

Series Editor: A. Maziar Zafari, MD, PhD, FACC

Physical Activity and the Metabolic Syndrome

Benjamin D. Mackie, MD

A. Maziar Zafari, MD, PhD, FACC

Total daily physical activity, which is the sum of all occupational, household, and leisure-time activities, has declined over the past few decades. Participation in leisure-time as well as occupational physical activities has declined in part because of increased automation and use of technology. Time spent at sedentary occupations or in work-related activities (eg, passive commuting) has been increasing and may be expected to have a negative impact on total physical activity, and in turn, physical fitness.

In the United States, physical inactivity is rampant and is prevalent among women and men (**Figure 1**). Data from the US Centers for Disease Control and Prevention (CDC) show that 21.4% of men and 25.9% of women are physically inactive (**Table 1**).¹ In parallel with the decline in total physical activity, the prevalence of obesity, hypertension, type 2 diabetes, and the metabolic syndrome has been rising dramatically worldwide. Cross-sectional studies have demonstrated that body mass index (BMI) is inversely related to objectively measured physical activity.²

The purpose of this review, the sixth part in a series on the metabolic syndrome,³⁻⁷ is to provide the reader with a general understanding of the relationship between physical activity and cardiovascular health, in particular the contribution of physical inactivity to the pathophysiology of metabolic syndrome and the role of increasing physical activity in the management of this syndrome.

PHYSICAL INACTIVITY AND SEDENTARY LIFESTYLE

Obesity has reached epidemic proportions in the Western world, with the most recent data from the 2003–2004 National Health and Nutrition Examination Survey (NHANES) showing that nearly two thirds of the adult population in the United States is either overweight or obese. Also, 17.1% of adolescents are overweight (BMI > 95th percentile for age and sex), and an additional 16.5% are at risk for overweight (BMI > 85th percentile for age and sex).⁸ A major contributing factor to this epidemic is a lack of exercise in a significant proportion of the population. According to a survey published by the CDC, over half of US adults do not

TAKE HOME POINTS

- Physical inactivity carries a relative risk for coronary heart disease of 1.5 to 2.4, which is comparable to that of smoking and hypercholesterolemia. Over half of US adults do not perform the minimum amount of exercise needed to prevent disease.
- Physical activity is inversely related to age, smoking, hypertension, body mass index, waist-to-hip ratio, total and non-high-density lipoprotein cholesterol, and triglycerides, whereas these factors are directly related to C-reactive protein concentrations.
- Strategies targeting the underlying risk factors of obesity, physical inactivity, and atherogenic diet are the most efficacious treatments for and the only effective prevention of metabolic syndrome.
- Greater cardiorespiratory fitness is associated with primary prevention of metabolic syndrome, especially in patients who have already started to develop components of the syndrome.
- Measuring ambulatory activity with an inexpensive, precise, accurate, and objective monitoring device, such as a pedometer, can help to encourage patients to achieve their daily activity goals.

perform the minimum amount of exercise needed to prevent diseases, despite the well-documented benefits of exercise, which include reducing the risk of cardiovascular disease, improving glycemic control in diabetes, improving blood pressure, and alleviating depression.⁹ In addition, the proportion of persons who do not exercise is higher among women than men and

Dr. Mackie is an internal medicine resident, Department of Medicine, Emory University School of Medicine. Dr. Zafari is an associate professor and director, Cardiovascular Training Program, Division of Cardiology, Emory University School of Medicine, Atlanta, GA.

