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Part G. Section 4: Energy Balance

Introduction

Overweight and obesity are linked to increased risk of morbidity from hypertension, dyslipidemia, type 2 diabetes, coronary heart disease, stroke, gallbladder disease, osteoarthritis, sleep apnea and respiratory problems, and endometrial, postmenopausal breast, prostate, and other cancers (1;2). In addition, obesity is associated with excess overall mortality (3). Unfortunately, the prevalence of overweight and obesity has increased dramatically over the past 20 years in the United States to 70.8% and 31.1% for adult men, and 61.8% and 33.2% for adult women, respectively (4). This increase has been attributed to changes in environment and lifestyle factors because the escalating prevalence has been occurring in a constant genetic milieu. The focus in this chapter is on the role that physical activity plays in energy balance.

Review of the Science

Overview of Questions Addressed

This chapter addresses 5 major questions related to physical activity and energy balance.

1. How much physical activity is needed for weight stability and weight loss?
2. How much physical activity is needed to prevent weight regain in previously overweight individuals?
3. What is the effect of physical activity on body composition parameters (e.g., waist circumference, intra-abdominal fat, abdominal obesity, total body fat) that are related specifically to metabolic disorders?
4. What effects do sex and age have on the role of physical activity in energy balance?
5. How do the physical activity requirements for weight maintenance differ across racial/ethnic and socioeconomic groups?

Data Sources and Process Used to Answer Questions

The Energy Balance subcommittee used the *Physical Activity Guidelines for Americans* Scientific Database as its primary source for each question (see **Part F. Scientific Literature Search Methodology**, for a complete description of the Database). It also used other

databases, reviews, and meta-analyses to obtain evidence bearing on each question. Specific search strategies are described for each question.

Caveats

Four points need to be mentioned at the outset of this chapter on physical activity and energy balance. First, in contrast to outcomes addressed in other chapters, in which physical activity can be discussed as the primary variable affecting the outcome, achieving energy balance is dependent on both energy intake and energy expenditure. With the availability of inexpensive and easily accessed high-calorie, highly palatable foods, it is far easier to increase energy intake than to increase energy expenditure in our society. In support, the 2005 Dietary Guidelines Advisory Committee Report (5) indicated that most Americans are consuming energy in excess of energy needs, and it is not likely to change in the near future. Consequently, final recommendations related to the level of physical activity needed for weight maintenance, weight loss, or prevention of weight regain after weight loss must consider energy intake issues as well.

Second, when a caloric deficit induced by exercise is compared with an equivalent caloric deficit created by a reduction in caloric intake, there is little or no difference in weight loss (6). However, in many weight loss studies, the proportion of the caloric deficit due to physical activity is only a small fraction of the overall caloric deficit, and consequently, the contribution that physical activity makes to weight loss is relatively small. This must be remembered as we address the role of physical activity **alone** on weight-related issues.

Third, secular trends have increased the use of automation and labor-saving devices on the job, at home and in the community and increased passive leisure-time physical activity (e.g., TV/VCR, computer use). These trends influence the amount of physical activity needed to achieve energy balance.

Finally, if we did not have an overweight and obesity problem in our society, we would still need a physical activity recommendation to maintain health and prevent disease. That simple message is lost on many who focus solely on the role of physical activity in preventing overweight and obesity. Consequently, the level of physical activity needed to maintain health and prevent disease is the baseline for any physical activity recommendation for energy balance.

Question 1: How Much Physical Activity Is Needed for Weight Stability and Weight Loss?

Conclusions

All study designs provide clear evidence of a dose-response relation between physical activity and weight loss. However, few data are available on weight stability over the long term. Available data on weight stability are from short-term clinical trials. Based on these

trials, a dose of physical activity in the range of 13 to 26 MET-hours per week resulted in a modest 1% to 3% weight loss, consistent with weight stability over time (7-9). Thirteen MET-hours per week is equivalent to walking at a 4 mile per hour pace for 150 minutes per week or jogging at a 6 mile per hour pace for 75 minutes per week. The magnitude of weight loss resulting from studies of resistance exercise is typically less than 1 kilogram (2.2 pounds). However, this result may be affected by the relatively short duration of these studies and gains in fat-free mass that accompany such interventions. In contrast, it is clear that if one wants to achieve weight loss (i.e., more than 5% decrease in body weight), a dietary intervention also is needed. The dietary intervention could include either a maintenance of baseline caloric intake, or a reduction in caloric intake to accompany the physical activity intervention. The magnitude of change in weight due to physical activity is additive to that associated with caloric restriction.

Definitions

To aid in the study of patterns of weight change, the scientific literature has operationally defined the concept of weight stability. St. Jeor and colleagues (10) define weight stability as a change of 2.3 kilograms (5 pounds) or less of initial body weight. In this study, participants' weights were monitored over a period of time using this criterion. It was determined that 62%, 52%, 49%, and 46% of participants were classified as maintaining their body weight at 1, 2, 3, and 4 years of follow-up, respectively. The Pound of Prevention Study also defined weight maintenance as a change of 2.3 kilograms (5 pounds) or less (11) of initial body weight. When examined over a 3-year period, 40% of men and 38% of women were classified as "maintainers," with a mean weight change of 0.3 kilograms (0.7 pounds) and 0.2 kilograms (0.4 pounds), respectively. Moreover, across the entire sample of 957 individuals, the mean weight gain over a 3-year period was 1.7 kilograms (3.7 pounds) for men and 1.8 kilograms (4 pounds) for women. This would suggest that the mean weight gain across the population may be approximately 0.6 kilograms (1.3 pounds) per year.

More recently, Stevens and colleagues (12) have recommended that weight maintenance be defined as less than a 3% change in body weight. Moreover, they recommended that a change in body weight of 3% to less than 5% of initial weight be considered as small fluctuations in body weight, and a change of 5% or more of body weight be considered clinically significant. Considering these standards, an obese individual weighing 91 kilograms (200 pounds) would need to reduce body weight by 4.5 kilograms (10 pounds) to have a significant weight loss, and a weight change of 2.7 kilograms (6 pounds) would be considered weight stability. These standards should be considered when evaluating the effect of physical activity on body weight change to determine whether various doses and modes of physical activity result in weight stability or clinically relevant weight loss.

Rationale

A search of the *Physical Activity Guidelines for Americans* Scientific Database identified 126 research articles on the effect of physical activity on weight loss and weight stability. Additionally, pertinent reviews available through a MEDLINE search were considered.

