD risk response to MS and weight gain.

	MS	Weight gain	Ref
Demyelination	Increase	?	20,36
Inflammation	Increase	Increase	10,20
Neurotrophic Factor	Decrease	?	1
Leptin	Increase	Increase	20,42
Adiponectin	Decrease	Decrease	20
Resistin	?	Increase	42
Insulin Resistance	?	Increase	42
LDL	?	Increase	23,31,35
HDL	?	Decrease	23,31,36
TG	?	Increase	31,35,39
Brain Function	Decrease	?	2,60
Muscle Mass	Decrease	Decrease	63,64
Fitness	Decrease	Decrease	2,20
Fatigue	Increase	Increase	2,20
Depression	Increase	Increase	5,15

LDL: Low-density lipoprotein; HDL: High-density lipoprotein; TG: Triglyceride; MS: Multiple Sclerosis.

2. Primary benefit of physical activity and exercise for weight management

2.1. Body composition

Despite the importance of body composition and its variation in MS (Fig. 1), there are few studies that consider body composition indices as a primary or secondary end-point (Table 2). One study investigated the effects of a 6-month internet-delivered physical activity behavioral intervention on the body composition of 82 pwMS²⁰ The researchers reported that an Internet-delivered behavioral intervention resulted in higher levels of physical activity compared with a control group. However, there were no significant differences recorded between groups (intervention vs. control) on body composition indicators using adjusted alpha analysis for multiple comparisons. Importantly, there was a significant improvement in percent body fat and whole-body fat mass favoring the intervention condition when the analysis was unadjusted. Moreover, there was a significant intervention effect on whole-body bone mineral content and bone mineral density using unadjusted criteria values (Table 2). Further studies²¹ reported that 12 weeks of high-intensity concurrent training (i.e., interval and strength training) did not change total, fat and lean body mass, however, there were improvements in resting heart rate and insulin resistance.

There are several studies that have included body composition indicators as secondary end-point outcomes^{22,23} Some studies have reported that physical activity and exercise are an important factor in weight loss and control, especially when using long-term exercise training^{23–25} For instance, Schmidt and Wonneberger investigated the effects of an individualized 12 month endurance exercise regime in pwMS (normal and overweight) and reported that there was a significant decrease in body fat in both non-fatigue (fatigue severity scale, FSS < 4) and fatigue (FSS > 4) groups.²⁴ A further study that included 24 weeks of combined endurance and resistance exercise reported significant improvements in body composition, especially lean tissue mass.²³ Petajan and coworkers reported that a 15 week combined arm and leg ergometry exercise program resulted in a significant decrease in skinfold thickness and percent body fat, but not in body weight and lean body mass in pwMS with mild disability²⁶ Moghadasi and colleagues recruited adult women with MS (women with a combination of obesity and overweight) to study the effect of resistance training²⁷ They reported that weight, BMI, waist to hip ratio and fat mass, but not fat percentage and lean body mass improved following the intervention. Further, research²² investigated the effects of aerobic interval exercise training on women with MS who were overweight. The authors reported that both BMI and body fat percent significantly reduced following the exercise intervention. Some studies have reported no effect of exercise training on body composition. For example, White and coworkers investigated the effects of 8 weeks progressive resistance training in pwMS with EDSS between 1–5, and reported that indicators of body composition including body weight, BMI and body fat percentage remained unchanged after the training program.²⁸ In addition, a study by Castellano and coworkers investigating the effects of a short term (8 weeks) of aerobic cycling at 60% maximal oxygen uptake (VO_{2max}) in PwMS and matched healthy controls reported that there were no significant effects of exercise training on weight, BMI, waist-to-hip ratio, and body fat percent in either group²⁹ Various reasons can be used to explain the lack of exercise effects on body composition in these studies. Firstly, the short term of exercise intervention duration (> 3 months) that was used to influence body composition indicators. Secondly, training intensity limited by work capacity in pwMS can prevent adaptations to exercise training in pwMS. Thirdly, lack of exercise specificity aimed at influencing body composition and use of a wide range of outcomes as body composition indicators would both influence the observed results (Table 2). Finally, since most studies did not focus on body composition as a primary endpoint, they often did not use correct methodologies (i.e., dual-