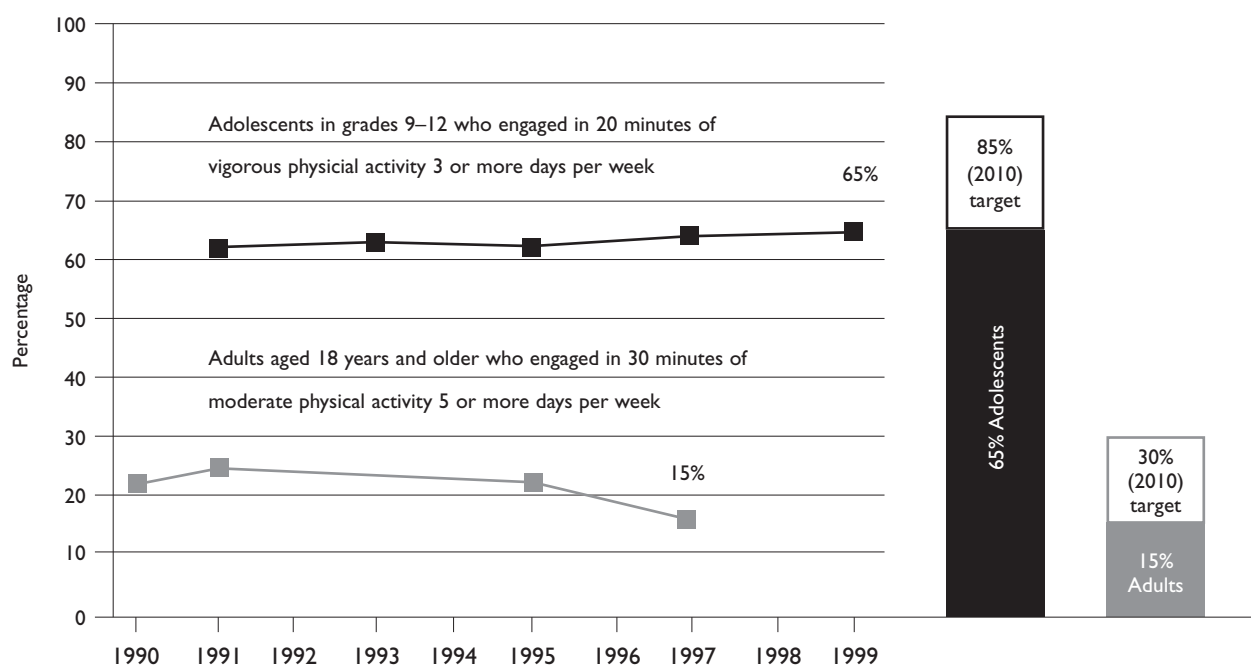


Figure 1. Participation in regular physical activity in the United States, 1990–1999. (Adapted from the Healthy People 2010 Slideshow. Physical activity leading health indicator. Slide 20. Available at www.healthypeople.gov/About/Slideshow_May_2001_files/frame.htm. Accessed 31 Jul 2006.)

among minority populations (Table 1). In recent years, the CDC survey underwent revision and used new criteria for defining exercise in order to give a more comprehensive picture of people’s daily lifestyles. Moderate activities were considered to be things such as walking, yard work, and some household activities. Although a greater percentage of people did exercise under this new definition, the proportions of adults who do not perform the minimum amount of exercise needed to prevent diabetes or hypertension (55%) and who do not exercise at all (15.6%) remain too high. Additionally, these figures may be underestimates due to reporting bias (ie, survey participants often try to respond in ways that make them appear healthy).

Effects on Cardiovascular Risk

Physical inactivity has significant consequences. The relative risk of coronary heart disease associated with physical inactivity ranges from 1.5 to 2.4, which is comparable to the relative risks for smoking or hypercholesterolemia.¹ Physical inactivity caused by television watching has an additional association with atherosclerosis risk factors and obesity (Table 2).¹⁰ A more active lifestyle generally leads to lower risk for cardiovascular disease, and recent research has concentrated on leisure-time physical activity. Data from an observational study showed that increasing physical activity had

Table 1. Prevalence of Leisure-Time Physical Inactivity by Gender and Race, in US Adults Aged 18 Years and Older

Population Group	Men (%)	Women (%)
Total	21.4	25.9
Non-Hispanic whites	18.4	21.6
Non-Hispanic blacks	27.0	33.9
Hispanic	32.5	39.6
American Indian/ Alaska native	23.8	31.8
Asian/Pacific Islander	20.4	24.0

Data from US Centers for Disease Control and Prevention (CDC). Trends in leisure-time physical inactivity by age, sex, and race/ethnicity—United States, 1994–2004. *MMWR Morb Mortal Wkly Rep* 2005;54:991–4.

a strong, graded, inverse association with the risk of coronary events and total cardiovascular events among white and black women, with a risk reduction of greater than 50% for women in the highest quintile of physical activity.¹¹ Walking and vigorous exercise were associated with similar risk reductions, and the results applied to women of all categories of race, age, and BMI. Fewer hours spent sitting daily also predicted lower risk.¹¹ Data from the Harvard Alumni Study showed that more exercise was inversely related to risk of myocardial infarction

Table 2. Influence of Leisure-Time Physical Activity and Television Watching on Carotid IMT*