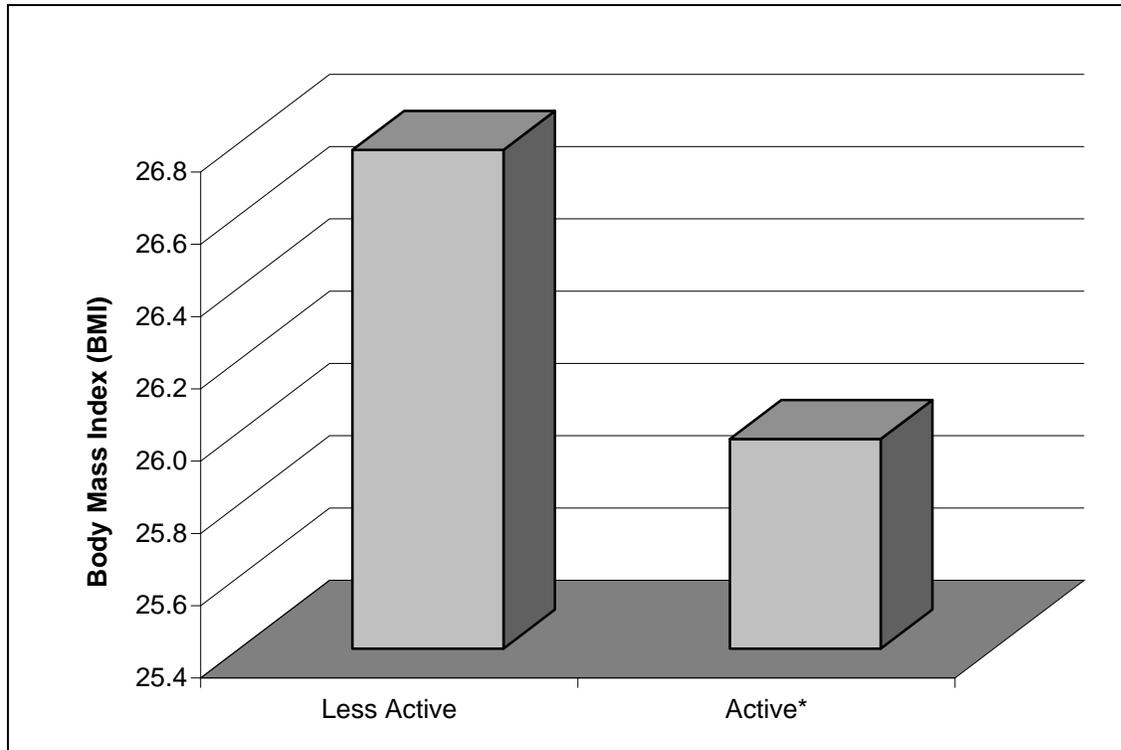
Cross-Sectional Studies

Twenty-four cross-sectional studies were identified that examined the association between physical activity and body weight. Of these 24 studies, 23 reported results suggesting an inverse relationship between physical activity and body weight and/or body mass index (BMI) (13-35). These studies tended to illustrate a dose-response relationship between physical activity and body weight or BMI. For example, Giovannucci and colleagues (14) reported that when 0.9, 4.8, 11.3, 22.6, and 46.8 MET-hours per week were used to define quintiles of physical activity, corresponding BMI values were 25.4, 25.3, 25.1, 24.7, and 24.4 kg/m², respectively. More recently, Kavouras and colleagues (15) reported that individuals participating in physical activity that is consistent with the current consensus public health recommendations of at least 30 minutes per day on 5 days a week had a significantly lower BMI (25.9 kg/m²) when compared to the BMI (26.7 kg/m²) of less active individuals (Figure G4.1). Thus, based on these findings, it appears that levels of physical activity that are consistent with a range of 30 to 60 minutes per day on at least 5 days per week (150 to 300 minutes per week) is sufficient to maintain and/or significantly reduce body weight.

Prospective Studies

Nine prospective studies were identified that reported on the benefits of physical activity to prevent weight gain and/or result in weight loss (36-44). Three studies, which had a follow-up period of 1 to 3 years, all reported a favorable association between physical activity and weight-related outcomes (36;37;39). The remaining 6 studies, which had a follow-up period of 6.5 years or greater, also reported a favorable association between physical activity and weight-related outcomes (38;40-44). Berk and colleagues (43) found that individuals who initially reported less than 60 minutes per week of physical activity and increased to 134 minutes per week of physical activity had an increase in BMI of 0.4 kg/m² across a 16-year follow-up period, but this was not significantly different from the 0.9kg/m² increase observed for individuals who remained sedentary (less than 60 minutes per week) at both assessment periods. These data suggest that less than 150 minutes per week of physical activity will result in a non-significant blunting of weight gain compared to individuals who remain sedentary. However, individuals who were classified as active at both assessment periods were participating in 261 minutes per week of physical activity, and had a significantly smaller change in BMI compared to individuals who were initially active (more than 60 minutes per week) at baseline but became inactive at follow-up (less than 60 minutes per week). This supports the need to maintain a physically activity lifestyle to manage body weight long-term.

Figure G4.1. Differences in Body Mass Index Due to Level of Physical Activity



*Active is defined as the consensus public health recommendation for physical activity (3 or more days per week of 20 minutes per day at vigorous intensity or 5 or more days per week of 30 minutes per day at moderate intensity). Source: Adapted from Kavouras and colleagues, 2007 (15).

Figure G4.1. Data Points

	Less Active	Active*
BMI	26.7	25.9

Randomized Trials

Endurance Exercise

Twenty studies were identified that examined the effect of endurance exercise on body weight. However, 7 studies were not reviewed due to the intent of the study to focus on marathon training, a dietary intervention to counter or enhance the weight loss effects of exercise, the inclusion of only subjects with serious psychiatric disabilities, the lack of a consistent training paradigm across the observation period, or the exercise volume not expressed in as minutes per week. The remaining 13 studies were reviewed in greater detail. Twelve used a randomized design, although 3 of them did not have a control group and/or the physical activity was in addition to a dietary intervention (45-47), and 1 used a non-randomized design to examine the effect of physical activity but did not include a comparison group (48). In addition, the primary purpose of 5 of the studies was on

something other than weight loss (49-53). The remaining 4 studies (7-9;54) had sufficient statistical power to evaluate the effect of physical activity on body weight and body composition.

These studies ranged in duration from 8 to 16 months, and physical activity level ranged from 180 minutes of moderate-intensity physical activity per week to 360 minutes of moderate- to vigorous-intensity physical activity per week. In addition, one study (9) evaluated 3 levels of physical activity, and 2 (7;8) established, post hoc, tertiles of physical activity participation (adherence) based on activity logs and/or pedometer records to evaluate a dose-response pattern. Typical weight losses were 1 to 3 kilograms (2.2 to 6.6 pounds), which corresponded to less than 3% change in body weight, but evidence of a dose-response relationship was clear, with those doing the greatest amount of physical activity achieving weight losses of 4% to 6% (the latter associated with an energy expenditure of 668 kcal per session, 5 days per week). A dose of physical activity in the range of 13 to 26 MET-hours per week resulted in a modest 1% to 3% weight loss, consistent with weight stability over time.