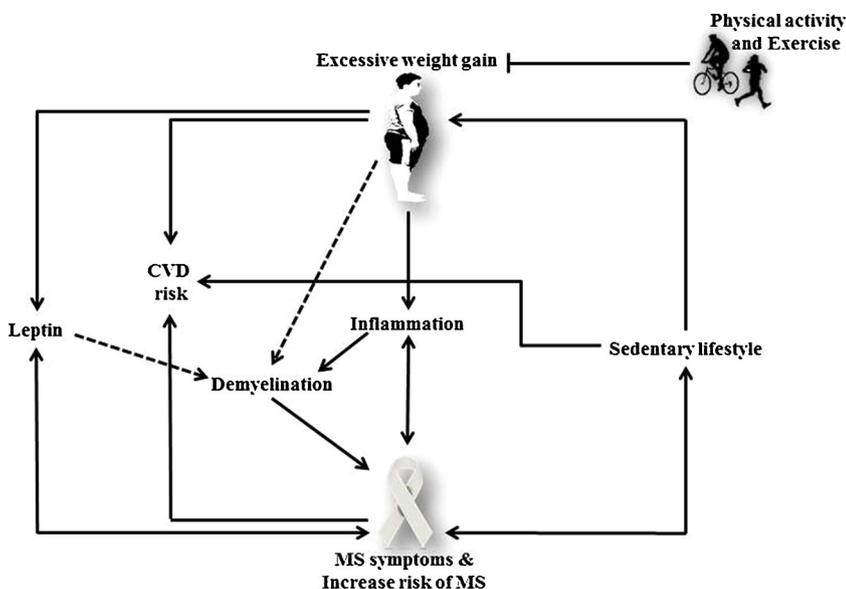


Fig. 1. Physical activity and exercise through weight control and coping with excessive weight gain can be helpful for MS. People with MS are commonly live inactively. The result of this lifestyle is gaining excessive weight, while overweight and obesity increase the risk of MS. Increased weight can exacerbate the symptoms of MS by exacerbate inflammation and increasing adipokines (i.e., leptin) production and concentration that play a pro-inflammatory role. Physical activity and exercise, besides having several benefits for people with MS, can help to losing and controlling weight in people with MS; therefore, it can help to managing disease course, therapy, well-being and preventing CVD risk. MS: Multiple sclerosis; CVD: Cardiovascular disease.

energy X-ray absorptiometry) to evaluate body composition, which reduces the accuracy and validity of the results.

In general, the existing evidence does not fully support a beneficial effect of exercise and physical activity for weight loss and management/control in patients with MS. This finding is partially based on body composition being included as a secondary end-point rather than the main focus of the studies examined. Future research should be designed to use body composition as the primary outcome, and focus on the change in a range of outcomes for quantifying the effect of exercise on body composition. It should be noted here that exercise training along with diet modification, can result in greater weight loss benefits³⁰ In addition, exercise has an effect on dietary habits (i.e., appetite and energy intake)³¹ and as a result, future studies should include and/or control the diet.

3. Secondary benefits of exercise induced weight loss and control

Although, there is no conclusive evidence for the role of exercise and physical activity for weight loss in pwMS, it is clear based on evidence from the general population, especially among overweight and obese persons, that exercise strategies (including dietary manipulations) are one of the most effective ways to achieve correct body weight status. In addition, weight loss with exercise has other important features that may be considered as secondary benefits of decreasing weight. Weight loss with exercise is characterized by increasing the amount of resting energy expenditure, reducing insulin resistance, reducing triglyceride levels, maintaining or increasing muscle mass and modifying the immune system (Fig. 1). In general, the benefits of weight loss with exercise can be divided in two main sections that include cardiovascular disease (CVD) risk factor improvement and benefits to the immune-adipokine system.