	Women			Men		
	Coefficient	SE	P	Coefficient	SE	P
Minimal model						
Age	0.0105	0.0005	0.0001	0.0129	0.0006	0.0001
Activity level at work	†	†	0.95	†	†	0.11
Leisure-time physical activity [‡]	-0.0001	0.0009	0.11	-0.00006	0.0007	0.93
Television watching	0.0019	0.0048	0.69	0.0006	0.0053	0.91
Extended model						
Age	0.0091	0.0006	0.0001	0.0125	0.0007	0.0001
Activity level at work	†	†	0.87	†	†	0.11
Leisure-time physical activity [‡]	0.0002	0.0008	0.81	0.0002	0.0006	0.80
Television watching	-0.0025	0.0048	0.61	-0.0038	0.0052	0.47
BMI*	-0.1259	0.0623	0.0439	-0.2718	0.1076	0.0120
Waist circumference	0.0026	0.0008	0.0013	-0.0024	0.0013	0.0703
HDL cholesterol	-0.0013	0.0004	0.0024	-0.0020	0.0020	0.0040
LDL cholesterol	0.0004	0.0002	0.609	0.0006	0.0002	0.0167
Blood glucose	0.0001	0.0008	0.90	0.0022	0.0009	0.0103
Alcohol (drink/day)	-0.0012	0.0021	0.57	0.0065	0.0021	0.0019
Systolic blood pressure	0.0020	0.0004	0.0001	0.0003	0.0006	0.59
Current smoking	0.0450	0.0191	0.0191	0.0305	0.0211	0.15

Adapted from Kronenberg F, Pereira MA, Schmytz MKH, et al. Influence of leisure-time physical activity and television watching on atherosclerosis risk factors in the NHLBI family heart study. *Atherosclerosis* 2000;153:441. Copyright 2000, with permission from Elsevier.

BMI = body mass index; HDL = high-density lipoprotein; IMT = intima-media thickness; LDL = low-density lipoprotein; MET = metabolic equivalents; SE = standard error.

*Carotid IMT and BMI were logarithmically transformed before inclusion into the model and investigated by multiple regression analysis.

†No estimates are given because activity level at work has more than 2 classes.

‡Coefficient and SE are based on a 100 weekly MET-minutes increment of total leisure-time physical activity.

over an 8-year interval.¹² This result and others showed that physical activity and greater fitness were important in reducing cardiovascular disease risk in men and women.¹³ Persons in the lowest quintiles of fitness have experienced the highest cardiovascular disease event rates; even modest degrees of fitness were related to lower risk of cardiovascular disease in studies of middle-aged men and women.¹⁴

Effects on Inflammation

There is increasing evidence that inflammation and oxidative stress not only contribute to the atherosclerotic process^{15,16} but are intricately involved in the development of other chronic conditions, such as hypertension, diabetes, metabolic syndrome, cancer, and Alzheimer's disease.^{17,18} C-reactive protein (CRP), a serum marker of acute and chronic inflammation, is a predictor of disease and has characteristics that make it conducive for clinical use.¹⁹ This inflammatory marker

has shown a dose-response relationship to cardiovascular disease that is independent of other major risk factors. It is well documented that physical activity has a role in preventing cardiovascular disease,¹⁹ mediated in part by changes in inflammation.²⁰

Cross-sectional studies have demonstrated an inverse relationship between regular physical activity and the serum concentration of inflammatory markers. In a study that examined the effect of leisure-time physical activity on inflammatory markers in 13,748 adults from NHANES III, physical activity was inversely associated with CRP levels.²¹ This association remained significant after adjusting for such potential confounders as age, gender, ethnicity, education, occupation, smoking, hypertension, BMI, waist-to-hip ratio, high-density lipoprotein cholesterol, aspirin use, chronic disease affecting CRP, and serum insulin. Another study examined changes in physical activity over 20 years and showed that inactive men who became active had CRP values

approaching those of men who remained at least lightly active.²⁰ Conversely, men who became inactive had CRP levels similar to those who remained inactive, suggesting that physical activity has to be continuous to maintain its effect on CRP, whereas starting physical activity in later life can still alter CRP levels.

To eliminate reporting bias, several studies have examined the relationship of cardiorespiratory fitness to CRP. A cross-sectional survey of 892 middle-aged men and women noted that cardiorespiratory fitness was inversely related to CRP levels in a stepwise fashion.²² For each 1-unit increase in metabolic equivalents, the mean CRP level decreased by 0.061 mg/L. These trials support the concept that increased physical activity reduces CRP levels by altering the inflammatory process.