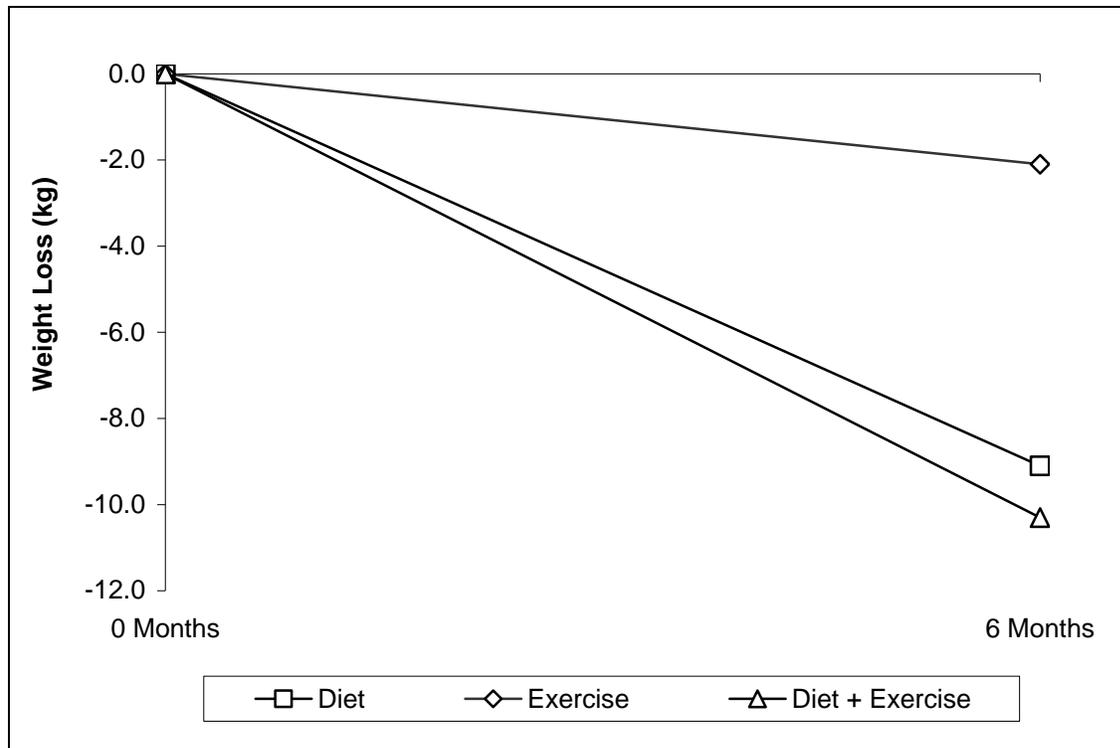
Resistance Exercise

An alternative form of physical activity is resistance exercise. Ten studies were reviewed that examined the impact of this form of exercise on change in body weight, and all of these studies showed a modest reduction (less than 1 kilogram) or a non-significant change in body weight (55-64). This finding of a modest impact of resistance exercise on body weight was confirmed in a literature review (65). A potential explanation for this lack of a reduction in body weight is that many of these studies reported an increase in fat-free mass resulting from resistance exercise training, which resulted in a reduction in percent body fat, but did not change absolute body weight or fat mass. Thus, changes in body composition may be a desirable outcome to examine when determining the effect of resistance exercise on body weight parameters. However, the lack of a sufficient dose of physical activity to elicit a significant energy deficit may also explain these findings, as many of these studies were relatively short in duration and included only 2 to 3 days per week of resistance exercise.

Five studies from the *Physical Activity Guidelines for Americans* Scientific Database examined the combination of endurance and resistance exercise on change in body weight. Two studies used randomized designs to assign participants to a physical activity group or a control group (66;67), 1 used a randomized cross-over design involving 8 weeks of physical activity and 8 weeks of no physical activity (68), and 2 examined the effect of physical activity but did not include a control group (69;70). Four of these studies reported no effect of combined endurance plus resistance exercise on change in body weight (66-69), and 1 study that did not include a control group (70) reported a significant effect. A potential limitation of these studies is that they ranged from 8 to 10 weeks in duration, which may have been too short a time to significantly affect body weight.

In general, regular participation in moderate-to-vigorous physical activity is associated with weight maintenance over time. In contrast, it is clear that if one wants to achieve clinically relevant weight loss (a decrease of 5% or more in body weight), a dietary intervention is usually needed. This is shown clearly in Figure G4.2, adapted from Wing, 1999 (71).

Figure G4.2. Weight Loss Related to a Diet Intervention, an Exercise Intervention, and a Diet + Exercise Intervention



Source: Adapted from Wing, 1999 (71)

Figure G4.2. Data Points—Weight Loss in kg

	0 Months	6 Months
Diet	0	-9.1
Exercise	0	-2.1
Diet + Exercise	0	-10.3

The magnitude of weight loss due to physical activity is additive to caloric restriction, but physical activity is generally insufficient by itself to bring about clinically significant weight loss. Consistent with this, McTiernan and colleagues (8) estimated that the physical activity intervention in their study should have produced a weight loss of 7.8 kilograms, rather than the 1.4 kilograms (women) and 1.8 kilograms (men) observed, **if caloric intake had remained stable**. Further, studies in which the caloric intake was held constant (by design) from baseline showed that the weight loss associated with the physical activity intervention

was what one would predict from the physical activity energy expenditure (6). Consequently, the addition of a dietary restraint **to not increase caloric intake** may have resulted in clinically significant weight loss, rather than just weight stability with the physical activity intervention mentioned above. The magnitude of weight loss reported in these studies is consistent with earlier reviews on this topic by Wing (71) and the Expert Panel of Clinical Guidelines for the Treatment of Obesity (1).

Question 2. How Much Physical Activity Is Needed to Prevent Weight Regain in Previously Overweight Individuals?

Conclusions

Most of the available literature indicates that “more is better” when it comes to the amount of physical activity needed to prevent weight regain following weight loss. However, the literature has some considerable shortcomings regarding the appropriate research design needed to directly address this question. Given these limitations, the estimated gross energy expenditure needed to achieve weight maintenance following substantial weight loss is about 31 kilocalories per kilogram week or $4.4 \text{ kcal}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$, which is equivalent to walking 54 minutes per day at a 4 mile per hour pace, walking 80 minutes per day at a 3 mile per hour pace, or jogging 26 minutes per day at a 6 mile per hour pace (72-74).

Rationale

Initial references were obtained with a search of the *Physical Activity Guidelines for Americans* Scientific Database. Key words included adults, exercise, physical activity, obesity, adiposity, weight, and BMI. Eight systematic reviews or meta-analyses also were reviewed for pertinent references. Studies that investigated special populations (e.g., physically disabled), included individuals with a disease known to affect weight (e.g., cancer), or weight loss drugs, were excluded. To be included, studies had to target a period of weight loss followed by a period of weight maintenance using physical activity as the strategy for preventing weight regain.

Eight randomized trials met the above criteria and were used for this review. Of the eight studies, only three had a design in which participants were randomized after weight loss and only two used a control group. Three observational or prospective cohort studies were identified that met the above criteria and were used for this review. Four position papers or reports also were used as references.

