PART F. CHAPTER 5. CARDIOMETABOLIC HEALTH AND PREVENTION OF WEIGHT GAIN

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INTRODUCTION

The Committee identified cardiometabolic health and weight management as key areas to include in this report, with a focus on preventing the onset of specific outcomes. The Committee considered the broad areas of cardiometabolic health and weight management when determining the specific areas to be examined in this *2018 Physical Activity Guidelines Advisory Committee Scientific Report*, and also considered how this report could expand the conclusions provided in the *Physical Activity Guidelines Advisory Committee Report, 2008*.[1] Within this context, the Cardiometabolic Health and Prevention of Weight Gain Subcommittee prioritized three areas for this chapter that included the association between physical activity and prevention of weight gain, incidence of hypertension, and incidence of type 2 diabetes mellitus. The rationale for inclusion of these areas within this report follows.

Excessive body weight has been shown to be associated with numerous negative health outcomes that include, but are not limited to cardiovascular disease (CVD), diabetes, some forms of cancer, and musculoskeletal disorders.[2, 3] Recent estimates indicate that prevalence of overweight (body mass index (BMI) 25 to $\leq$30 kg/m^2) in the United States for adult men is approximately 40 percent and for women is 30 percent,[4] with estimates of obesity (BMI $\geq$30 kg/m^2) for men being approximately 35 percent and for women being 40 percent.[5] Thus, an ongoing need for effective treatments for both overweight and obesity is recognized. From a public health perspective, however, the strategies that prevent or minimize weight gain, which may result in a lower prevalence of overweight and obesity, are important to lower the health consequences of excessive body weight. This chapter focuses on physical activity and its potential influence on body weight, with a particular focus on minimizing weight gain, maintaining body weight, and preventing overweight and obesity in adults. The potential influence of physical activity on body weight in youth is addressed in *Part F. Chapter 7. Youth* and during pregnancy is addressed in *Part F. Chapter 8. Women Who are Pregnant or Postpartum*, and the potential influence of sedentary behavior on body weight is addressed in *Part F. Chapter 2. Sedentary Behavior*.

CVD is the leading cause of death in the United States and the world, accounting for approximately 1 in 3 deaths (807,775, or 30.8%) in the United States and 17.3 million (31%) worldwide.[6, 7] Hypertension is the most common, costly, and preventable CVD risk factor. According to the *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure* (JNC 7)[8] blood pressure classification scheme, hypertension affects 86 million (34%) adults in the United States and 1.4 billion (31%) adults globally.[6, 7] Hypertension also is the most common primary diagnosis in the United States, and the leading cause for medication prescriptions among adults older than age 50 years.[9] Another 36 percent of adults in the United States have prehypertension, and one in five adults with prehypertension is estimated to develop hypertension in 4 years.[6, 10] By 2030, it is estimated that 41 percent of adults in the United States will have hypertension, and almost an equal amount will have prehypertension. From 2010 to 2030, the total direct costs attributed to hypertension are projected to triple ($130.7 to $389.9 billion), while the indirect costs due to lost productivity will double ($25.4 to $42.8 billion).[6] Curbing this growing and expensive public health crisis is a national and global priority.[7, 11] This chapter focuses on physical activity and its potential influence to prevention hypertension. The influence of physical activity on resting blood pressure in adults with hypertension is addressed in *Part F. Chapter 10. Individuals with Chronic Conditions*.

Diabetes mellitus, more commonly referred to as diabetes, is a chronic disease characterized by a deficiency and/or defect in the action of insulin. Type 2 diabetes is characterized by a relative resistance to insulin usually accompanied by resistance to the effect of insulin and comprises 90 to 95 percent of all cases of diabetes. The risk of developing type 2 diabetes is reduced by regular participation in moderate-to-vigorous physical activity. An estimated 23 million people (9.4% of the U.S. population) are known to have type 2 diabetes.[12] The prevalence rises from about 3 percent among people ages 18 to 44 years to 13 percent of people ages 45 to 64 years, and 21 percent of people ages 65 years and older.[12] Common complications of diabetes affect the eyes, kidneys, nerves, and blood vessels, leading to, among other problems, loss of vision, kidney failure, and lower limb amputations. Risk factors for these conditions are common among people with diabetes: 88 percent have overweight or obesity, 41 percent report no moderate-to-vigorous physical activity, 74 percent have high blood pressure, 16 percent have a hemoglobin A1c (HbA1c) value greater than 9 percent. In 2012, the total estimated cost of diabetes in the United States was $176 billion in direct medical costs and $69 billion in reduced productivity.[13] People with type 2 diabetes have medical expenditures about 2.3 times higher than they would if they did not have the disease. This chapter focuses on type 2 diabetes prevention because the risk of developing the condition is reduced by regular participation in moderate-to-vigorous physical activity. Gestational diabetes is addressed in *Part F. Chapter 8. Women Who are Pregnant or Postpartum*. The relationship between sedentary behavior and the incidence of type 2 diabetes is described in *Part F. Chapter 2. Sedentary Behavior*. Among individuals who already have type 2 diabetes, the effect of habitual moderate-to-vigorous physical activity on the development of other chronic diseases, quality of life, physical function, and the prevention of disease progression is described in *Part F. Chapter 10. Individuals with Chronic Conditions.*

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses 3 major questions and related subquestions:

1. What is the relationship between physical activity and prevention of weight gain?
    a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
    b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
    c) Does the relationship vary based on levels of light, moderate, or vigorous physical activity?

2. In people with normal blood pressure or prehypertension, what is the relationship between physical activity and blood pressure?
    a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
    b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, weight status, or resting blood pressure level?

  c) Does the relationship vary based on frequency, duration, intensity, type (mode), or how physical activity is measured?

3. In adults without diabetes, what is the relationship between physical activity and type 2 diabetes?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
   c) Does the relationship vary based on: frequency, duration, intensity, type (mode), and how physical activity is measured?

Data Sources and Process Used to Answer Questions

For Question 1 (prevention of weight gain) the Subcommittee determined that existing reviews (systematic reviews, meta-analyses, pooled analyses, and reports) identified from an initial search did not answer the research question. A complete de novo search of original research was conducted.

The Subcommittee determined that systematic reviews, meta-analyses, pooled analyses, and reports provided sufficient literature to answer research Questions 2 and 3. In an effort to reduce duplication of efforts, the searches for existing reviews and title triage for Question 2 (blood pressure) and Question 3 (incidence of type 2 diabetes) were done concurrently with the Chronic Conditions Subcommittee's Question 3 (individuals with hypertension) and Question 4 (individuals with type 2 diabetes). The search strategies for each of these questions were developed to address the needs of both Subcommittees. Title triage addressed the inclusion criteria of both Subcommittees. Abstract and full-text triage were done separately for each Subcommittee. For complete details on the systematic literature review process, see *Part E. Systematic Review Literature Search Methodology.*

Question 1. What is the relationship between physical activity and prevention of weight gain?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship vary based on levels of light, moderate, or vigorous physical activity?

Sources of evidence: Original research articles

Conclusion Statements

Strong evidence demonstrates a relationship between greater amounts of physical activity and attenuated weight gain in adults, with some evidence to support that this relationship is most pronounced when physical activity exposure is above 150 minutes per week. **PAGAC Grade: Strong.**

Limited evidence suggests a dose-response relationship between physical activity and the risk of weight gain in adults, with greater amounts of physical activity associated with lower risk of weight gain. **PAGAC Grade: Limited.**

Limited evidence suggests that the relationship between greater amounts of physical activity and attenuated weight gain in adults varies by age, with the effect diminishing with increasing age. The evidence from studies of older adults, however, is inconsistent. **PAGAC Grade: Limited.**

Moderate evidence indicates that the relationship between greater amounts of physical activity and attenuated weight gain in adults does not appear to vary by sex. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether the relationship between greater amounts of physical activity and attenuated weight gain in adults varies by race/ethnicity. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between greater amounts of physical activity and attenuated weight gain in adults varies by socioeconomic status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between greater amounts of physical activity and attenuated weight gain in adults varies by initial weight status. **PAGAC Grade: Not assignable.**

Strong evidence demonstrates that the significant relationship between greater time spent in physical activity and attenuated weight gain in adults is observed with moderate-to-vigorous physical activity. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine an association between light-intensity activity and attenuated weight gain in adults. **PAGAC Grade: Not assignable.**