3.1. Cardiovascular risk factors

Excess weight is a primary determinant of CVD and other metabolic risk factors both in the general population and in people with MS. Moreover, it has been suggested that pwMS are more susceptible to CVD or other risk factors including metabolic syndrome and fat mass than healthy subjects^{17,32,33} Studies suggest that the prevalence of coronary heart disease is 11% among pwMS³⁴ and 15% of pwMS dying from CVD.³³ Recently, a systematic review written by Wens and coworkers indicated that dying from CVD risk and prevalence of CVD increased slightly in pwMS.³² The study reviewed 34 previous studies,

and it was reported that glucose intolerance, dyslipidemia and hypertension were the most prevalent CVD risk factors that were directly affected by obesity and body composition parameters. Several mechanisms can be used to explain the cause of the higher CVD risk in pwMS. Firstly, some commonly used MS treatments (i.e., corticosteroids) increase the risk and prevalence of CVD, and insulin resistance.³² Secondly, MS comorbidities such as sleep deprivation are other factors that enhances CVD and metabolic syndrome risk.^{32,35} Thirdly, deconditioning and inactive life styles increase the risk of CVD^{25,36} and puts pwMS at risk of weight gain and obesity that contribute to increased prevalence of CVD and mortality rates^{22,37,38}

The presence of a multitude of MS comorbidities (i.e., sleep deprivation), obesity and inactive life style leads to a worsening of the patient's CVD risk profile (Fig. 1). Removing some of the comorbidities, particularly inactivity, leads to improvements in the patient's body composition and cardiovascular status. Regular physical activity directly contributes to the cascade of events that restricts abdominal fat accumulation, decreases levels of triglyceride (TG) and low-density lipoproteins (LDL), increases levels of high-density lipoproteins (HDL) and reduces insulin resistance³² Therefore, regular physical activity can be considered as an important non-pharmacological therapy used for minimizing CVD risk in pwMS. Unfortunately, there are few studies that have examined the role of physical activity or exercise training as an effective intervention for CVD risk in MS. Wens and coworkers²⁵ examined the impact of 24-weeks of resistance and endurance training (mild to moderate workload corresponding to 12–14 ratings of perceived exertion) on factors related to CVD risk including glucose tolerance, lean tissue mass and body weight in 44 pwMS. Results demonstrated that exercise had no benefits on an oral glucose tolerance test. However, improved lean tissue mass was observed, with no changes in body weight and BMI. A further study by Wens and coworkers³⁶ reported that 12 weeks of a combination of high intensity resistance and endurance training improved oral glucose tolerance test results and muscle glucose transport 4 (GLUT4) content in pwMS in the absence of any changes in weight loss. Although, CVD risk studies in MS are limited, investigations relating to the benefits of exercise in healthy people explicitly confirm the positive role of exercise training.³⁹ Another limitation is that most studies have not studied specifically pwMS with obesity to determine the effects of exercise in this population. Petajan and coworkers reported that long term aerobic exercise (15 weeks) significantly reduced TG, but cholesterol, HDL, and LDL did not change significantly.²⁶ White and coworker⁴⁰ reported that lower-extremity progressive resistance-training reduced a coronary artery

Table 2
Summary of training program characteristics and the results of some studies.