Mechanisms of reduction in CRP levels with physical activity. Physical activity is related to several risk factors that are independently associated with lower CRP levels. For example, physical activity is inversely related to age, smoking, hypertension, BMI, waist-to-hip ratio, total and non-high-density lipoprotein cholesterol, and triglycerides, whereas these factors are directly related to CRP concentrations.²¹ Similarly, physical activity is directly related to the proportion of white participants included in studies, education level, insulin sensitivity, alcohol consumption, and fruit and vegetable intake, all factors that are inversely associated with CRP.²¹

Physical activity may also mitigate inflammation by improving endothelial function. Endothelial cells are known to produce interleukins and adhesion molecules that induce inflammation. Physical training reduces peripheral inflammatory markers associated with endothelial dysfunction²³ and improves endothelial function by preserving nitric oxide availability.²⁴ Nitric oxide is critical for maintaining vascular tone, inhibiting platelet aggregation and monocyte adhesion to the endothelium, inhibiting vascular smooth muscle growth, and finally, inhibiting the oxidation of low-density lipoprotein cholesterol.²⁵ Although exercise acutely increases oxidative metabolism and thereby induces oxidative stress, there is evidence that long-term physical activity increases antioxidant defenses through the upregulation of endothelial nitric oxide synthase and antioxidant enzymes.²⁶ Furthermore, this antioxidant effect of exercise reduces the susceptibility of low-density lipoprotein cholesterol to oxidation, which in turn helps to further prevent vascular injury and inflammation.²⁷ Thus, it is likely that physical activity reduces CRP by reducing cytokine production and oxidative stress as well as by increasing insulin sensitivity, improving nitric oxide bioavailability and endothelial function, and reducing body weight.

Table 3. Examples of Moderate Amounts of Physical Activity

Walking 2 miles in 30 minutes
Gardening for 30–45 minutes
Washing windows or floors for 45–60 minutes
Stair-walking for 15 minutes
Bicycling 5 miles in 30 minutes
Dancing fast for 30 minutes
Swimming laps for 20 minutes

FORMS OF ACTIVITY THAT IMPROVE RISK FACTORS

Physical activity can be characterized as any movement that requires skeletal muscles and therefore increases energy expenditure over resting metabolic rate.²⁸ Forms of exercise include aerobic activity and resistance exercise. Physical fitness is defined as the combination of cardiorespiratory fitness, muscle strength, and flexibility. Aerobic exercise consists of rhythmic, repeated, and continuous movements of the same large muscle for at least 10 minutes at a time.²⁹ When aerobic exercise is performed at sufficient intensity and frequency for several months, maximal oxygen uptake improves by 15% to 25% in previously sedentary individuals. Examples of aerobic activity include walking, jogging, bicycling, and swimming (**Table 3**). Resistance exercise consists of activities that use muscular strength to move a weight or move against a resistive load. When performed regularly and at moderate to high intensity, resistance exercise increases muscular fitness and muscular endurance. By increasing muscle mass and endurance, resistance exercise training can produce more rapid changes in functional status and body composition than aerobic training. Resistance exercise also improves insulin sensitivity to a similar extent as aerobic exercise. Examples of resistance exercise include weight lifting and exercises using weight machines.

Moderate physical activity can improve cardiorespiratory function, produce weight loss and changes in body composition, and improve risk factors for the metabolic syndrome and cardiovascular disease. In addition, studies indicate that multiple daily short bouts of moderate physical activity produce similar improvements in risk factors for disease compared with a single daily session (> 30 min) of moderate physical activity.³⁰ Physical activity does not need to be vigorous (> 60% maximal oxygen uptake; > 70% maximal heart rate) to produce positive health benefits. Based on the above data, moderate intensity activity has an important role to play in the modification of risk factors for cardiovascular disease and the metabolic syndrome.