Review of the Evidence

To answer this question, the Subcommittee reviewed evidence from 33 original research studies.[14-46] Most of the studies showing an association between greater physical activity and attenuated weight gain (N=26) were prospective cohort studies,[14-18, 20, 22-24, 27-31, 34-36, 38-46] with follow-up periods ranging from 1 to 22 years and one study involving 6-year follow-up after a block randomized controlled trial (RCT). For the seven studies not showing an effect, six were cohort studies with the follow-up period ranging from 1 to 20 years.[19, 21, 25, 32, 33, 37] Three of these studies had follow-up periods of 2 or fewer years,[21, 24, 33] and one was a secondary analysis of data from a randomized study.[26]

Of studies showing an inverse association with weight gain, 7 studies assessed physical activity at one time point to examine the association with weight gain,[17, 22, 27, 28, 31, 35, 41] whereas 19 studies assessed physical activity at two or more time points to assess this association with weight gain.[14-16, 18, 20, 23, 24, 29, 30, 34, 36, 38-40, 42-46] For the seven studies that examined the association with weight gain but did not show an effect, three studies measured physical activity at one time point[21, 32, 33] and four studies measured physical activity at multiple time points.[19, 25, 26, 37]

The studies reviewed provided substantial information to allow for evaluation of an overall association between physical activity and either weight gain, increase in BMI, or development of obesity. Although data were available to examine whether these associations were influenced by sex and age, very limited information was provided within the studies reviewed to examine the influence of race/ethnicity, socioeconomic status, initial weight status, or dietary intake and eating behaviors, on the relationship between physical activity and weight gain. Moreover, although substantial information was provided for moderate-to-vigorous physical activity, few studies provided data for light-intensity physical activity.

Evidence on the Overall Relationship

Twenty-six of 33 studies demonstrate a significant relationship between greater amounts of physical activity and attenuated weight gain in adults.[14-18, 20, 22-24, 27-31, 34-36, 38-46] Eleven of the 26 studies that demonstrated a relationship reported data for the volume of physical activity where the effect is observed.[17, 20, 27, 29, 30, 34, 36, 40, 41, 43, 45] The evidence for a specific volume threshold of physical activity that is associated with prevention of weight gain in adults is inconsistent. Studies find that at least 1 hour per week of moderate intensity reduces the risk of developing obesity in both normal weight women (incidence rate ratio (IRR)=0.81; 95% confidence interval (CI): 0.71-0.93) and overweight women (IRR=0.88; 95% CI: 0.81-0.95)[39]; however, a similar result may be observed with less than 1 hour per week if the activity is of vigorous intensity, rather than moderate intensity. Williams and Wood[45] have reported that running equivalent to 4.4 km per week (~2.8 miles per week (~28 minutes per week at a 10-minute per mile pace) in men and 6.2 km per week (~3.8 miles per week (~38 minutes per week at a 10-minute per mile pace) in women may be sufficient to prevent weight gain associated with aging. Some evidence also supports the need to achieve at least 150 minutes per week of moderate intensity physical activity to minimize weight gain or to prevent increases in BMI.[29, 30, 43] Studies also support greater amounts of physical activity to prevent or minimize weight gain, with some studies reporting this effect with greater than 150 minutes per week at a moderate intensity,[36] 500 or more MET-minutes per week (≥167 minutes per week at a 3-MET intensity),[20, 41] or more than 300 minutes per week.[17, 27, 34]

Dose-Response: Some of the reviewed studies provided data on the dose-response relationship of physical activity and weight gain,[17, 27, 36, 41] maintenance of a healthy weight,[20] and development of obesity.[39]

Sims et al[41] reported a trend (*P*<0.08) for minimized weight gain in women engaging in more than 8.3–20 MET-hours per week (>167-400 minutes per week at a 3-MET intensity) or more than 20 MET-hours per week (>400 minutes per week at a 3-MET intensity) of physical activity, compared with those engaged in less than 1.7 MET-hours per week (<33 minutes per week at a 3-MET intensity). A physical activity volume of 1.7-8.3 MET-hours per week was not protective against weight gain, however.

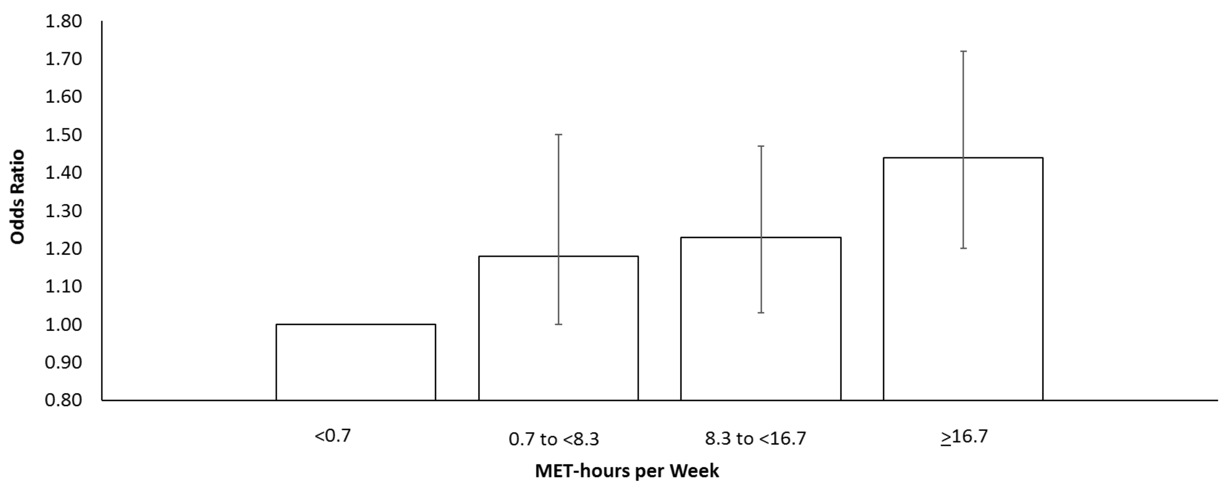
Two studies provide evidence of a dose-response to prevent weight gain of approximately 2 kg. Moholdt et al[36] identified four groups based on physical activity ("Inactive": no leisure-time physical activity; "Below Recommended": active <150 minutes per week in moderate intensity or <60 minutes per week in vigorous intensity leisure-time physical activity; "Recommended": active at 150 minutes per week in moderate intensity or 60 minutes per week in vigorous intensity leisure-time physical activity; "Above Recommended": active >150 minutes per week in moderate intensity or >60 minutes per week minutes per week in vigorous intensity leisure-time physical activity). For men, compared with those in the "Inactive" category, the risk of gaining ≥2.3 kg was 0.97 (95% CI: 0.87-1.08) for those in the "Recommended" category and 0.79 (95% CI: 0.69-0.91) for those in the "Above Recommended" category. A similar pattern was observed in women, with the risk of 0.97 (95% CI: 0.88-1.07) for those in the "Recommended" category and 0.69 (95% CI: 0.59-0.82) for those in the "Above Recommended" category. Gebel et al[27] reported a 10 percent reduction in the odds of ≥2kg weight gain with 300 or more minutes per week of moderate-to-vigorous physical activity compared with less than 150 minutes per week of moderate-to-vigorous physical activity; however, 150-249 minutes per week was not predictive of weight change.

Blanck et al[17] reported that the odds of gaining 10 or more pounds (≥4.5 kg) was significantly lower with 18 or more MET-hours per week (0.88; 95% CI: 0.77-0.99) in women with normal weight compared with the reference of more than 0 but less than 4 MET-hours per week (1.0). Compared to the reference, the odds of gaining this magnitude of weight did not differ with 0 MET-hours per week (1.01; 95% CI: 0.82-

1.01), 4 to less than 10 MET-hours per week (0.93; 95% CI: 0.80-1.08), and 10 to less than 18 MET-hours per week (0.99; 95% CI: 0.87-1.14).