It is generally accepted that individuals can lose weight but most cannot maintain significant weight loss. Because it has an energy equivalent, physical activity is universally promoted as a necessary component of strategies to maintain weight loss (1;75;76). Indeed, physical activity is often cited as the best predictor of weight maintenance after weight loss (77;78). A systematic review of physical activity to prevent weight regain subsequent to weight loss was completed by Fogelholm and Kukkonen-Harjula (79). The majority of studies included

in this review were observational studies and studies of individuals who were randomized at baseline to exercise or no exercise, or to different levels of physical activity. Follow-up varied from several months to several years and generally showed that individuals who engaged in exercise experienced less regain than those individuals who did not, and those individuals who engaged in greater amounts of physical activity experienced less regain than those who did more moderate levels. Only 3 studies used a design in which individuals were randomized to physical activity after weight loss (80-82), and the results were inconsistent, showing that physical activity had an indifferent, negative, or positive effect on prevention of weight regain.

Despite the accepted concept that physical activity is necessary for successful weight maintenance after weight loss, the amount that is needed remains uncertain. The 1995 Centers for Disease Control/American College of Sports Medicine (CDC/ACSM) recommendations for physical activity specified the accumulation of 30 minutes of moderate-intensity physical activity for most days of the week (83). These guidelines were provided for health promotion and disease prevention. However, they were widely interpreted to also be useful for weight management. Minimum levels of 150 minutes per week (30 minutes per day, 5 days a week) of moderate-intensity physical activity were also recommended by the ACSM Position Stand for “Appropriate Intervention Strategies for Weight Loss and Prevention of Weight Regain for Adults” (75). However, recent evidence suggests that greater levels of physical activity may be necessary to prevent weight regain after weight loss. For example, individuals in the National Weight Control Registry who have maintained weight loss have shown levels of energy expenditure equivalent to walking about 28 miles a week (77). Schoeller and colleagues (74) used doubly-labeled water to study women who recently lost 23 ± 9 kilograms of weight in order to estimate the energy expenditure needed to prevent weight regain. Retrospective analyses of these data were performed to determine the level of physical activity that provided maximum differentiation between gainers and maintainers. Based on these analyses, it was determined that individuals would need to expend about 4.4 kilocalories per kilogram per day in physical activity (which is equivalent to about 80 minutes per day of moderate-intensity physical activity or 35 minutes per day of vigorous physical activity) to prevent weight regain.

Jakicic and colleagues (73;84) and Andersen and colleagues (85) provided data from randomized trials showing that individuals who performed large amounts of physical activity maintained weight loss better at follow-up of 18 months, 12 months, and 12 months, respectively, than did those doing smaller amounts of physical activity. In particular, Jakicic and colleagues (73;84) showed very little weight regain in individuals who performed more than 200 minutes per week of moderate-intensity physical activity. Ewbank and colleagues (72) also found similar results 2 years after weight loss by very-low-energy diet. Retrospectively grouping participants by levels of self-reported physical activity, individuals who reported greater levels (i.e., walking about 16 miles per week,) had significantly less weight regain than individuals reporting less physical activity per week (4.8 to 9.1 miles per week). However, it is important to note that individuals in all 3 studies above were grouped into physical activity categories retrospectively and were not randomly assigned to those

groups after weight loss. Thus, the amount of physical activity was self-selected and therefore does not provide clear evidence for the amount needed to prevent weight regain.

To explore the effects of levels of physical activity greater than those normally recommended in weight management programs, Jeffery and colleagues (86), targeted energy expenditures of 1,000 kilocalories per week and 2,500 kilocalories per week for 18 months in 2 groups of participants; these levels were randomly assigned at baseline. The actual reported energy expenditure at 18 months was $1,629 \pm 1,483$ and $2,317 \pm 1,854$ kilocalories per week for the 1,000 and 2,500 kilocalories per week groups, respectively. At 6 months, weight loss did not differ between the groups, but there were significant differences at 12 and 18 months (weight maintenance) follow-up, with the 2,500 kilocalories per week group showing significantly greater weight losses (6.7 ± 8.1 kilograms versus 4.1 ± 8.3 kilograms). The energy equivalent for walking for the 2,500 kilocalories per week group and 1,000 kilocalories per week group was about 3.3 miles per day and about 2.3 miles per day, respectively. This study showed that greater levels of physical activity resulted in significantly lower levels of weight regain. However, the results must be interpreted with caution, as the percentage of individuals meeting the targeted energy expenditure varied greatly, and the behavioral interventions were not equal.

In general, large volumes of physical activity are needed to prevent weight regain in those who have lost a great deal of weight. Studies by Ewbank and colleagues (72), Jakicic and colleagues (73), and Schoeller and colleagues (74) indicate that the volume of physical activity needed for that purpose is approximately 31 MET-hours per week or 4.4 MET-hours per day.

Question 3. What Is the Effect of Physical Activity on Body Composition Parameters (e.g., Waist Circumference, Intra-Abdominal Fat, Abdominal Adiposity, Total Body Fat) That Are Specifically Related to Metabolic Disorders?

Conclusions

A dose-response relation exists between volume of physical activity and decreases in total and abdominal adiposity in overweight and obese individuals. In the absence of coincident caloric restriction, aerobic physical activity in the range of 13 to 26 MET-hours per week results in decreases in total and abdominal adiposity that are consistent with improved metabolic function. Thirteen MET-hours per week is equivalent to walking at a 4 mile per hour pace for 150 minutes per week or jogging at a 6 mile per hour pace for 75 minutes per week (7-9). However, larger volumes of physical activity (e.g., 42 MET-hours per week) result in decreases in intra-abdominal adipose tissue that are 3 to 4 times those seen with 13 to 26 MET-hours per week, even without weight loss. The evidence thus far suggests that abdominal fat loss with increased physical activity is proportional to overall fat loss.

Definitions

The obesity phenotype that conveys the greatest health risk of metabolic disorders, such as the metabolic syndrome and type 2 diabetes, is one that favors an accumulation of adipose tissue in the abdominal region. Regular physical activity is recognized as an effective method of preventing excessive weight and fat gain throughout adulthood, and although physical activity is commonly prescribed to reduce overall obesity, the influence of exercise-induced weight loss on abdominal adiposity is not clear. Abdominal adiposity is characterized several ways in the scientific literature. Modern imaging techniques such as MRI, DXA, and CT provide highly-precise quantification of total body fat content (expressed in relative [%] or absolute [kilogram] terms), as well as specific measures of abdominal fat, such as the subcutaneous and visceral (intra-abdominal) fat areas (cm²). Although less precise than the imaging measures, the waist circumference (measured in centimeters and usually defined at the level of the lowest rib) is the most widely-used anthropometric measure of abdominal adiposity and therefore has the most clinical utility of all these measures.

Rationale

The *Physical Activity Guidelines for Americans* Scientific Database was accessed using the following delineation terms: 1) **population sub-group:** adults/older adults; 2) **study design:** randomized controlled trials (RCTs); longitudinal experimental studies (before/after); and prospective observational studies; and 3) **health outcomes:** adiposity measures (e.g., total fat, percent fat, abdominal fat area [visceral and subcutaneous], waist circumference) related specifically to metabolic disorders. Evidence obtained using the Scientific Database was supplemented with recently-published scientific papers and review articles.