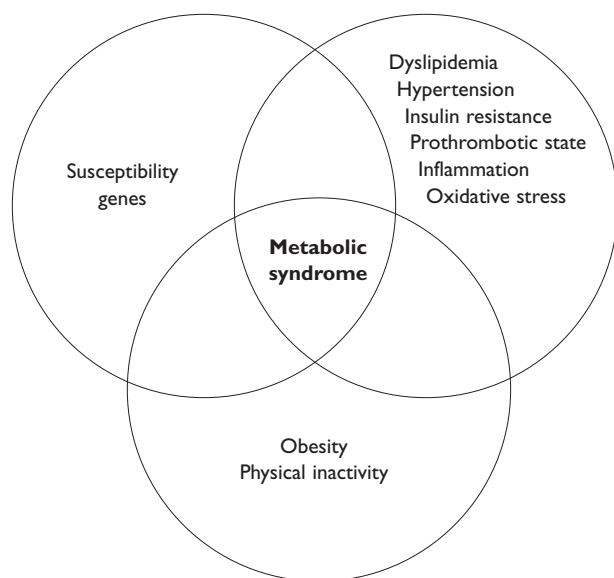


Figure 2. Complexity of the causes of metabolic syndrome.

PHYSICAL ACTIVITY AND THE METABOLIC SYNDROME

The metabolic syndrome is characterized by the presence of obesity, hypertension, insulin resistance, glucose intolerance, and dyslipidemia.³ Moreover, individuals exhibiting 1 or more signs of the metabolic syndrome tend to be 20% to 30% less active than healthy subjects. Inactivity is associated not only with body weight but with the other elements of the metabolic syndrome as well (Figure 2). The most efficacious treatments and the only effective approaches to preventing the metabolic syndrome are aimed at the underlying risk factors of obesity, physical inactivity, and atherogenic diet. Most recently, LaMonte and colleagues³¹ reported evidence from their prospective follow-up database of subjects examined at the Cooper Aerobic Center showing that cardiorespiratory fitness is a strong and independent predictor of the risk of developing metabolic syndrome in men and women over time (Figure 3).

All 5 criteria of the metabolic syndrome are improved by exercise. Skeletal muscle is the most insulin-sensitive tissue in the body and, therefore, a primary target for impacting insulin resistance. Physical training has been shown to improve skeletal muscle insulin sensitivity and insulin resistance.³² Lack of physical exercise and excess caloric intake lead to the development of obesity, which is associated with an increase in plasma free fatty acid (FFA) availability. The structural imbalance between FFA uptake, lipid storage, and fatty acid oxidation results in progressive intramuscular ac-

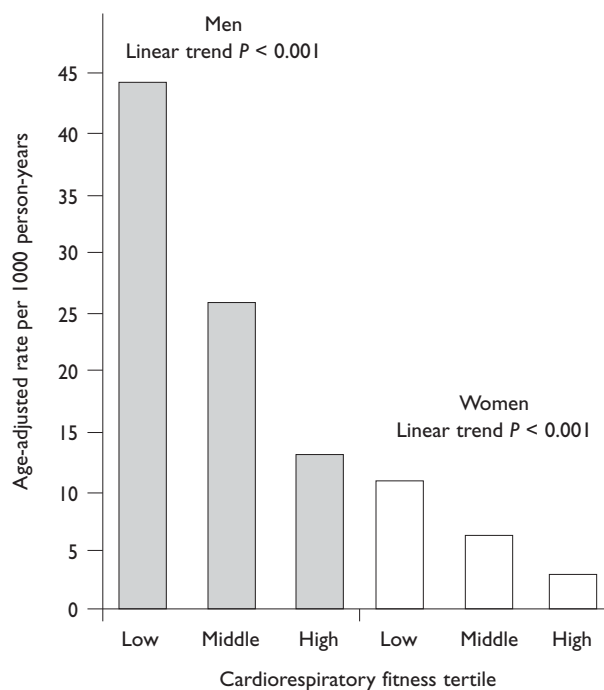


Figure 3. Age-adjusted incidence rates (per 100 person-years) of metabolic syndrome by thirds of cardiorespiratory fitness in men and women. (Adapted with permission from LaMonte MJ, Barlow CE, Jurca R, et al. Cardiorespiratory fitness is inversely associated with the incidence of metabolic syndrome. *Circulation* 2005;112:508.)

cumulation of both lipids and fatty acid metabolites, which could cause abnormal insulin signaling, leading to skeletal muscle insulin resistance (Figure 4).³² Furthermore, it has been suggested that excess lipid deposits are prone to enhanced lipid peroxidation, which could also lead to the development and/or progression of skeletal muscle insulin resistance by increasing tumor necrosis factor- α and/or by inducing mitochondrial damage. This results in an imbalance between plasma FFA uptake and fatty acid oxidation. In contrast, greater intramuscular lipid storage capacity in lean and physically active individuals could represent an adaptive response to physical training, allowing a greater contribution of the intramuscular lipid levels as a substrate source during exercise.