Brown et al[20] report on a dose-response relationship for physical activity and the odds of maintaining a healthy weight (i.e., BMI of ≥18.5 to <25 kg/m^2). Compared with less than 0.7 MET-hours per week, the odds ratio (OR) for maintaining a normal BMI was 1.18 (95% CI: 1.00-1.40) for 0.7 to less than 8.3 MET-hours per week, 1.23 (95% CI: 1.03-1.47) for 8.3 to less than 16.7 MET-hours per week, and 1.44 (95% CI: 1.20-1.72) for 16.7 or more MET-hours per week (Figure F5-1).[20]

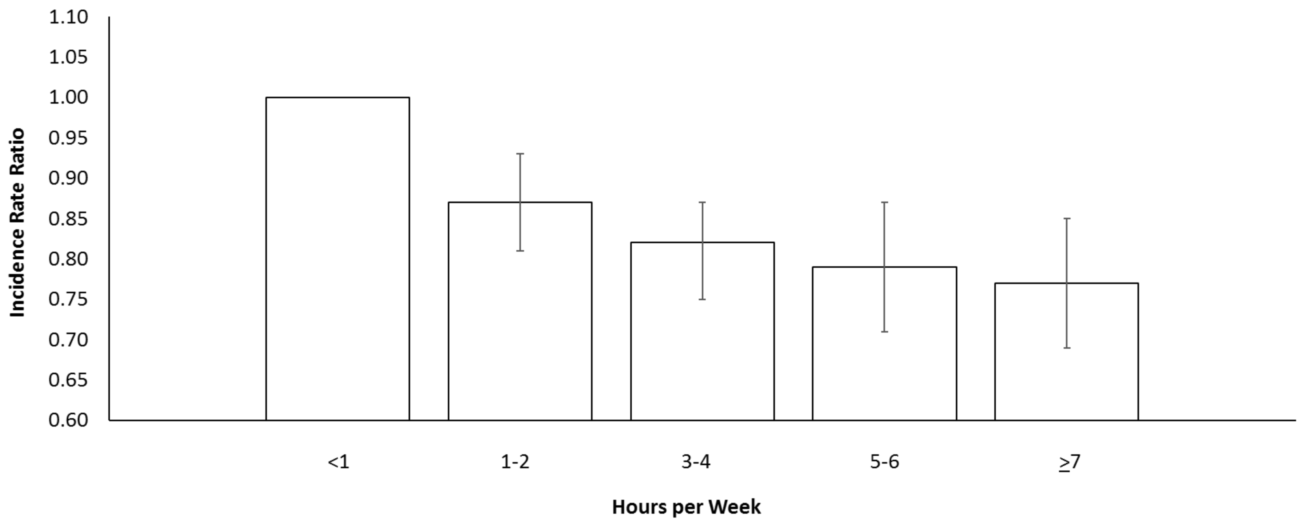
Figure F5-1. Odds of Maintaining a Healthy Weight by Level of Physical Activity



Source: Adapted from data found in Brown et al., 2016.[20]

Rosenberg et al[39] reported on the dose-response relationship for vigorous intensity physical activity and the likelihood of developing obesity. In women with normal weight and overweight, when compared to less than 1 hour per week, the incidence of developing obesity was significantly reduced in a graded manner, with vigorous intensity activity of 1 to 2 hours per week (0.87; 95% CI: 0.81-0.93), 3 to 4 hours per week (0.82; 95% CI: 0.75-0.88), 5 to 6 hours per week (0.79; 95% CI: 0.71-0.87), and 7 or more hours per week (0.77; 95% CI: 0.69-0.85) (Figure F5-2).[39]

Figure F5-2. Incidence Rate Ratio of Developing Obesity at Various Levels of Vigorous Physical Activity



Source: Adapted from data found in Rosenberg et al., 2013.[39]

Evidence on Specific Factors

Age: In general, the 26 studies in which a significant inverse association between physical activity and weight gain was observed encompassed a broad age range that included young, middle-aged, and older adults. Six studies analyzed the data specifically by age, with the evidence suggesting attenuation of this association with increasing age in both men and women.[34-36, 41, 44, 46] This pattern of results was inconsistent in the studies that included both men and women, however. MacInnis et al[35] reported a significant inverse association between physical activity and magnitude of weight gain across a mean follow-up of approximately 12 years in adults ages 40 to 49 years, with this association not observed in adults ages 50 to 59 years or 60 to 69 years. Williams[46] reported that running attenuated weight gain in men younger than 55 years of age and in women younger than 50 years of age.

These results are not consistent with the finding of Moholdt et al,[36] who reported that physical activity was significantly associated with reduced odds of gaining 2.3 or more kg in both men and women. Additional analyses, however, showed a significant interaction with age with a lower odds of a 2.3 or more kg weight gain in physically active adult men ages 40 years or older but not in those younger. In contrast, the inverse association between physical activity and odds of a 2.3 or more kg weight gain was observed across the age spectrum (younger than age 40 years, age 40 to 59 years, and age 60 years and older) in women. Moreover, Williams and Thompson[44] reported that the weight gain associated with the cessation of running was consistent between men less than 45 years of age and 45 years or older.

However, among women, weight gain was greater in women ages 45 years or older compared with their younger counterparts.

Two studies examined the association between physical activity and weight gain only in women. Lee et al[34] examined data from the Women's Health Initiative study and reported a trend for greater weight gain with lower levels of activity in women younger than age 64 years, but not in women ages 65 years and older. Similar findings were reported by Sims et al[41] in a study of post-menopausal women ages 50 to 79 years, which showed attenuated weight gain with greater amounts of physical activity in women ages 50 to 59 years, but not in those of ages 60 to 69 years or 70 to 79 years.

Sex: The 26 studies in which a significant inverse association between physical activity and weight gain was observed included either women (N=10)[14, 16, 17, 20, 22, 28, 31, 34, 39, 41] or both men and women (N=16).[15, 18, 23, 24, 27, 29, 40, 43-46] Of the 16 studies that included both men and women, 6 did not analyze the data separately by sex.[18, 24, 27, 29, 40, 43] Of the 10 studies that presented findings separately by sex, 8 reported that the association between physical activity and weight gain was consistent for both men and women.[15, 23, 30, 35, 36, 38, 42, 44-46]

Race/ethnicity: In general, the 26 studies in which a significant inverse association between physical activity and weight gain was observed encompassed diverse races and ethnicities. When specified, for studies conducted based on adults residing in the United States, a broad range of races and ethnicities appeared to be represented in the study samples[18, 24, 30, 31, 41] or the sample included only black/African Americans.[39] Some of the studies were conducted in countries outside of the United States, including Australia,[20, 27, 35, 43] France,[42] Great Britain,[38] Norway,[36] South Africa,[28] Spain,[15] Sweden,[23] and the Philippines.[14, 22] Although some studies included race or ethnicity as a covariate in the analyses, none of them presented data separately by race or ethnicity to allow for comparisons.

Socioeconomic status: Of those studies showing an inverse association between physical activity and weight gain, some studies provided a measure of socioeconomic status as a descriptive variable or as a covariate in analyses. Only one study isolated the effect of socioeconomic status on the association between physical activity and weight gain, and it was reported that socioeconomic status attenuated this association even though it remained statistically significant.[18]

Weight status: The 26 studies in which a significant inverse association between physical activity and weight gain was observed included adults of normal, overweight, and obese weight status. However, 19 of these studies did not report on whether the association between physical activity and weight gain varied by initial weight status. Of the remaining seven studies, two reported that the association did not differ by weight status,[39, 41] three reported the association to be more favorable in adults who had normal weight versus overweight or obesity,[17, 31, 34] and two studies reported results showing a more favorable pattern in adults with overweight compared to those with normal weight.[15, 36]

Light, moderate, or vigorous physical activity: In the 26 studies in which a significant inverse association between physical activity and weight gain was observed, investigators examined a variety of domains of physical activity. These included leisure-time/recreational activity, occupational activity, household activity, walking, and total steps of physical activity. Moreover, various intensities of physical activity (light, moderate, vigorous, moderate-to-vigorous) were assessed across these studies.

Total leisure-time physical activity was consistently inversely associated with weight change across the studies reviewed.[17, 23, 34, 35, 38, 41, 42] Studies reporting on moderate intensity,[15, 24] vigorous intensity,[18, 28, 29, 35, 39, 44-46] and moderate-to-vigorous intensity[20, 27-31, 36, 40] physical activity showed consistent patterns of inverse associations with weight gain. Light-intensity physical activity, however, was either not associated with weight change[29] or was associated with weight gain.[24]

Walking was not consistently associated with change in weight or BMI[28, 35] or with the incidence of developing obesity.[39] In contrast, however, Smith et al[43] reported that achieving 10,000 steps or more per day attenuated weight gain compared with not achieving 10,000 steps per day.

Studies also examined occupational and household activity. Occupational activity was inversely associated with weight gain,[14, 22, 35] with this association being observed with moderate- and vigorous intensity occupational activity,[14, 35] but not with light-intensity occupational activity.[14] Household activity does not appear to minimize weight gain.[22, 35]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The *Physical Activity Guidelines Advisory Committee Report, 2008*[1] concluded physical activity was associated with modest weight loss,[1] prevention of weight gain following weight loss,[1] and reductions in total and regional adiposity.[1] This evidence review expands these previous findings by providing evidence from prospective studies for an inverse association between physical activity and both weight gain and incidence of obesity, and a positive association between physical activity and maintenance of a BMI within a range of ≥18.5 to <25 kg/m^2. Evidence also exists to support that attenuation of weight gain is most pronounced when physical activity exposure is more than 150 minutes per week.