First author (Year)	BMI at baseline (kg/m ²)	Modality	Duration	Frequency	Intensity	Session duration (min)	Results
Keytsman (2017)	23.5 ± 3.3	high-intense concurrent training	12 weeks	5 per 2 weeks	85–100% HR _{max}	–	Weight: unchanged; Fat mass: unchanged; Lean body mass: unchanged; Fat percentage: unchanged
Pilutti (2014)	I: 27.9 ± 7.7 C: 27.6 ± 6.4	Internet-delivered physical activity behavioral intervention	24 weeks	–	–	–	BMI: unchanged; PBF: ↓; BMC: ↑; BMD: ↑
Mokhtarzade (2017)	I: 27.08 ± 2.49 C: 26.21 ± 1.67	Aerobic cycling	8 weeks	3 per week	60–75% W _{max}	42–66	BMI: ↓; Weight: ↓; PBF: ↓
Wens (2016)	NR	Combined training	24 weeks	5 per 2 weeks	12–14 RPE	45–75	Weight: unchanged; Fat mass: unchanged
Schmidt (2014)	24.7 ± 4.2	Endurance training	52 weeks	3 per week	65–70% HR _{peak}	30	Weight: unchanged; PBF: ↓
Wens (2015)	I: 22.6 ± 0.9 C: 22.9 ± 1.3	Combined training	24 weeks	5 per 2 weeks	12–14 RPE	45–75	Weight: unchanged; Lean tissue mass: ↑
Petajan (1996)	NR	Leg and arm cycling	15 week	3 per week	60% VO _{2max}	40	Weight: unchanged; PBF: unchanged; skinfold thickness: ↓
Moghadasi (2015)	I: 25.8 ± 6.5 C: 25.3 ± 4.9	Resistance training	8 weeks	3 per week	NR	NR	Weight: ↓; BMI: ↓; PBF: ↓;
White (2004)	27 ± 6	Resistance training	8 weeks	2 per week	50–70% MVC	30	Weight: unchanged; BMI: unchanged; PBF: unchanged
Castellano (2008)	24 ± 4	Aerobic cycling	8 weeks	3 per week	60% VO _{2peak}	30	Weight: unchanged; BMI: unchanged; WHR: unchanged
Mokhtarzade (2018)	20–30	Aerobic cycling	8 weeks	3 per week	60–75% W _{max}	42–66	BMI: unchanged; Weight: unchanged

I: intervention; C: control; W_{max}: maximum watt; RPE: rating of perceived exertion; VO_{2max}: maximum rate of oxygen consumption; VO_{2peak}: peak rate of oxygen consumption; MVC: maximal voluntary contraction; HR_{max}: maximal heart rate; BMI: body mass index; PBF: percentage of body fat; BMC: bone mineral content; BMD: bone mineral density; ↓: significant decrease; ↑: significant increase.

disease risk factor (i.e., TG level) in women with MS. Furthermore, Slawta and coworkers⁴¹ reported that women with MS who participated in low- to moderate-intensity leisure-time physical activity had lower coronary heart disease risk factors, smaller waist circumferences, TG, and glucose levels. The authors concluded that physical activity can protect pwMS from coronary heart disease and contribute to important health-related benefits.

3.2. Immune and adipokine markers

In recent years, many studies have been conducted to explain the upstream mechanisms of inflammation. Numerous studies suggested that inflammation occurs as a consequence of weight gain, and the production and development of inflammation plays an important role in increasing CVD risk, including insulin resistance, glucose intolerance, dyslipidemia, and hypertension^{42,43}. Interestingly, obesity-induced inflammation is unique compared to other recorded inflammatory paradigms that involve tonic activation of the immune system. This may be related to the fact that obesity-induced inflammation is related to multiple organs, that include adipose tissue, heart, skeletal muscle and the brain⁴². Therefore, obesity-induced inflammation has some features that are challenging to control and difficult to treat in pwMS. This may help explain why some treatments and drugs have little effect in pwMS. We have previously demonstrated in our lab that in the absence of weight loss, there were no positive effects from exercise training on inflammation markers including IL-10 and TNF-α in pwMS. Therefore, it is rational to consider weight loss in pwMS with obesity as a treatment priority. However, further comprehensive studies are required to confirm this theory.

The precise mediators of obesity-induced inflammation are poorly understood. The production of adipokines and cytokines from adipocytes is one of the most popular mechanisms involved in cellular cross talk in MS^{42,44}. In addition, the secretion of pro-inflammatory cytokines, including interleukin (IL)-6 and tumour necrosis factor (TNF)-α, especially from visceral fat, increases along with weight gain; unlike, anti-inflammatory mediators (i.e., IL-1B) are downregulated⁴³. Therefore, obesity stimulates inflammation and contributes to the initiation and progression of MS.