Favorable body composition changes (reduced fat mass and increased lean mass) occur with the adoption of regular physical activity — even among individuals aged 75 years and older, and evidence suggests that current activity is more protective than past activity (87;88). What is not clear at this time is the amount and type of activity necessary to result in meaningful alterations in abdominal fat, which in turn can preserve or improve metabolic function. Unfortunately, few large-scale RCTs have been directed toward this question. The data that do exist are from relatively small RCTs and controlled intervention studies. Nonetheless, these studies paint a consistent picture of energy expenditure requirements for minimizing fat gain and/or reducing excess total and abdominal fat.

Several RCTs and controlled interventions report the benefits of moderate- to vigorous-intensity aerobic exercise to overall improvements in body weight, body fat, and lean mass in middle-aged and older adults (7;8;89-93). The data are equivocal, however, with regard to the ability to significantly alter regional distribution of body fat with endurance training (7-9;54;91;93-95). In general, aerobic exercise, without dieting, appears to have a beneficial effect on overall and abdominal adiposity. However, the exercise dose necessary to result in these alterations is rather high. In Irwin and colleagues (7), 176 minutes per week of moderate- to vigorous-intensity physical activity performed over 12 months resulted in a

reduction in subcutaneous fat and intra-abdominal fat of 5.4% and 5.8%, respectively, with the impact being even larger when contrasted with the control group. In addition, McTiernan and colleagues (8) used a higher volume/longer duration aerobic exercise regimen (60 minutes or more of moderate- to vigorous-intensity physical activity on 6 days per week) over 12 months of training and also reported modest decreases in the subcutaneous abdominal fat (5% in women and 11% in men) and intra-abdominal fat (6% in women and 8% in men) depots and in the waist circumference (2% in women and 3% in men). Data from the Studies of Targeted Risk Reduction Interventions through Defined Exercise (STRRIDE) show that the highest amount of exercise performed (equivalent of jogging approximately 20 miles per week) over 8 months resulted in, at best, a 7% decrease in visceral and subcutaneous fat in men and women aged 40 to 65 years (9). Ross and colleagues (93) report an 18% reduction in total fat and a 20% reduction in abdominal fat among non-dieting abdominally-obese women who exercised every day for about 60 minutes (or 500 kilocalorie expenditure) for 14 weeks. Together, these findings (7-9;93) and others (6) support the contention that in the absence of coincident caloric restriction, aerobic physical activity in the range of 13 to 26 kilocalories per kilogram per week results in decreases in total and abdominal adiposity that are consistent with improved metabolic function. However, as mentioned above, when more physical activity is done per week (e.g., 42 MET-hours per week), decreases in intra-abdominal adipose tissue approach 3 to 4 times the level seen with 13 to 26 MET-hours per week, even without weight loss (93).

A recent study employing 45 minutes of resistance exercise training twice weekly also reports small, yet favorable changes in total and abdominal fat (56) in middle-age and older adults, but not in younger, non-obese women (96). In a 2-year study of resistance training in overweight and obese premenopausal women, Schmitz and colleagues (56) report a 4% decrease in total fat in the exercise group versus a negligible change in the control group ($P < 0.01$). Interestingly, intra-abdominal fat increased over 2 years by 7% in the exercise group and by 21% in the control group, underscoring the benefits of resistance training (without caloric restriction) in at least minimizing intra-abdominal fat gain in middle-aged women. The benefits of resistance training may be most noticeable among obese and older populations, who typically have the greatest amount of abdominal fat.

Generally, short-term (less than 6 months) exercise interventions will have a positive effect on body composition. However, the magnitude of these alterations in body fat or lean mass may be of limited biological significance (48). Studies that employ moderate- to vigorous-intensity aerobic exercise of at least 55-75% $\text{VO}_{2\text{peak}}$ (4.5-6 METs), on most days of the week (i.e., 4 or more days), over intervention periods of at least 9 months, report the most significant changes in body composition (7-9;91;93). In general, the amount of adiposity present in study subjects at baseline will affect the amount of fat lost with a given intervention. Indeed, studies employing overweight or obese subjects (7;8;56;92;93) report greater improvements in body composition than those studies using subjects of normal weight (48;96). Also important is the dose-response relation highlighted by Ross and colleagues (93) between exercise-induced weight loss and fat loss — that is, greater total weight loss will result in greater fat loss (7;93). Nonetheless, Ross and colleagues (93)

report that, even without coincident weight loss, 60 minutes per day of vigorous-intensity exercise (approximately 500 kilocalories per day) on 7 days per week still resulted in statistically significant reductions in total (7%), abdominal (10%), and intra-abdominal (18%) fat in abdominally-obese premenopausal women.

Overall, regular participation in aerobic physical activity causes decreases in both total and abdominal adiposity, changes that are consistent with improved metabolic function. The greater the volume of physical activity, the larger the change in adiposity.

Question 4: What Effects Do Sex and Age Have on the Role of Physical Activity in Energy Balance?

Conclusions

Some evidence indicates that the amount of physical activity needed to maintain a constant weight differs between men and women and increases with age. This may be due to a number of physiologic and behavioral factors that also vary by sex and by age. However, the evidence is not sufficient to recommend differential physical activity prescriptions based on sex or on age alone.

Rationale

The *Physical Activity Guidelines for Americans* Scientific Database was accessed using the following delineation terms: 1) **population sub-group:** adults/older adults; 2) **study design:** randomized controlled trials, longitudinal experimental studies (before/after), prospective observational studies, and cross-sectional studies; 3) **health outcomes:** body weight; and 4) **search term:** aging, age, gender, men, women. Studies identified using the Scientific Database were supplemented by recently-published or in press scientific papers and review articles. Findings presented here were limited to studies having a forward study design (i.e., prospective observational and/or longitudinal experimental studies) with adequate statistical power to distinguish moderate effect sizes from chance alone.

Sex

The prevalence of obesity is higher among women compared with men, particularly among women from ethnic minority groups (4;97). Although women report less physical activity than men, it is not clear whether this is actually so, or whether it is a consequence of measurement error resulting from the low sensitivity of traditional physical activity surveys (83;98;99). In any case, potential sex differences in the influence of physical activity on weight stability are important to consider in maximizing the utility of future public health guidelines.

Cross-sectional and longitudinal epidemiologic studies generally have demonstrated inverse associations between physical activity and weight gain in both men and women (e.g., 100-105). Dose-response relationships have been somewhat less consistent in women

than in men. However, as stated previously, this may be attributable to measurement error associated with self-reported data (100;106). Indeed, objective measurements of energy expenditure (e.g., doubly-labeled water) have either stronger inverse associations in men than in women or no biological sex differences in response to different amounts of physical activity (107). The few intervention studies that included both men and women (along with sex-specific analyses) report weight or fat losses only in men (107), no change in either sex (67), or similar changes in both men and women (e.g., 8;58;89;108;109).