Public Health Impact

Weight gain that results in overweight or obesity is associated with increased risk for numerous chronic conditions. This is a significant health concern in the United States due to the high prevalence of both overweight and obesity. Thus, while it is important to focus on effective treatments for overweight and obesity, there is also a need to implement effective public health strategies to prevent weight gain and the onset of both overweight and obesity. The scientific evidence supports that physical activity can be an effective lifestyle behavior to prevent or minimize weight gain in adults. Therefore, public health initiatives to prevent weight gain, overweight, and obesity should include physical activity as an important lifestyle behavior.

Question 2. In people with normal blood pressure or prehypertension, what is the relationship between physical activity and blood pressure?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, weight status, or resting blood pressure level?
c) Does the relationship vary based on frequency, duration, intensity, type (mode), or how physical activity is measured?

Source of evidence: Systematic reviews, meta-analyses

Conclusion Statements

Strong evidence demonstrates that physical activity reduces blood pressure among adults with prehypertension and normal blood pressure. **PAGAC Grade: Strong.**

Strong evidence demonstrates an inverse dose-response relationship between physical activity and incident hypertension among adults with normal blood pressure. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and incident hypertension among adults with prehypertension. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and blood pressure varies by age, sex, race/ethnicity, socioeconomic status, or weight status among adults with normal blood pressure and prehypertension. **PAGAC Grade: Not assignable.**

Strong evidence demonstrates the magnitude of the blood pressure response to physical activity varies by resting blood pressure level, with greater benefits occurring among adults with prehypertension than normal blood pressure. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether the relationship between blood pressure and physical activity varies by the frequency, intensity, time, and duration of physical activity, or how physical activity is measured among adults with normal blood pressure and prehypertension. **PAGAC Grade: Not assignable.**

Moderate evidence indicates the relationship between resting blood pressure level and the magnitude of benefit does not vary by type (mode, i.e., aerobic, dynamic resistance, combined) of physical activity among adults with normal blood pressure and prehypertension. **PAGAC Grade: Moderate.**

Review of the Evidence

To answer this question, the Subcommittee reviewed 10 meta-analyses (Supplemental Table 5-1).[47-56] The coverage dates ranged from earliest coverage to 2016, the total number of included studies ranged from 9 to 93, and the total included study sample size consisted of 485,747 adults ranging from 233 to 330,222 participants. Two meta-analyses examined longitudinal prospective cohort studies,[55, 56] and eight meta-analyses examined randomized controlled trials.[47-54] The 10 meta-analyses[47-56] included adults with hypertension and normal blood pressure, while five included adults with prehypertension.[47, 48, 50, 51, 53] Because the literature reviewed for this question was based upon the JNC 7 blood pressure classification scheme, the Subcommittee used the JNC 7 blood pressure classification scheme[8] for data extraction purposes. The JNC 7 defines these blood pressure classifications as follows: Hypertension is defined as having a resting systolic blood pressure of 140 mmHg or greater and/or a resting diastolic blood pressure 90 mmHg or greater, or taking antihypertensive medication, regardless of the resting blood pressure level. Prehypertension is defined as a systolic blood pressure from 120 to 139 mmHg and /or diastolic blood pressure from 80 to 89 mmHg. Normal blood pressure is defined as having a systolic blood pressure less than 120 mmHg and diastolic blood pressure less than 80 mmHg. However, it should be noted that during the preparation of the 2018 Scientific Report, the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines released the 2017

Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults.[57] The new guidelines define hypertension as a resting systolic blood pressure of 130 mmHg or greater and/or a resting diastolic blood pressure 80 mmHg or greater, or taking antihypertensive medication, regardless of the resting blood pressure level. Furthermore, the term prehypertension was eliminated and elevated blood pressure was added indicating a resting systolic blood pressure between 120 to 129 mmHg and a diastolic blood pressure < 80 mmHg. However, the new guidelines did not alter the conclusion statements made in this report.

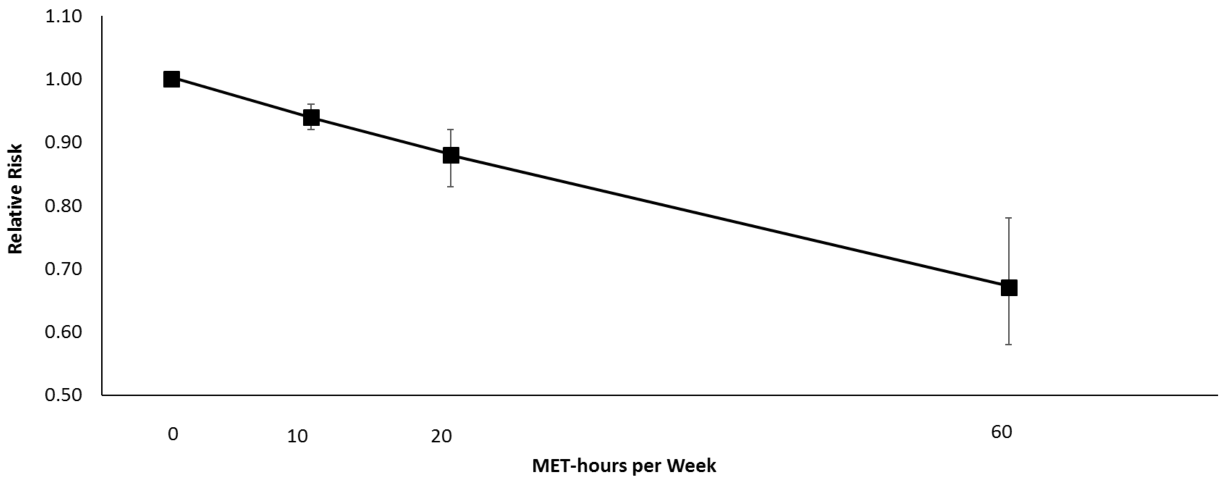
Evidence on the Overall Relationship

Strong evidence demonstrates that physical activity reduces blood pressure among adults with prehypertension and normal blood pressure. Eight meta-analyses of RCTs examined the blood pressure response to physical activity among initially sedentary adults with prehypertension[47, 48, 50, 51, 53] and/or normal blood pressure.[47-49, 51-54] Of the five meta-analyses involving adults with prehypertension, five reported a statistically significant reduction in systolic blood pressure and four reported a statistically significant reduction in diastolic blood pressure (see Supplementary Table S-F5-2). Of the seven meta-analyses involving adults with normal blood pressure, three reported a statistically significant reduction and one reported a statistically significant rise in systolic blood pressure, and six reported a statistically significant reduction in diastolic blood pressure (see Supplementary Table S-F5-2). Blood pressure reductions of the magnitude observed in these meta-analyses of about 2 to 5 mmHg for systolic blood pressure and 1 to 4 mmHg for diastolic blood pressure may be sufficient to reduce the risk of coronary heart disease by 4 to 5 percent and stroke by 6 to 8 percent among adults with prehypertension and normal blood pressure.[8, 58, 59] Furthermore, they may be of sufficient magnitude to lower the resting blood pressure of some samples with prehypertension into normotensive ranges. When studies disclosed the information, the frequency of physical activity ranged from 1 to 7 days per week, with 3 days per week most common; the intensity ranged from low to vigorous, with low to moderate most common; the time ranged from 8 to 63 minutes per session, with 30 to 60 minutes per session most common; and the study duration ranged from 4 to 52 weeks, with 16 to 20 weeks most common.

The Subcommittee also regarded the association between physical activity and the risk of developing hypertension (referred to as incident hypertension) as an indicator of the blood pressure response to physical activity. Huai et al[55] examined this association among 136,846 adults with normal blood pressure at baseline. After an average of 10 years (2 to 45 years) of follow up, 15,607 adults developed hypertension (11.4% of the sample). In this meta-analysis, high amounts (i.e., volume and/or intensity) of leisure-time physical activity were associated with a 19 percent decreased risk of incident hypertension compared to the referent group engaging in low amounts of leisure-time physical activity (relative risk (RR)=0.81; 95% CI: 0.76-0.85). Moderate amounts of leisure-time physical activity were associated with an 11 percent decreased risk of hypertension compared to the referent group engaging in low amounts of leisure-time physical activity (RR=0.89; 95% CI: 0.85-0.94). However, Huai et al[55] found no significant associations with occupational and commuting physical activity and incident hypertension.