Previously, it has been reported that some adipokines including leptin and resistin increase in MS, however, adiponectin and visfatin decrease compared to healthy individuals^{45,46}. Leptin as an inflammatory mediator can be upregulated by pro-inflammatory cytokines (i.e., TNF-α and IL-6), which results in immune response modulation^{45,47}. Furthermore, peripheral leptin concentration is closely associated with weight gain⁴⁸. Therefore, in addition to weight gain, resting levels of leptin increase and are able to shift T cell balance thereby increasing the Thelper1/Thelper2 balance (observed in MS), which induces an inflammatory state^{44,45}.

Studies have not been limited to the role of leptin in MS, they have also shown that adiponectin, as an adipokine is involved in metabolic diseases^{44,49}. Interestingly, Piccio and coworkers⁵⁰ studied the role of adiponectin in an animal model of MS (experimental autoimmune encephalomyelitis, EAE). They observed higher CNS inflammation, demyelination, and axonal injury in adiponectin deficient mice in addition to higher production of TNF-α, IL-17 and IL-6. Piccio and coworkers⁵⁰ concluded that adiponectin has a pivotal role in MS severity.

The controlling of mass and phenotype fatty tissue is an effective approach to regulate adipokines and their underlying pathways (Fig. 1). Our recent review observed that research regarding the effects of exercise training on adipokines and cytokines in pwMS is in its infancy⁵¹. We are aware of only three original investigations that studied the effects of exercise intervention on adipokines in pwMS. Our research observed that the level of leptin reduced only in the relapse phase of MS after exercise. Other inflammatory mediators (adiponectin, TNF-α, IL-10 and IL-6) observed similar responses in the relapsing and remitting

phase of MS compared to both healthy and control subjects⁵² We concluded that exercise in relapse can be considered as a complementary therapy during the relapse phase, however, further study is needed to confirm this observation. We have also previously demonstrated that 8-weeks of interval exercise training (upper and lower cycling with 60–75% maximal power) decreased leptin and TNF- α levels but increased adiponectin levels in women with MS. Moreover, the leptin to adiponectin ratio decreased.²² A further study that used 10-weeks of vibration exercise found that leptin and gerlin did not change in PwMS.⁵³ Failure to see significant change in this recent study may result from the nature and intensity of the vibration training. Furthermore, in this study,⁵³ body composition indicators did not significantly change, while in our investigation,²² leptin and adiponectin significantly decreased and increased, respectively. Moreover, we observed that leptin and adiponectin changes had strong positive and negative correlations with changes in body composition indicators, respectively.²² In fact, this study²² emphasized the importance of weight loss for improving adipokine status. However in this study,²² only BMI and bodyweight were used as body composition indicators, and BMI underestimates adipose tissue in MS⁵⁴ Therefore, the use of more reliable tools and methods to elevate body composition can enhance our understanding of body composition changes in MS.

Additional research⁵⁵ indicated that in the absence of weight loss, overweight MS subjects did not show any significant improvement in cytokine concentrations. The main limitation of the previous studies is the lack of a control group that is obese or overweight. Some of the studies have used an intervention group with a wide range of BMI's or a combination from different body types (i.e., normal and obese)^{22,29,56,57}

4. Skeletal muscle mass importance

Fat mass is not the only important consideration during weight loss, in fact, skeletal muscle mass is another important measurement. Skeletal muscle (all skeletal muscles) is one of the heaviest organs in the body and is classified as one of the largest consumer tissues^{58,59} Consequently, many of the circulatory substrates, such as glucose and lipids, are consumed by skeletal muscle and therefore, this helps to reduce CVD and mortality risk. Over recent years, science has demonstrated the benefits of exercise on skeletal muscle. Skeletal muscle is considered as an endocrine organ that is able to produce and secrete important myokines, such as irisin and IL-6^{60,61} Therefore, skeletal muscle is one of the most effective organs for regulating adipose tissue and immune system status (Fig. 2). Recent research has gone further, suggesting that exercising skeletal muscle can have positive effects on the brain^{62,63} Interestingly, strong evidence suggests that skeletal muscle is also able to produce neurotrophic factors that include brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF)^{61,64} In addition, a strong relationship has been observed between enhancing skeletal muscle mass and function with improvements in fatigue, depression, risk of falling and cognitive performance.^{59,65,66} All these benefits emphasize the importance of muscle mass maintenance (Fig. 2).