Recent studies in type 2 diabetes patients show that intramuscular lipids and muscle glycogen use can be increased by combining exercise with pharmacologic inhibition of adipose tissue lipolysis.³³ These findings could be clinically relevant to the prevention and/or treatment of skeletal muscle insulin resistance in the metabolic syndrome. Depletion of both intramuscular

lipids and glycogen content is associated with an exercise-induced increase in skeletal muscle insulin sensitivity.³⁴ Furthermore, exercise also stimulates muscle glycogen use.³⁵ The extent of muscle glycogen depletion and its subsequent repletion are closely linked to the exercise-induced increase in insulin sensitivity.³⁶ Consequently, a combined exercise and pharmacologic intervention that elevates both intramuscular lipid and/or glycogen use could potentially be more effective in increasing skeletal muscle insulin sensitivity. More research is warranted to establish the long-term effects of combining physical activity with lipolytic inhibition to enhance the benefits of exercise intervention to prevent and/or treat skeletal muscle insulin resistance in the metabolic syndrome.

Management of all patients with the metabolic syndrome includes both weight reduction and a systematic program of physical activity. Although caloric restriction is the hallmark of dietary management of the metabolic syndrome, a formal program to increase physical activity is part of the management of every patient with metabolic syndrome because maintenance of successful weight loss is unlikely without a systematic program of physical activity. The standard recommendation is for a daily minimum of 30 minutes of moderate physical activity. More exercise (1 hour/day) is even more effective. One promising trend is the “lifestyle exercise” approach used in the Diabetes Prevention Program, in which exercise is broken down into multiple short bouts of activity (eg, 10 minutes of brisk walking).²⁹ The effect of this fragmented exercise program appears to be similar to that of a single daily exercise session of comparable total duration and intensity.

Enhancing Compliance with the Physical Activity Program

As with other lifestyle changes, adhering to a physical activity program can be challenging; it is estimated that nearly 50% of participants drop out within 1 year of beginning an exercise training program.³⁷ One way to enhance compliance is to work collaboratively with the patient to individualize the goals of the physical activity program and to choose activities that are convenient, accessible, and enjoyable to the patient. Focusing on simple ways to increase activity in the patient’s daily routine (eg, using the stairs instead of an elevator, parking further away from a destination, or increasing recreational activity) will increase patient compliance with daily physical activity requirements.³⁸ For many, brisk walking (3.0–3.5 miles/hr) is an easy, safe, low-cost activity that can be readily fit into the day’s activities. Patients need to plan the activity and

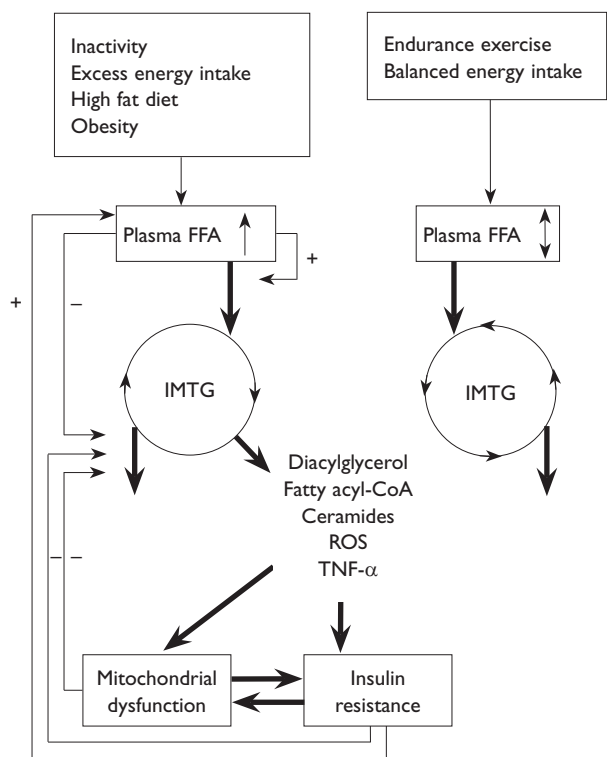


Figure 4. Schematic overview of the divergent metabolic pathways responsible for the elevated intramuscular lipid content in the insulin-resistant or trained state. CoA = coenzyme A; FFA = free fatty acid; IMTG = intramuscular triacylglycerol; ROS = reactive oxygen species; TNF = tumor necrosis factor. (Adapted with permission from van Loon LJ, Goodpaster BH. Increased intramuscular lipid storage in the insulin-resistant and endurance-trained state. *Pflugers Arch* 2006;451:606–16. Copyright 2006, Springer-Verlag.)

keep a record to monitor compliance as well as progress towards goals. Decreasing the time spent watching television as a first step may be a rewarding adjunct to increasing physical activity, especially during childhood and adolescence.