Dose-response: Strong evidence demonstrates an inverse dose-response relationship between physical activity and incident hypertension among adults with normal blood pressure. Two meta-analyses investigated the relationship of physical activity and incident hypertension among adults with normal blood pressure.[55, 56] Of these, Liu et al[56] quantified the dose-response relationship between physical activity and incident hypertension among adults with normal blood pressure (Figure F5-3). Among 330,222 adults with normal blood pressure, after 2 to 20 years of follow up, 67,698 incident cases of hypertension occurred (20.5% of the sample). The risk of hypertension was reduced by 6 percent (RR=0.94; 95% CI: 0.92-0.96) at 10 MET-hours per week of leisure-time light, moderate, and vigorous physical activity (LMVPA) among adults with normal blood pressure. The protective effect increased by about 6 percent for each further increase of 10 MET-hours per week. For adults with 20 MET hours per week of leisure-time LMVPA, the risk of hypertension was reduced by 12 percent (RR=0.88; 95% CI: 0.83-0.92); and for those for 60 MET-hours per week of leisure-time LMVPA, the risk of hypertension was reduced by 33 percent (RR=0.67; 95% CI: 0.58-0.78). The relationship between leisure-time physical activity and incident hypertension was linear, with no cutoff of benefit, and slightly weaker with (RR=0.94; 95% CI: 0.92-0.96) than without (RR=0.91; 95% CI: 0.89-0.93) BMI adjustment. These same dose-response trends were seen for total physical activity such that for each 50 MET-hours per week increase in total physical activity, the risk of hypertension was reduced by 7 percent (RR=0.93; 95% CI: 0.88-0.98); and for 64.5 MET-hours per week of total physical activity, the risk of hypertension was reduced by 10 percent. The relationship between total physical activity and incident hypertension was linear, with no cutoff of benefit, and slightly stronger with than without BMI adjustment. The authors acknowledged their meta-analysis was limited by the considerable variety of physical activity self-report questionnaires used in the primary level studies.

Figure F5-3. Inverse Relationship Between Incident Hypertension and Leisure-Time Physical Activity, by MET-Hours per Week Among Adults with Normal Blood Pressure



Source: Adapted from data found in Liu et al., 2017.[56]

The available evidence is insufficient to determine whether a dose-response relationship exists between physical activity and incident hypertension among adults with prehypertension, as the magnitude and precision of the effect cannot be ascertained from findings that are too scarce to synthesize.

Evidence on Specific Factors

Demographic characteristics and weight status: The available evidence is insufficient to determine whether the relationship between physical activity and blood pressure varies by age, sex, race/ethnicity, socioeconomic status, or weight status among adults with prehypertension and normal blood pressure. In the few instances where age, sex, race/ethnicity, socioeconomic status, and weight status were examined as moderators of the blood pressure response to physical activity, the findings were too disparate to synthesize because they were often not reported separately by blood pressure classification but were reported for the overall sample that included adults with hypertension, prehypertension, and normal blood pressure.

Three meta-analyses found age not to be a significant moderator of the blood pressure response to physical activity,[47, 48, 56] but two of these contained samples with mixed blood pressure levels, and the other did not stratify analyses by age. One meta-analysis reported that men exhibited blood pressure reductions twice as large as did women following aerobic exercise training among samples with mixed blood pressure levels,[48] and another found no difference by sex.[56] Race/ethnicity was poorly reported, and when reported in three of the meta-analyses,[53, 55, 56] the samples primarily included White and some

Asian participants. Three meta-analyses reported the weight status of their samples, which ranged from normal weight to overweight.[47, 51, 53] Among a large sample of 330,222 adults with normal blood pressure who were followed for 2 to 20 years, Liu et al[56] found that the inverse dose-response relationship between leisure-time physical activity and incident hypertension was slightly weaker with (RR=0.94; 95% CI: 0.92-0.96) than without BMI adjustment (RR=0.91; 95% CI: 0.89-0.93), but these analyses were not stratified by BMI. These authors also found that the relationship between total physical activity and incident hypertension was slightly stronger with than without BMI adjustment, but these analyses were also not stratified by BMI. Cornelissen and Smart[48] found the systolic blood pressure reductions resulting from aerobic exercise training tended to be larger with greater ($\beta1=0.49$, $P=0.08$) than less ($\beta1=0.45$, $P=0.06$) weight loss among a sample of 5,223 adults with mixed blood pressure levels. Therefore, no conclusions can be made regarding the influence of age, sex, race/ethnicity, socioeconomic status, or weight status on the relationship between physical activity and blood pressure.

African Americans have the highest prevalence of hypertension of any ethnic group in the world.[60] The progression from prehypertension to hypertension is also faster among African Americans than Whites.[11] African Americans are more likely to have their hypertension identified and treated, but less likely to have their hypertension controlled than are Whites, despite using more antihypertensive medications.[61-63] As verified by this review, surprisingly little published research in the form of meta-analyses and systematic reviews exists on the association between physical activity and incident hypertension among African Americans. There are findings, however, from recent original studies, such as the Jackson Heart Study, that may also inform the association between physical activity and incident hypertension in African Americans.[64]

Resting blood pressure level: Strong evidence demonstrates the magnitude of the blood pressure response to physical activity varies by resting blood pressure level, with greater benefits occurring among adults with prehypertension than with normal blood pressure. Of the six meta-analyses examining blood pressure classification as a moderator of the blood pressure response to physical activity,[47-49, 51, 53, 54] four[48, 49, 51, 53] found that the greatest blood pressure reductions occurred among samples with hypertension (5 to 8 mmHg, 4 to 6 percent of resting blood pressure level) followed by samples with prehypertension (2 to 4 mmHg, 2 to 4 percent of resting blood pressure level), and normal blood pressure (1 to 2 mmHg, 1 to 2 percent of resting blood pressure level) (see online Supplemental Table 2). Consistent with the law of initial values,[65, 66] adults with prehypertension experience blood pressure reductions from exercise training that are about 2 to 4 times greater than the blood pressure reductions that occur among adults with normal blood pressure. Blood pressure reductions of this magnitude may be sufficient to reduce the resting blood pressure of some of the samples with prehypertension into normotensive ranges. They also may be sufficient to reduce the risk of coronary heart disease by 4 to 5 percent and stroke by 6 to 8 percent among adults with normal blood pressure and prehypertension.[8, 58, 59]

Frequency: The frequency of physical activity was reported in seven meta-analyses,[47-51, 53, 56] and ranged from 0 to 7 days per week. However, no conclusions can be made about the influence of frequency on the blood pressure response to physical activity because the findings were too scarce and too disparate to synthesize.

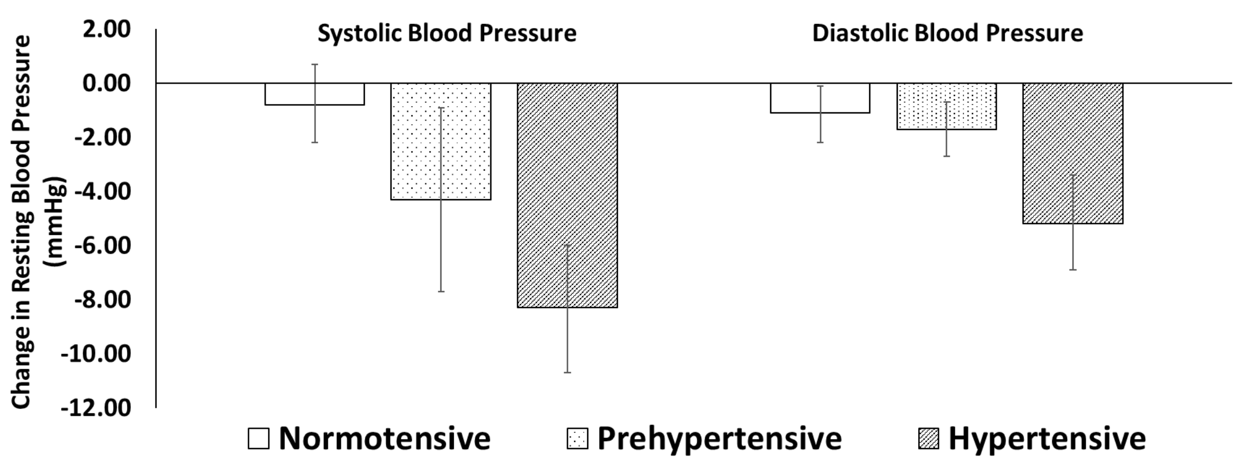
Intensity: The intensity of physical activity was reported in all meta-analyses,[47-56] and ranged from low to vigorous intensity. However, no conclusions can be made regarding the influence of intensity on the blood pressure response to physical activity as the magnitude and precision of the effect could not be determined from findings that were too scarce to synthesize.

Time: The time of the exercise session was reported in six meta-analyses,[48-51, 54, 56] and ranged from 12 to 63 minutes. Time was not disclosed in three meta-analyses.[47, 52, 53] However, no conclusions can be made regarding the influence of time on the blood pressure response to physical activity, as the magnitude and precision of the effect could not be determined from a lack of findings on the time of the exercise session.