Data has indicated that 12 weeks of high intensity interval cycling increased mean fiber, type II and IIa CSA of the *Vastus medialis* muscle while body fat percentage tended to decrease.⁶⁵ Another study by Dalgas and coworkers⁶⁶ used progressive resistance training as one of the most effective modalities for skeletal muscle hypertrophy and reported an increase in mean and type II CSA of *Vastus lateralis* in pwMS. Alternatively, exercise training helps maintain skeletal muscle mass and associated hypertrophy, decrease intramuscular adipose tissue content and induce changes in the body composition phenotype of pwMS.

5. Recommendations for the application of exercise

There are currently no guidelines or recommendations for exercise

training or physical activity for weight loss, and/or controlling or preventing weight gain in MS; but there are guidelines for exercise for patients with MS for other benefits. The first guideline⁶⁷ recommends the application of different modalities of exercise including resistance, endurance and combined training based on the beneficial effects of exercise training in pwMS (with a focus on fitness, muscle strength and endurance and psychological parameters). For endurance training, 2–3 sessions per week, 50–70% VO_{2max} , 10–40 min duration for each session in the initial months, was recommended. Resistance training with moderate intensity, 8–15 repetitions, 1–4 sets and 4–8 exercises in each session (2–3 day per week) was also recommended. Finally, combined training based on equal proportions of resistance (2 day per week) and endurance (2 day per week) exercise separated by a rest interval of 24–48 h was recommended. A further gridline after reviewing the effects of exercise training on fitness, mobility, fatigue and health-related quality of life in pwMS recommended that moderate intensity exercise, 2 days per week for adult pwMS with mild to moderate disability for improving fitness in health-related indicators in pwMS⁶⁸ Based on previous data^{18,69–72} 150–250 min per week moderate physical activity (energy expenditure ~ 1200–2000 kcal per week) is required for modest weight loss (2–3 kg) and to prevent further weight gain. Furthermore, for higher weight loss (5–7.5 kg), 225–420 min per week moderate physical activity is required. Although, both mentioned guidelines^{67,68} were based on many benefits for pwMS, but given the number of sessions per week (2 or 3 sessions per week) and the duration of each session (< 40 min), these guidelines do not appear to be able to meet the required amount of energy expended. As a result, it seems unlikely that these guidelines^{67,68} would be suitable for weight management in pwMS. This suggests the importance of designing and considering new guidelines for weight control in MS that might yield appropriate caloric expenditure. The most comprehensive weight loss and controlling guidelines are outlined in the ACSM Position Statement.^{18,70} They recommended that 1) at least 150 min per week of moderate intensity physical activity is needed to prevent weight gain, and decrease chronic disease risk factors, 2) 150–250 min per week (approximate 1200–2000 kcal per week) of moderate intensity physical activity is needed to prevent weight gain greater than 3% and is associated with modest weight loss, and 3) approximate 250–300 min per week (approximate 2000 kcal per week) of moderate intensity physical activity is needed for greater weight loss and prevention of weight regain^{18,70} It should be noted that the energetic cost of exercise/walking is elevated in MS,⁷³ and thus probably more energy would be expended in MS than controls for a given bout of exercise. This might support the notion that slightly less physical activity could yield similar effects on weight control and loss, or that meeting the ACSM guidelines could have a larger effect in pwMS with low to moderate disability.

6. Conclusion

In general, one of the most important and effective approaches in weight management is an active lifestyle and increasing physical activity. However, there is no evidence-based guidelines regarding a comprehensive and accurate exercise program for weight management in MS, and previous exercise guidelines do not appear to be able to meet the required amount of energy expenditure for this population. It seems that weight management guidelines recommended by the ACSM that include 150–250 and 225–420 min per week moderate physical activity is suitable for pwMS in preventing weight gain and weight loss, respectively. However, further studies are required for the definitive acceptance or suggestions of a more suitable guideline for exercise prescription in patients with MS.