Measuring physical activity. Physical activity assessment is important for surveillance, screening, and evaluating exercise program effectiveness. Physical activity is evaluated based upon frequency, intensity, and duration and can ultimately be quantified as energy expenditure. The assessment of physical activity can be separated into 3 types of methodologies: criterion methods, objective methods, and subjective methods. Criterion methods include techniques such as the doubly labeled water (DLW) method, which is similar to indirect calorimetry and is accurate to within 3% to 10% of calorimeter values in adults. Although it is very accurate, the DLW method has proven expensive and

labor intensive because it requires the use and analysis of carbon and hydrogen isotopes, which is not practical to implement on a large scale. Additionally, DLW only measures total energy expenditure and does not differentiate between energy expenditure from physical activities versus other causes. The DLW method can be expanded and combined with indirect calorimetry, which calculates energy expenditure based upon oxygen consumption, to further differentiate the sources of energy expenditure, specifically that related to physical activity.³⁹

The concept of metabolic equivalent tasks (METs) was created to overcome the need to directly measure oxygen consumption and/or calorimetric expenditure as described above. A metabolic equivalent is defined as follows: 1 unit of sitting/resting oxygen uptake = 3.5 mL oxygen/kg of body weight/min. METs can be converted into energy expenditure via the following formula:

$$\frac{\text{METs} \times 3.5 \times \text{body weight [kg]}}{200}$$

Differing MET values have been assigned to multiple activities as defined by the American Heart Association. Evidence suggests that expenditure of more than 700 kcal/week is associated with improved cardiovascular fitness; this equates to 30 minutes of moderate physical activity 5 times per week.⁴⁰ The concept of METs is most useful when applied to self-report methods in attempts to quantify intensity and energy expenditure and is a commonly applied construct.

Objective assessment of physical activity is accomplished with multiple devices, the most common of which are motion sensors (accelerometers and pedometers) that register body movement. Accelerometers register the electrical charge resulting from bodily movement, allowing for the measurement of the frequency and velocity of movement in multiple planes. Energy expenditure can be estimated with their use since activity intensity is inferred from velocity.³⁹ Accelerometers register activity counts that are the product of frequency and intensity of movement; these data are then available for computer analysis, a potential benefit for researchers. A major drawback of accelerometers is their expense (\$US 50–\$US 400), which makes them impractical for large-scale use.⁴¹ In contrast to accelerometers, pedometers are devices that measure movement in the vertical plane only. The newer models are electronic and are much more accurate than their older mechanical counterparts. They are most appropriately used to measure physical activity when the predominant activity is walking. In comparison to ac-

celerometers, pedometers are much more affordable (\$US 10–\$US 50 per device) and therefore are practical to use on a large scale; they have become the preferred method for measurement of physical activity.^{39,41}

Subjective assessment of physical activity is accomplished through surveys and questionnaires. Self-report methods are advantageous because of their ease of use and affordability; however, they are not without problems and are notoriously susceptible to measurement bias.⁴² For example, it has become abundantly apparent that walking is unreliably recalled, even though it is a commonly reported leisure-time physical activity and a requirement of daily mobility. Self-report does have utility when combined with an objective method as described above. Additionally, motion sensors are not accurate measures for all physical activities (eg, cycling, swimming, rowing). Self-report methods are integral for assessing these activities and when correlated with METs are a reasonable estimation of the physical activity performed.