Duration: All chronic (i.e., training) meta-analyses reported the duration of the physical activity intervention, and they ranged from 4 to 52 weeks.[47-51, 53, 54] However, no conclusions can be made regarding the influence of duration on the blood pressure response to physical activity as the magnitude and precision of the effect could not be determined from findings that were too scarce to synthesize.

Type (Mode): Moderate evidence indicates the relationship between resting blood pressure level and the blood pressure response to physical activity does not vary by type (i.e., aerobic, dynamic resistance, combined) of physical activity. Three meta-analyses examined the blood pressure response to aerobic exercise training,[48-50] three meta-analyses examined the blood pressure response to resistance exercise training (one acute[52] and two chronic),[47, 53] one meta-analysis examined the blood pressure response to combined aerobic and resistance exercise training (also referred to as concurrent exercise training),[51] and one meta-analysis examined the blood pressure response to isometric resistance training.[54] Cornelissen and Smart[48] examined aerobic exercise training performed, on average, at moderate to vigorous intensity for 40 minutes per session 3 days per week for 16 weeks and reported systolic/diastolic blood pressure reductions of -8.3 (95% CI: -10.7 to -6.0)/-5.2 (95% CI: -6.9 to -3.4), -4.3 (95% CI: -7.7 to -0.9)/-1.7 (95% CI: -2.7 to -0.7), and -0.8 (95% CI: -2.2 to +0.7)/-1.1 (95% CI: -2.2 to -0.1) mmHg among adults with hypertension, prehypertension, and normal blood pressure, respectively (Figure F5-4). MacDonald et al[53] examined dynamic resistance training performed, on average, at moderate intensity for 32 minutes per session 3 days per week for 14 weeks, which approximates 90 minutes of moderate intensity or 45 minutes of vigorous intensity physical activity per week, and reported systolic/diastolic blood pressure changes of -5.7 (95% CI: -9.0 to -2.7)/-5.2 (95% CI -8.4, -1.9), -3.0 (95% CI: -5.1 to -1.0)/-3.3 (95% CI: -5.3 to -1.4), and 0.0 (95% CI: -2.5 to 2.5)/-0.9 (95% CI: -2.1 to 2.2) mmHg among adults with hypertension, prehypertension, and normal blood pressure, respectively. Corso et al[51] examined combined aerobic and dynamic resistance exercise training performed, on average, at moderate intensity for 58 minutes per session 3 days per week for 20 weeks and reported systolic/diastolic blood pressure changes of -5.3 (95% CI -6.4 to -4.2)/-5.6 (95% CI -6.9 to -3.8), -2.9 (95% CI -3.9 to -1.9)/-3.6 (95% CI -5.0 to -0.2), and +0.9 (95% CI 0.2 to 1.6)/-1.5 (95% CI -2.5 to -0.4) mmHg among adults with hypertension, prehypertension, and normal blood pressure, respectively.

Figure F5-4. Blood Pressure Response to 16 Weeks of Aerobic Exercise Training



Source: Adapted from data found in Cornelissen and Smart, 2013.[48]

Carlson et al[54] investigated the blood pressure response to 4 or more weeks of isometric resistance training at 30 percent to 50 percent maximal voluntary contraction with 4 contractions held for 2 minutes with 1 to 3 minutes of rest between contractions among adults with hypertension (N=61) and normal blood pressure (N=162). Systolic, diastolic, and mean arterial blood pressure were reduced among the adults with hypertension, all of whom were on medication, by -4.3 (95% CI: -6.6 to -2.2)/-5.5 (95% CI: -7.9 to -3.3)/-6.1 (95% CI: -8.0 to -4.0) mmHg, and by -7.8 (95% CI: -9.2 to -6.4)/-3.1 (95% CI: -3.9 to -2.3)/-3.6 (95% CI: -4.4 to -2.7) mmHg among adults with normal blood pressure, respectively. Carlson et al[54] were unable to explain the larger reductions in systolic blood pressure among the adults with normal blood pressure compared to adults with hypertension, and the reverse pattern of blood pressure response for diastolic blood pressure and mean arterial pressure. The sample size of the meta-analysis by Carlson et al[54] investigating isometric resistance training was much smaller than the sample size of the meta-analyses investigating aerobic,[48] dynamic resistance,[53] and combined[51] exercise training. For these reasons, any conclusions made about the blood pressure benefits of isometric resistance training should be made with caution. It also should be noted that the existing literature included in this report on physical activity and blood pressure has examined aerobic, resistance, and combined types of physical activity.

Collectively, these findings indicate the blood pressure response to aerobic, dynamic resistance, and combined types of physical activity elicit blood pressure reductions of 2 to 4 mmHg (2 to 4 percent of resting blood pressure level) among adults with prehypertension and 1 to 2 mmHg (1 to 2 percent of resting blood pressure level) among adults with normal blood pressure, independent of type (mode). These blood pressure reductions are about 2 to 4 times greater among adults with prehypertension than normal blood pressure. These blood pressure benefits occurred at about 6 MET hours per week of moderate-to-vigorous physical activity.

How physical activity was measured: All meta-analyses that examined the blood pressure response to physical activity included interventions that were structured by the frequency, intensity, time, duration, and type (mode) of physical activity, but the details of these features of the physical activity interventions were not well disclosed. None of these meta-analyses reported any physical activity measure outside of the structured physical activity intervention. No conclusions can be made regarding how physical activity was measured, as the magnitude and precision of the effect could not be determined from findings that were too scarce to synthesize.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for Supplementary Tables S-F5-1 and S-F5-2 and the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report concluded that both aerobic and dynamic resistance exercise training of moderate-to-vigorous intensity produced small but clinically important reductions in systolic and diastolic blood pressure in adults, with the evidence more convincing for aerobic than dynamic resistance exercise.[1] The 2018 Scientific Report extends these findings in four ways. First, the 2018 Scientific Report provides strong evidence that physical activity reduces blood pressure among adults with prehypertension and normal blood pressure. Second, it provides strong evidence of an inverse dose-response relationship between leisure-time physical activity and incident hypertension among adults with normal blood pressure. Third, due to an accumulating amount of highly consistent evidence over the past decade, the 2018 Scientific Report provides strong evidence demonstrating the magnitude of the blood pressure response to physical activity is greater among adults with prehypertension than with normal blood pressure. Fourth, reflecting on the accumulating evidence over the past decade, the 2018 Scientific Report indicates aerobic and dynamic resistance exercise may be equally effective in reducing blood pressure at a lower volume of physical activity.

Public Health Impact

Hypertension is the most common, costly, and preventable cardiovascular disease risk factor. According to the JNC 7 blood pressure classification scheme, by 2030 it is estimated that nearly 40 percent of adults in the United States will have hypertension and almost an equal amount will have prehypertension. Due to the clinically important role of physical activity in the prevention of hypertension, adults with normal blood pressure and prehypertension are encouraged to engage in at least 90 minutes per week or more of moderate intensity or at least 45 minutes per week or more of vigorous intensity aerobic and/or dynamic resistance physical activity, or some combination of these. Because there appears to be no cut off to the amount of physical activity that confers benefit, even greater amounts of physical activity should be encouraged. These recommendations are particularly important for African Americans to reduce the high disease burden of hypertension among this population group.

Question 3. In adults without diabetes, what is the relationship between physical activity and type 2 diabetes?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship vary based on: frequency, duration, intensity, type (mode), and how physical activity is measured?