Conflict of interest

All authors report no disclosures.

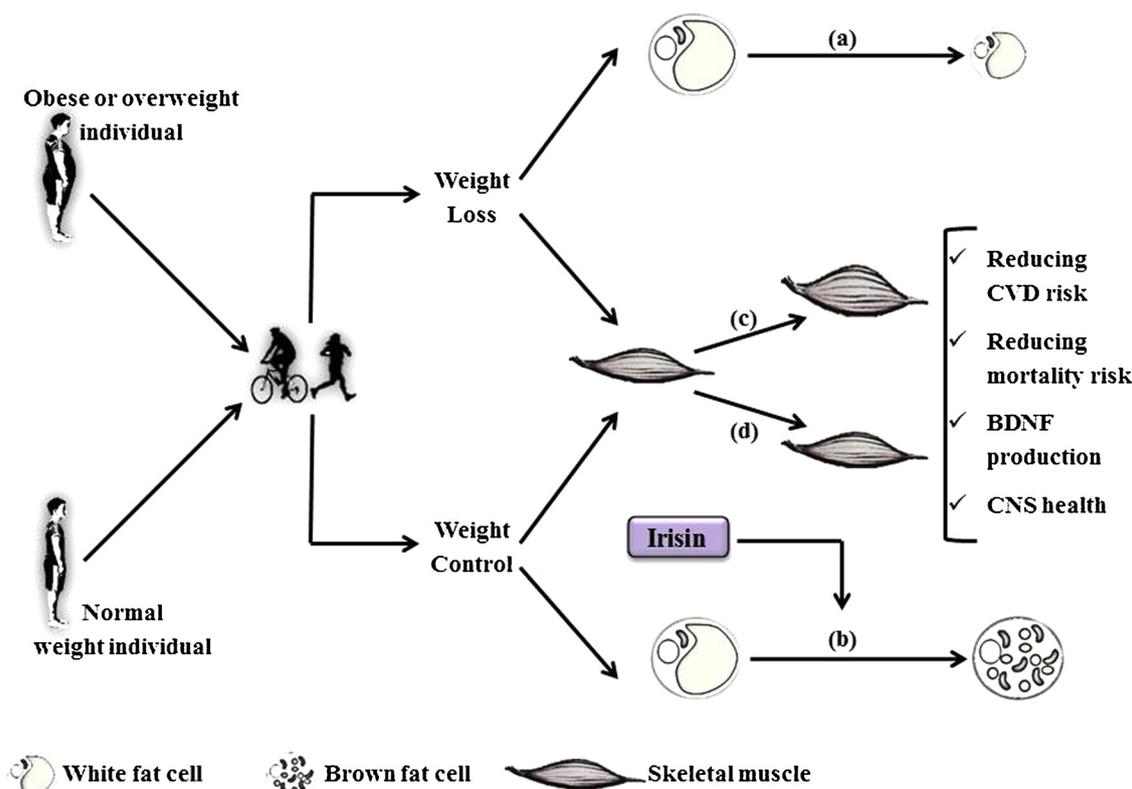


Fig. 2. Importance of exercise and physical activity on skeletal muscle mass and function. Physical activity and exercise can be designed for weight loss and control in obese or health people, respectively. From the perspective of fat tissue, exercise can reduce the size of the fat cell (a) which often seen in obese and overweight people, and shift the white fat cell phenotype to the brown fat cell (b).⁶¹ Brown fat cell are characterized by consuming more energy and high mitochondria density. One of the most important mechanisms influence body expenditure and fat cell phenotype is relate to the Irisin that release from skeletal muscle.⁶¹ Exercise can lead to skeletal muscle hypertrophy (c) or increase skeletal muscle performance (d), resulting in the improvement of many health-related indicators such as reducing mortality, CVD risks, producing BDNF, increasing CNS health, and etc.^{62,63,65} Therefore, weight control and coping with excessive weight gain through physical activity and exercise can be helpful for pwMS through these mechanisms.

CVD: Cardiovascular disease; BDNF: Brain-derived neurotrophic factor; CNS: Central nervous system.

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