It is likely that differences in findings among these intervention studies reflect dissimilarities among study protocols. However, even within particular study samples, observed sex differences in weight loss responses to exercise can be attributed to a number of factors. For instance, several highly controlled laboratory-based intervention studies have noted that women are more resistant to weight loss or may require greater energy expenditure compared with men to maintain a healthy body weight (54;100;107). Indeed, this suggests that a similar absolute energy expenditure (e.g., 1,200 kilocalories per week) may not yield the same results in men and women. This may be due to a greater proportion of less lipolytically responsive gluteofemoral adipose tissue in younger and middle-aged women than in men of the same age. Animal studies also have observed a sex dimorphism in the control of energy homeostasis that might be attributed to a differential interaction between adiposity hormones and food intake control systems in the brain (110;111). These biological sex differences in responsiveness to weight change may be difficult to discern in large community-based interventions or at the population level, however, due to measured or unmeasured sex differences in: 1) how a similar level of physical activity is performed (walking vs. water aerobics vs. running); 2) adherence to a given exercise prescription; or 3) dietary intake. Because a number of other physiological (body mass, peak aerobic capacity) or behavioral factors (cigarette smoking, drinking, hormone replacement therapy) also may vary between men and women, studies that measure sex differences in weight loss responses to exercise must be careful to control for these covariables either by matching in experimental designs or by appropriate statistical adjustments when feasible.

Age

Because the risk of chronic disease increases markedly with sedentary lifestyles and with age, the public health burden associated with inactivity is substantial among middle-aged and older adults (88). In general, lower levels of physical activity are associated with higher body weight and body fat in middle-aged and older adults (4;87;112-114). The epidemiologic studies to date provide clear longitudinal evidence linking habitual physical activity to the prevention of excess weight gain in both men and women (100-105;115) and this is true even in older age. Although the effect sizes from these observational studies appear small, over the lifespan these small savings in excess weight gain accumulate into net savings that are quite meaningful with regard to minimizing the risk of obesity-related disorders. Moreover, the longitudinal epidemiologic evidence suggests that as people progress from young adulthood to old age, they require increasing amounts of daily energy expenditure to maintain a constant body weight (37;104;105;115). More than likely, this is due to a combination of physiologic (e.g., sex hormone depletion, decline in peak aerobic

capacity) and lifestyle changes (e.g., retirement) that occur with aging that make older people more susceptible to positive energy balance and thus to weight gain.

An active lifestyle also is beneficial in preventing weight **loss**, an increasingly important concern for the oldest sectors of the population (those older than 85 years) because of its relation to metabolic disorders and functional ability. Several observational studies have demonstrated the longitudinal benefits of even modest levels of physical activity on preventing excess weight loss in older age, presumably through the maintenance and preservation of lean mass (116-118).

Among intervention studies, training protocols are too variable and sample sizes are often too small to establish dose-response relations between changes in weight and activity type, duration, and intensity for different age subgroups. Nonetheless, some intervention studies have demonstrated statistically significant improvements in various weight-related outcomes (e.g., BMI, body fat distribution) with aerobic and resistance training in older participants (e.g., 8;89;108), whereas others have not (104;105). The magnitude of improvement observed in many of these intervention studies is similar, but is smaller than what is often observed in younger populations given the same relative exercise dose. A similar relative stimulus (say 75% of VO_{2peak}) will translate into a lower absolute exercise dose in older compared with younger people (due to lower levels of lean mass and aerobic capacity) and therefore, may not result in an adequate stimulus for fat loss in older people. This may be especially true for older women.

Question 5: How Do the Physical Activity Requirements for Weight Maintenance Differ Across Racial/Ethnic and Socioeconomic Groups?

Conclusions

Although some evidence suggests possible ethnic differences, the paucity of data, particularly from the stronger longitudinal cohort or randomized, controlled intervention study designs, makes it unwise to draw conclusions as to whether physical activity requirements for weight stability or reduction differ by racial/ethnic or socioeconomic groups.

Overview

Racial/ethnic disparities in obesity prevalence are robust and persistent across socioeconomic groupings (e.g., 119-121). African Americans, American Indians/Alaska Natives, Latinos and Pacific Islanders have substantially higher BMIs than do whites and Asian Americans, and a significant interaction exists between ethnicity and sex (122). For example, 54% of African American women are obese, compared with 42% of Mexican American women and 30% of white women (4). This contrasts with the similar obesity rates

among men: 34% of African Americans, 32% of Mexican Americans, and 31% of whites (4).

Greater obesity implies a lesser ability to maintain weight and avoid weight gain, which may be associated with less physical activity, more physical inactivity, or both. However, racial/ethnic differences in the contribution of physical activity to weight maintenance have been systematically examined only infrequently. Therefore, in addition to the reasons to examine whether general physical activity recommendations should differ between racial/ethnic groups (See *Part G. Section 11: Understudied Populations*, for a detailed discussion of this topic), specifically exploring the possible need for different recommendations to promote weight maintenance also is warranted. Available evidence suggests at least 2 possible reasons for differential influences of physical activity on weight maintenance by race/ethnicity:

1. Differences in the energy cost of physical activity, such that some ethnic groups would appear to derive lesser benefits for weight maintenance at the same level of physical activity (e.g., 123).
2. Differences in the relative contribution of physical activity and excess calories (energy expenditure versus energy intake) to weight gain, such that some ethnic groups would receive less benefit than others because physical activity contributes less to the overall equation (124).

Experimental studies in exercise physiology have suggested that lower resting energy expenditures and/or activity-related energy expenditures may contribute to higher rates of obesity in Pima Indians and African Americans than in whites (123;125;126). However, recent studies have demonstrated that these physiological differences may, in fact, be explained by racial variations in body morphology (e.g., trunk versus limb length, organ size) (127-129) that would not necessarily influence the ability to maintain weight. The precise role in weight maintenance of racial/ethnic differences in resting or activity-related energy metabolism (as opposed to age or sex-related differences) in body composition is an important area for future research.

Rationale

The Energy Balance subcommittee used a search strategy to generate 236 articles from the *Physical Activity Guidelines for Americans* Scientific Database (all age group combinations except youth, with weight and BMI as the outcome of interest, excluding studies focused on weight loss). These articles were further screened to identify studies that linked physical activity to weight-related outcomes and met the following criteria: 1) targeting an ethnic minority group; **or** 2) including subgroup analyses by ethnicity, not simply treating race/ethnicity as a co-variate and adjusting for it; **and** 3) specifying the racial/ethnic minority groups included in the analyses, not aggregating in the analyses as “non-white;” **and** 4) having a sample size of 30 or more participants or at least 30 participants per study arm; **and** 5) having a “general audience” sample (i.e., not focusing on a specific subgroup

such as elite athletes or postpartum women). Even very recent studies in US locations that have large ethnic minority populations, such as Baton Rouge, LA (130) and St. Louis, MO (131), did not characterize their samples by race/ethnicity. A MEDLINE search using similar parameters to those of the Scientific Database (key words: ethnic groups AND (body composition OR body weight OR obesity) AND (physical activity OR exercise OR walking) yielded 399 articles, most of which were already included in the Scientific Database. These articles were then further screened by applying the above racial/ethnic minority inclusiveness and sample size criteria, and eliminating those intervention studies in which physical activity was not the dominant intervention component (i.e., nutrition was equally strong or stronger). Reviews of relevant studies published after 1996 (132-135) and expert referral produced an additional in press publication.