Sources of evidence: Systematic reviews, meta-analyses, pooled analysis

Conclusion Statements

Strong evidence demonstrates a significant relationship between a higher volume of physical activity and lower incidence of type 2 diabetes. **PAGAC Grade: Strong.**

Strong evidence demonstrates that an inverse curvilinear dose-response relationship exists between the volume of physical activity and incidence of type 2 diabetes, with a decreasing slope at higher levels of physical activity. **PAGAC Grade: Strong.**

Moderate evidence indicates no effect modification by weight status. An inverse relationship exists between a higher volume of physical activity and lower incidence of type 2 diabetes for people who have normal weight, overweight, or obesity. **PAGAC Grade: Moderate.**

Limited evidence suggests that the relationship between a higher volume of physical activity and lower incidence of type 2 diabetes is not influenced by age, sex, or race/ethnicity. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between physical activity and the incidence of type 2 diabetes varies by socioeconomic status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and the incidence of type 2 diabetes varies by the frequency, intensity, duration, or type of physical activity, or how physical activity is measured. **PAGAC Grade: Not assignable.**

Review of the Evidence

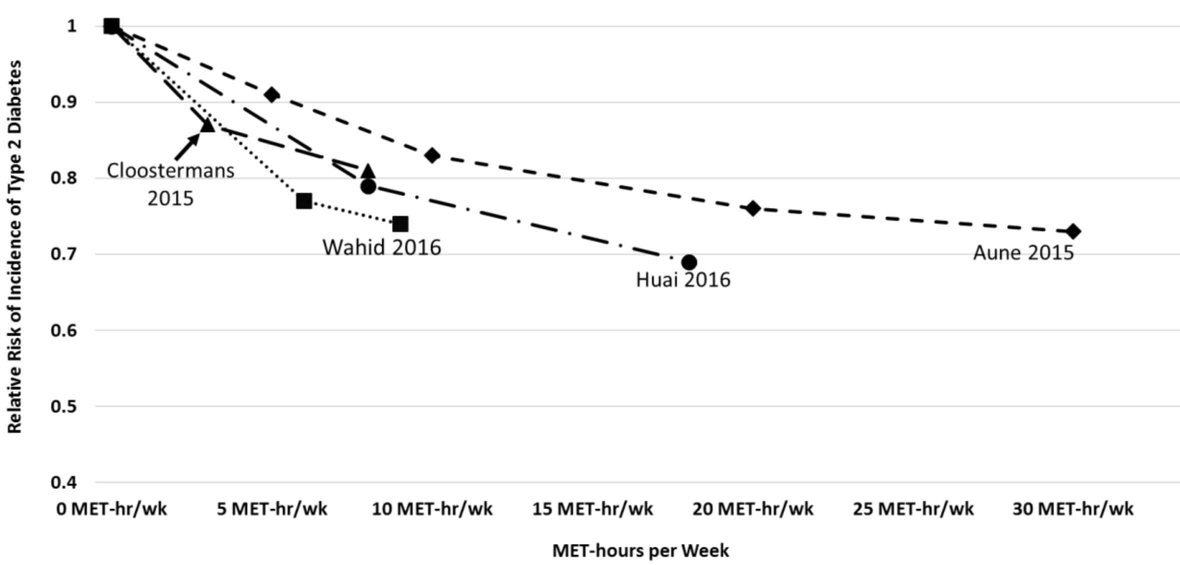
The evidence base comprised seven meta-analyses,[67-73] four systematic reviews,[74-77] and one pooled analysis.[78] Ten[68-71, 73-78] of the articles included only cohort studies, one included cohort and experimental studies,[72] and one included cohort, experimental, and case-control studies.[67] The number of studies included in each review ranged from 2 to 81, with a median of 8.5. For the eight reviews for which data on number of participants were provided, the total number ranged from 4,550 to about 300,000, with a median of 140,000. All reviews except one, which had no age restrictions,[67] included only adults. Mean age was not commonly provided; the three studies for which it was provided reported a mean age of 50[68, 72] and 52[78] years. Almost all physical activity behavior was self-reported leisure-time moderate-to-vigorous, though a few studies included other domains (i.e., occupational, transportation, household).[67, 68, 71, 77] Seven reviews provided risk estimates for at least three doses of physical activity, enabling an assessment of dose-response.[67-69, 71, 73, 74, 76]

Evidence on the Overall Relationship

All meta-analyses,[67-73] systematic reviews,[74-77] and the pooled analysis[78] reported an inverse relationship between volume of physical activity and the incidence of type 2 diabetes. Three meta-analyses,[67, 70, 72] one systematic review,[77] and the pooled analysis[78] provided quantitative estimates of the reduction in risk comparing participants engaging in "high" volume of physical activity with participants engaging in "low" volume of physical activity. The volume of physical activity represented by "high" and "low" was not provided. It is expected that "high" is at or near the target zone recommended in the 2008 Scientific Report for moderate-to-vigorous physical activity (i.e., 150 to 300 minutes per week of moderate intensity physical activity, 75 to 150 minutes per week of vigorous intensity physical activity, or an equivalent combination)[1] and "low" is at or near zero reported moderate-to-vigorous physical activity. The estimated relative risks and 95% confidence interval for these four studies were: 0.65 (95% CI: 0.59-0.71) for total physical activity and 0.74 (95% CI: 0.70-0.79) for leisure-time physical activity[67]; 0.69 (95% CI: 0.58-0.83) without adjustment for BMI and 0.83 (95% CI: 0.76-0.90) with adjustment for BMI[70]; odds ratios of 0.53 (95% CI: 0.40-0.70)[72]; and 0.45 (95% CI: 0.31-0.77).[78] Warburton et al,[77] a systematic review including 20 pertinent cohort studies, reported that all 20 studies found an inverse relationship between volume of moderate-to-vigorous physical activity and risk of type 2 diabetes, and that comparing the highest with the least active participants, the average risk reduction was 42 percent. These findings suggest that a reasonable estimate of the reduction in type 2 diabetes associated with 150 to 300 minutes per week of moderate to vigorous physical activity would be about 25 to 35 percent.

Dose-response: Five of the meta-analyses provided estimates for at least three levels of moderate-to-vigorous physical activity (Figure F5-5). Aune et al[67] reported that "there was evidence of a nonlinear association between MET-hours per week of leisure-time physical activity and type 2 diabetes ($P_{\text{nonlinearity}}$ <0.0001), with a slightly more pronounced reduction in risk at low levels of activity than at high levels." Cloostermans et al[68] calculated OR of 1.0 for 150 or more minutes per week of moderate-to-vigorous physical activity, OR of 1.08 (95% CI: 1.04-1.13) for more than 0 to less than150 minutes per week of moderate-to-vigorous physical activity, and OR of 1.23 (95% CI: 1.04-1.39) for 0 minutes per week of moderate-to-vigorous physical activity. All the Cloostermans et al[68] values have been divided by 1.23 in Figure F5-5, below, to match the orientation of the other meta-analyses (i.e., lowest activity group is the referent group with relative risk of 1.0). Huai et al[69] calculated hazard ratios for participants grouped into those with low (HR=1.0), moderate (HR=0.79; 95% CI: 0.70-0.89), and high (HR=0.69; 95% CI: 0.61-0.78) volumes of physical activity. Wahid et al[73] provided relative risk estimates of 0.77 (95% CI: 0.71-0.84) at 6 MET-hours per week and 0.74 (95% CIs not provided) at 11.25 MET-hours per week. The dose-response curves from these four reviews are shown in Figure F5-5. The shape of the dose-response curve for the fifth review that provided estimates for at least three levels of physical activity is similar to the curves from the four studies shown in Figure F5-5.[71] The curve is not included because the units for volume of physical activity are incompatible with the other studies. Kyu et al[71] combined and extrapolated domain-specific moderate-to-vigorous physical activity into total MET-minutes per week of MVPA and, using <600 MET-minutes per week as the referent value, reported risk reductions of 14 percent for 600 to 3,999 MET-minutes per week, 25 percent for 4,000 to 7,999 MET-minutes per week, and 28 percent for 8,000 or more MET-minutes per week. In a systematic review, Warburton et al[77] reported that the majority (84%) of the 20 included studies revealed incremental reductions in the risk for type 2 diabetes with increasing activity/fitness levels.

Figure F5-5. Dose-response Curves for Moderate-to-Vigorous Physical Activity and Relative Risk of Type 2 Diabetes



Source: Adapted from data found in Cloostermans et al., 2015,[68] Wahid et al., 2016,[73] Huai et al., 2016,[69] Aune et al., 2015.[67]

These findings indicate an inverse curvilinear relationship between volume of moderate-to-vigorous physical activity and the reduction in risk of type 2 diabetes, with a decreasing slope at higher levels of physical activity. This indicates that less active individuals who add a certain amount of physical activity to their daily routine reduce their risk of developing type 2 diabetes to a larger extent than more physically active individuals who add the same amount of physical activity to their daily routine. The absolute risk of the more physically active individuals remains below that of the less active individuals; their relative reduction in risk per unit of added physical activity is merely lower. Two of the articles included statistically significant risk reduction estimates for volumes of physical activity below the current target of 150 to 300 minutes per week of moderate-to-vigorous,[68, 73] confirming that benefit accrues below the target zone.

Evidence on Specific Factors

Physical activity, weight status, and risk of type 2 diabetes: The relationship between physical activity, weight status, and risk of type 2 diabetes is complicated because weight status affects risk of type 2 diabetes and physical activity affects risk of type 2 diabetes and weight status (for more details on this relationship see Question 1 in this chapter). When populations are stratified by BMI, higher levels of physical activity are associated with reduced risk of type 2 diabetes at all strata of BMI. For example, in a joint analysis of three physical activity behavior groups (low = 0 minutes per week of self-reported moderate-to-vigorous, middle = >0 to <150 minutes per week, high = ≥150 minutes per week) and BMI strata, among individuals with overweight (25 to <30 kg/m^2), the hazard ratio for the high active group was 2.26 (95% CI: 1.74–2.93), the middle active group was 2.45 (95% CI: 1.87–3.20), and the low active group was 2.86 (95% CI: 1.93–4.22). Among individuals with obesity (≥30 kg/m^2), the hazard ratio for the high active group was 6.13 (95% CI: 4.25–8.84), the middle active group was 6.93 (95% CI: 4.20–11.43), and the low active group was 7.43 (95% CI: 3.47–15.89).[68] Similar findings are reported in the systematic review by Fogelholm.[74]

Evidence also suggests that the combination of low levels of physical activity and high levels of adiposity, usually assessed as BMI, is a stronger risk factor for type 2 diabetes than one would expect if they were acting independently of each other. Qin et al[75] identified five articles that provided enough information for them to calculate estimates of the "biological interaction." The "attributable portion(s) due to biological interaction" were 46 percent,[79] 42 percent,[80] 29 percent,[81] 22 percent,[82] and 5 percent.[83] The analyses indicate that a substantial portion of the reduction in risk for type 2 diabetes (median value 29% of the five studies) is due to the combined effect of physical activity and adiposity.

Given this interaction and the known contribution of obesity to the risk of developing type 2 diabetes, it is not surprising that adjusting for BMI reduces the magnitude of the risk reduction attributable to physical activity.[67, 68, 70, 76, 77] For example, Jeon et al[70] in a high versus low comparison, reported a relative risk of 0.69 (95% CI: 0.58-0.83) without adjustment for BMI and a relative risk of 0.83 (95% CI: 0.76-0.90) with adjustment for BMI.

Age, sex, race/ethnicity, socioeconomic status: Although the importance of weight status as a risk factor for type 2 diabetes was uniformly acknowledged in these reports, the studies provide little information about demographic factors such as age, sex, or race/ethnicity. Information in a few suggest age, sex, and race/ethnicity have little or no impact on the relationship between physical activity and type 2 diabetes.[67, 68, 78] No conclusion could be made about the impact of socioeconomic status because none of the studies provided information about this variable.

Type of physical activity: The physical activity of interest in these papers was largely restricted to moderate-to-vigorous aerobic physical activity. The Subcommittee was unable to draw a conclusion because the studies provided no information about whether frequency, duration, intensity, type of physical activity, or the way physical activity was measured had any influence on the relationship between physical activity and the incidence of type 2 diabetes.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report[1] concluded that "approximately 30 minutes of moderate intensity exercise at least 5 days per week provides a substantial (25% to 36%) reduction in the risk of type 2 diabetes".[1] This evidence review confirms that estimate and expands on the previous findings by providing evidence for an inverse curvilinear dose-response association, demonstrating that risk reductions accrue at levels below the target range of 150 to 300 minutes per week of moderate-to-vigorous physical activity, and providing evidence of an interaction, but no effect modification, between physical activity and weight status.

Public Health Impact

Currently about 9.4 percent of the U.S. adult population has type 2 diabetes, with associated annual direct medical costs and lost productivity of about $245 billion per year.[12, 13] The evidence presented here confirms that about 150 to 300 minutes per week of moderate-to-vigorous physical activity reduces the risk of developing type 2 diabetes by 25 to 35 percent. This applies to people with normal weight, overweight, or obesity. Given that less than half of the U.S. population currently participates in 150 minutes or more per week of moderate-to-vigorous physical activity, the potential reduction in incidence and costs of type 2 diabetes is substantial.[84] Moreover, the fact that physical activity reduces the risk of excessive weight gain means that the reduction in risk could be even greater because excessive weight is an independent risk factor for type 2 diabetes.

NEEDS FOR FUTURE RESEARCH

1. Conduct longitudinal research on lower exposure levels of physical activity to allow for an enhanced understanding of the dose-response associations between physical activity and weight gain, hypertension, and type 2 diabetes across a wider spectrum of exposure.

   Rationale: Only limited evidence is currently available on the effect of physical activity less than 150 minutes per week on prevention of weight gain, hypertension, and type 2 diabetes. Thus, limited data are currently available to inform whether lower amounts of physical activity can be effective for preventing these conditions. Having this knowledge is important and will inform public health recommendations regarding the minimum physical activity exposure that can be effective for preventing weight gain or the development of obesity, hypertension, and type 2 diabetes.

2. Conduct large research trials with ample sample sizes to allow for stratum-specific analyses to determine whether the influence of physical activity on the prevention of weight gain, hypertension, and type 2 diabetes varies by age, sex, race/ethnicity, socioeconomic status, or initial weight status.

   Rationale: Only limited evidence is currently available on whether the influence of physical activity on weight gain or risk of hypertension or type 2 diabetes varies by age, sex, race/ethnicity, socioeconomic status, weight status. Moreover, little is known about whether the influence of physical activity varies when the exposure to physical activity is consistent across individuals with different demographic characteristics. Having this information will inform public health recommendations regarding whether physical activity exposure to prevent weight gain needs to vary by age, sex, race/ethnicity, socioeconomic status, weight status, and other demographic characteristics, and may allow for more precise individual-level physical activity recommendations. Thus, adequately designed and statistically powered studies are needed to allow for comparisons across the various strata of demographic characteristics to examine whether the influence of physical activity varies by these factors.

3. Conduct experimental research on varying intensities (light, moderate, and vigorous) of physical activity, while holding energy expenditure constant, to determine the independent effects of physical activity intensity on weight gain, hypertension, and type 2 diabetes.

   Rationale: Limited evidence is available on whether the influence of physical activity on weight gain, hypertension, or type 2 diabetes is consistent across intensities (light, moderate, vigorous) when total energy expenditure is held constant, and only limited evidence is available on the influence of light-intensity physical activity on weight gain. This information will inform public health recommendations regarding whether the emphasis to prevent weight gain, hypertension, or type 2 diabetes should be on total volume of physical activity regardless of intensity, or whether the emphasis needs to be on volume of physical activity that is performed at a specific intensity.

4. Conduct observational and experimental research that quantifies energy intake and eating behavior to determine whether these factors influence the association between physical activity and weight gain.

   Rationale: The majority of the studies examined regarding weight gain either did not report that diet and eating behavior were measured or considered in the analysis. Given that both dietary factors, primarily energy intake, and energy expenditure from physical activity can influence body weight regulation, it is important to understand whether the physical activity exposure necessary to limit weight gain will vary based on diet or eating behavior patterns.

5. Within research that is conducted, disclose the standard criteria and methods that were used to determine the blood pressure status of the study sample to better isolate samples with hypertension from those with normal blood pressure and prehypertension, and report results separately by blood pressure classification.

   Rationale: Strong evidence demonstrates the magnitude of the blood pressure response to physical activity varies by resting blood pressure, with greater benefits occurring among adults with prehypertension than normal blood pressure. However, study samples often include mixed samples of adults with hypertension, prehypertension, and normal blood pressure, and findings are frequently not reported separately by blood pressure classification. Consistent with the law of initial values, this practice underestimates the blood pressure benefits of physical activity. In addition, samples with prehypertension are underrepresented as they are often mixed with samples with hypertension. Reporting findings by blood pressure classification will inform public health recommendations on the magnitude and precision of the blood pressure reductions that result from physical activity among adults with normal blood pressure and prehypertension.

6. Conduct randomized controlled trials to examine the influence of types of physical activity other than aerobic, dynamic resistance, or combined aerobic and dynamic resistance physical activity on blood pressure and other health outcomes among adults with normal blood pressure and prehypertension.

   Rationale: Limited evidence on these topics is available among adults with normal blood pressure and prehypertension. Gaining this information will inform the public health recommendations on the types of physical activity that optimize blood pressure benefit.

7. Conduct experimental research that examines both the acute (i.e., short-term or immediate, referred to as postexercise hypotension) and the chronic (i.e., long-term or training) blood pressure response to physical activity among adults with prehypertension and normal blood pressure.

   Rationale: Insufficient evidence exists on the acute blood pressure response to physical activity despite primary-level reports suggesting a close relationship between the blood pressure response to acute and chronic exercise. Developing a better understanding of acute blood pressure responses will inform public health recommendations on possible behavioral strategies to increase adherence to physical activity for blood pressure benefit.

8. Conduct observational and experimental research examining the relationship between physical activity and blood pressure using the 2017 *Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults*[57] new blood pressure classification scheme.

   Rationale: The literature that was reviewed to answer this question was based upon The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) blood pressure classification scheme.[8] The new guideline increases the number of people with hypertension, eliminates the category of prehypertension, and adds the category of elevated blood pressure. The relationship between physical activity and blood pressure according to this new blood pressure classification scheme remains to be determined.

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