Of the 24 articles identified by this systematic review, half reported on studies that were conducted outside the United States, including 9 in Asia/Pacific Islands (China, Japan, Taiwan, India, New Zealand), 2 in Africa (Nigeria, South Africa), and 1 in Central America (Mexico). Three were longitudinal cohort studies, 7 were interventions, and 14 were cross-sectional studies.

Few of the 24 studies were population-based, and thus, findings may not be representative even of subgroups with similar sociodemographic characteristics to those studied. Relatively few studies included Latinos, currently the largest minority group in the United States, and even fewer studies included American Indians, with their tremendous intra-ethnic heterogeneity from diverse tribal origins and affiliations. Most studies of Asian Americans or Pacific Islanders took place outside of the United States, introducing further complexity. International studies were included, however, because so few domestic studies included substantive racial/ethnic diversity, particularly among those with more rigorous designs. These studies may assist in clarifying any influence of some biological or cultural differences which may persist after migration to the United States, though they are likely to be less applicable with regard to differences influenced by the specific environmental or sociocultural context.

Of the 14 cross-sectional studies, which were conducted across a broad variety of racial/ethnic minority groups, including African Americans, Nigerians, South Africans, Pima Indians, Latinos, Asian Americans, Asians, and East Indians, most found an inverse association between physical activity level and weight/waist circumference/body fat percentage (29;103;113;136-146). This finding was consistent with studies in predominantly white populations (147). Among elderly Chinese, tai chi or swimming were associated with body fat distribution (lower levels in the thigh and/or abdomen), but not with total body adiposity (145). The exceptions were found in: (1) a study of 7,503 Mexican-American immigrants in Harris County, Texas, in which physical inactivity was correlated with obesity in women but not in men (103); (2) a study of 44 African American women (14% BMI less than 25, 25% to 30% Class II or III obese) in rural areas and small cities in North Carolina, in which 3-day pedometer step counts were not correlated with BMI or waist circumference (146); and (3) a study of 263 middle-aged Chinese in Hong Kong

(40% obese, 30% completely sedentary), in which low levels of physical activity were not correlated with BMI or waist circumference (144). In these instances, it is likely that BMI and/or physical activity was insufficiently variable to detect an effect.

Longitudinal studies in predominantly white populations generally demonstrate associations between increases in physical activity and decreases in the magnitude of weight gain (147). Of the 3 longitudinal studies identified in ethnic minority populations, however, only one, a 4-city convenience sample across several US regions, The Study of Women's Health Across the Nation or SWAN, replicated this association (113). SWAN study outcomes revealed associations between increases in daily routine physical activity (active transportation and less TV viewing) and exercise/sports, and less weight gain. On the other hand, increases in physical activity, compared to baseline, were not associated with smaller increases in weight, as reflected in findings of no change or decreases in waist circumference (113). The findings of the two nationally representative samples in the United States and Japan (114;148) were essentially null. He and Baker (148) found that, between 1992 and 2000, regular recreational physical activities, of any intensity, and work-related activities were not associated with less weight gain. Race (Asian or white), education, and income were not correlated with weight gain in multivariate analyses (148). However, although data were adjusted for race/ethnicity, it is not clear whether differences in the physical activity-weight gain association were analyzed by ethnicity. Lee and colleagues (114) found no baseline association between physical activity and weight, though the mean BMIs were 23.5-23.7 across activity levels. This study apparently did not examine the relationship between changes in physical activity and BMI changes. Thus, too few studies are available to draw conclusions about the influence of race/ethnicity on the association between physical activity and weight change over time.

Intervention studies selected for this review generally demonstrated that resistance training, alone or in combination with moderate- to vigorous-intensity aerobic physical activity, was necessary to produce changes in BMI or body composition/distribution in ethnic minority populations (48;67;89;149-152), despite the effectiveness of aerobic physical activity alone in improving non-weight-related aspects of the metabolic profile, such as reducing blood pressure (67;149). Wilmore and colleagues (48) presented the only within-study "head-to-head" inter-racial comparisons, with subgroup analyses after endurance training using advancing intensity and duration on cycle ergometers. The magnitude of weight loss for both whites and blacks was small; 0.2 kilogram (0.4 pound) mean weight loss in both groups. The change was statistically significant in whites but not blacks likely due to the larger sample size for whites (n=398) than blacks (n=159). Changes in various measures of body fat followed a similar pattern, with small but somewhat greater changes occurring in whites than blacks (e.g., change in sum of skinfolds for whites = -7.1 ± 0.8 , blacks = -4.1 ± 1.5 , $P < 0.05$ for both). The ages (34.8 and 32.3 years for whites and blacks, respectively) and BMI (25.0 and 26.6 kg/m², respectively) were similar. Adjustments for the subtle racial/ethnic variations identified in experimental exercise physiology studies (e.g., 128) apparently were not performed (48). Wilmore and colleagues (48) concluded that the magnitude of the changes in body composition was not biologically significant in either

blacks or whites and that a physical activity intervention of greater volume or longer duration was needed to produce meaningful changes in body weight and fat. In another study, in Japan, even quantities/intensities of walking sufficient to increase VO_{2max} (13,500 to 14,500 steps per day in the experimental groups versus 5,800 in the control group) did not alter BMI, although the participants in this study were normal weight or minimally overweight (24.6 to 24.7 and 25.2 kg/m^2 , respectively) (149). Participants were presumably Japanese, although race/ethnicity of study samples is rarely specified in these international studies. Contrasting findings were reported in another international study. In this secondary analysis of data collected routinely on government health and social services workers in Mexico, Lara and colleagues (152) demonstrated a 0.32 kg/m^2 BMI decrease, a 1.0 kilogram (2.2 pound) weight loss, and a 1.6 centimeter (1.6 inch) decrease in waist circumference at the end of 1 year after integrating mandatory 10-minute structured group aerobic-calisthenic exercise breaks during paid work time in this group of mostly middle-aged, overweight and abdominally obese workers. Although the study had no control group, secular trends documented in Mexico at that time were similar to the United States mean increases of 1 to 2 pounds (0.45 to 0.9 kilograms) in body weight and 0.5 inches (1.27 centimeters) in waist circumference per year (113;152). The fact that the subjects of the Mexican study were not volunteer participants, but rather a sample more typical of the general population, and their overweight status, compared with the mostly normal weight Japanese sample, may account for the discrepant findings.

As noted in earlier reviews (e.g., 132-134;153) there is an extreme paucity of evidence on racial/ethnic minority groups with regard to the effects of physical activity on weight maintenance. In this review, no 2 studies examined the same ethnic-sex samples — Japanese middle-aged men, Japanese elderly adults, Japanese adults 30 to 69 years of age, Alaska Native women, African American peri-menopausal women, African American and white young and middle-aged adults, Mexican middle-aged adults — much less measures of activity duration or intensity. Consequently, broad generalizations about the influence of race/ethnicity on the physical activity requirements for weight stability or reduction are premature.

Overall Summary and Conclusions

The overall conclusions of this chapter on physical activity and energy balance can be summarized as follows:

Physical Activity, Weight Stability, and Weight Loss

Regular participation in physical activity provides benefits for weight stability, but with few data on this topic from long-term studies, the optimal amount is not known. Available data from short-term clinical trials indicate that a dose of physical activity in the range of 13 to 26 MET-hours per week results in a modest 1% to 3% weight loss, consistent with weight stability over time (7-9). Thirteen MET-hours per week is equivalent to walking at a 4 mile per hour pace for 150 minutes per week or jogging at a 6 mile per hour pace for 75 minutes

per week. Aerobic physical activity done at this level would reduce upward migration of individuals from one BMI category to the next. The wide range of physical activity levels (13 to 26 MET-hours per week) needed for weight stability probably reflects individual variation in the inherent (non-structured) level of physical activity and the degree to which caloric intake is increased over time when a physical activity intervention is initiated. The magnitude of weight loss resulting from resistance exercise in this review was typically less than 1 kilogram (2.2 pounds). However, this may have been affected by the relatively short duration of the study period and the increase in fat-free mass associated with this type of intervention. Although a weight loss of 5% or more of body weight can be achieved with large volumes of physical activity, a coincident dietary intervention is typically needed to achieve this goal. The dietary intervention could include maintenance of (at pre-intervention levels) or an actual reduction in caloric intake.

Physical Activity and Weight Regain

Most of the available literature indicates that “more is better” when it comes to the amount of physical activity needed to prevent weight regain following weight loss. However, as indicated above, the literature has some considerable shortcomings regarding the appropriate research design needed to directly address this question. Studies by Ewbank and colleagues (72), Jakicic and colleagues (73) and Schoeller and colleagues (74) indicate that the volume of physical activity needed to prevent weight regain following weight loss is approximately 31 MET-hours per week or 4.4 MET-hours per day. This is equivalent to walking 54 minutes per day at 4 miles per hour or 80 minutes per day at 3 miles per hour, or jogging for 26 minutes per day at 6 miles per hour.

Physical Activity and Body Composition Parameters

Ample evidence exists for a positive dose-response relation between the volume (frequency, intensity, and duration) of endurance and/or resistance exercise, the training duration, and the amount of total and regional fat loss. Moreover, the evidence suggests that regional fat loss is greater with greater amounts of exercise-induced total weight loss and among those with the greatest levels of adiposity. In the absence of coincident caloric restriction, aerobic physical activity in the range of 13 to 26 MET-hours per week results in decreases in total and abdominal adiposity that are consistent with improved metabolic function (7-9). Thirteen MET-hours per week is equivalent to walking at a 4 mile per hour pace for 150 minutes per week or jogging at a 6 mile per hour pace for 75 minutes per week. However, when more physical activity is done (e.g., 42 MET-hours per week), decreases in intra-abdominal adipose tissue approach 3 to 4 times the level seen with this range of physical activity (93).

The Effect of Sex and Age on Physical Activity and Energy Balance

Some evidence suggests that the amount of exercise necessary to maintain a constant body weight differs between men and women and increases with age due to a variety of physiological and lifestyle factors. Moreover, even within a given sex- or age-group, weight loss responses to exercise vary substantially. Thus, it is quite difficult to make a standard daily activity recommendation that relates to optimal weight maintenance for everyone. On the other hand, the evidence base is too sparse at this time to recommend differential physical activity prescriptions based on sex or on age alone.

Physical Activity Requirements Across Race/Ethnicity and Socioeconomic Groups

Although some evidence suggests possible ethnic differences, the paucity of data, particularly from longitudinal cohort or randomized, controlled intervention study designs, makes it unwise to draw conclusions as to whether the effects of physical activity on weight maintenance or loss differ by race/ethnicity or socioeconomic groups. Some of the questions outlined in this section have yet to be fully addressed, although evidence is suggestive, for example, that socioeconomic constraints, cultural preferences, and baseline levels of sedentariness or obesity make low-intensity, social-environmental interventions feasible, sustainable, and effective in many racial/ethnic minority groups (152;154-160). However, simply conducting studies that include representative sample populations will not suffice, because there likely will be too few members of any one group to disaggregate findings by socioeconomic status, race/ethnicity, and sex, or to examine interactions between these critical sociodemographic factors.

Research Needs

This review of physical activity and energy balance identified a number of research needs in each of the topic areas covered in the chapter.

Physical Activity, Weight Stability, and Weight Loss

Studies that are appropriately designed, with sufficient statistical power, and of sufficient length are needed to specifically examine the effects of varying doses of physical activity on weight loss and weight stability across a variety of population groups, especially for those in the normal BMI range. Further examination of effects of physical activity mode, intensity, duration, and frequency on weight loss and/or weight stability also would make a valuable contribution to this area. Finally, research is needed to further examine intervention strategies that are most effective at promoting and maintaining sufficient doses of physical activity that will facilitate weight loss and/or weight stability.

Physical Activity and Weight Regain

Most available literature is observational or has relied on retrospective analysis of self-selected and self-reported levels of physical activity. Use of state-of-the-art technology and complete energy balance designs are absent from the literature. Specifically, adequately powered studies of sufficient duration with randomization to different levels of physical activity after weight loss appear to be lacking. This limitation needs to be addressed to adequately explore the question of how much physical activity is needed to prevent weight regain following weight loss.

Physical Activity and Body Composition Parameters

There remains a need for more RCTs to distinguish exercise effects on total and regional fat loss from those of weight loss *per se*. In addition, the large-scale use of imaging techniques is necessary to distinguish the responsiveness of subcutaneous and visceral fat depots to endurance and/or resistance training. The ability of studies to translate imaging findings into simple anthropometric measures, such as waist or abdominal circumference, would increase the clinical and personal utility of the research. Finally, there is a need to identify and to study people who are very susceptible to weight gain in the current social environment and who thus may be most resistant to weight or fat loss with exercise.

The Effect of Sex and Age on Physical Activity and Energy Balance

Journal requirements stipulating that sex- and age-specific analyses be conducted with sufficient statistical power would help to address the dearth of information pertaining to individual and population differences in body weight response to physical activity. In addition, it would be helpful to identify and study people in the current social environment who are very susceptible to weight gain and who thus may be most resistant to weight or fat loss with exercise. Studies of how susceptibility to weight gain or resistance to weight/fat loss may vary by sex and age would contribute substantially to the obesity literature.

Physical Activity Requirements Across Race/Ethnicity and Socioeconomic Groups

Two clear mandates emerge from this research synthesis. The first is to increase attention and resources for studies that focus on diverse race/ethnicity groups and lower socioeconomic status populations, or that include sufficient numbers to permit subgroup analyses by race/ethnicity or socioeconomic status. The second is to establish standards for peer-review journals that require investigators to report race/ethnicity of samples. These standards also should require investigators to conduct subgroup analyses by race/ethnicity and/or socioeconomic status if sample sizes are sufficient, rather than simply treating these as co-variables and adjusting for them.

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