Using pedometers to measure and enhance physical activity. Objective assessment of physical activity in large populations has been limited by the complexity of measuring oxygen consumption and/or energy expenditure as described above. Recent advances in motion sensing using accelerometers and pedometers have opened new opportunities to comprehensively assess leisure-time activity and occupational activity as the major components of total daily activity.⁴³ A growing body of evidence is now available to substantiate the claim that simple and inexpensive pedometers agree acceptably with more expensive accelerometers, direct but time-consuming observation, estimates and measures of energy expenditure, and self-reported physical activity.⁴⁴ Previous studies of working age, ostensibly healthy adults have shown that pedometer-determined activity (steps/day) is associated inversely with percentage body fat, waist circumference, and BMI⁴³ (Table 4). Also greater numbers of steps per day have been significantly related to ventilatory threshold, an index of fitness,⁴⁵ and inversely correlated with heart rate kinetics.⁴⁶

A recent investigation studied the cross-sectional relationship between an objective measure of walking (pedometer-determined steps/day) and general indicators of health, a prior diagnosis of 1 or more components of the metabolic syndrome, and self-reported occupational activity in a generally sedentary working population.⁴⁷ Low occupational activity was a contributing factor to low total ambulatory activity, and fewer steps per day were associated with increased BMI, waist circumference, diastolic blood pressure, and components of the metabolic syndrome (Table 5). Furthermore, these data

Table 4. Relationship Between Pedometer-Determined Ambulatory Activity and Body Composition Variables

Permission to electronically reproduce this table
not granted by copyright holder.

Note: Values are means \pm standard deviation. Categories of pedometer-assessed physical activity were determined using percentiles of distribution: low, < 25th; moderate, 25th–75th; high, > 75th.

Adapted with permission from Tudor-Locke C, Ainsworth, BE, Whitt, MC, et al. The relationship between pedometer-determined ambulatory activity and body composition. *Int J Obes Rel Metab Disord* 2001;25:1575. Copyright 2001, MacMillan Publishers, Ltd.

*Means significantly different, $P < 0.05$.

were consistent with the observation that individuals who walk more than 9000 steps per day are more likely to be within the normal weight range and that those who walk less than 5000 steps per day are more likely to be classified as obese. In addition, increasing activity levels using a pedometer-based program or lifestyle changes that include exercise counseling can lower blood pressure in hypertensive individuals⁴⁸ and protect against type 2 diabetes⁴⁹ (Figure 5). In another study, occupational activity (stratified as “sitting,” “standing,” “moderate effort,” or “heavy work”) was associated with steps per day in men but not in women.⁵⁰ Men with “sitting” job types recorded 8800 ± 3600 steps per day compared with those performing “heavy work,” who accumulated $12,400 \pm 5400$ steps per day.⁵⁰ Pedometer-determined steps per day has been positively related to self-reported occupational activity across all workplaces.

By collecting objective activity data such as these and comparing them with known health risks such as metabolic syndrome, experts can work toward establishing benchmarks of physical activity vis-à-vis health risks. Thus, accurate assessment of physical activity is imperative and such data are necessary as health professionals and policy makers struggle to advise the public on how best to improve their health.

RECOMMENDATIONS

Physical inactivity is one of the leading major causes of obesity and the metabolic syndrome. Although increasing daily physical activity and exercise are effective therapeutic interventions for primary and secondary prevention of chronic diseases, most people do not engage in any significant physical activity. Low rates of physical activity can be attributed to several features,

Table 5. Effects of Occupational Activity on Body Mass Index and Waist Circumference

Occupational Activity	Steps/Day	BMI (kg/m ²)	Waist Circumference (cm)
Highly sedentary	6490 \pm 317	30.4 \pm 0.7	90.9 \pm 1.5
Moderately sedentary	7891 \pm 439	28.2 \pm 0.7	87.5 \pm 2.1
Moderately active	7798 \pm 769	28.9 \pm 1.0	90.6 \pm 3.2
Highly active	10,510 \pm 1069	28.9 \pm 1.7	88.1 \pm 3.8
P value	0.0002	0.26	0.61

Note: Data are means \pm standard error. Within-column comparisons were done by ANOVA.

Adapted with permission from Chan CB, Spangler E, Valcour J, Tudor-Locke C. Cross-sectional relationship of pedometer-determined ambulatory activity to indicators of health. *Obes Res* 2003;11:1566.

including the fact that health care professionals generally do not discuss the need for exercise. Physical activity length, frequency, and intensity should be discussed and monitored by patient and health care professionals with a general recommendation of a minimum of moderate activity for 30 minutes every day of the week. Most people will experience difficulty in initiating and sustaining exercise. Therefore, measuring ambulatory activity with an inexpensive, precise, accurate, and objective monitoring device, such as a pedometer, can be used to support and encourage patients to achieve their goals of daily activity. Strategies that increase activity levels should be beneficial in decreasing the proportion of those at risk of compromised health, including metabolic syndrome, cardiovascular disease, and other chronic conditions.

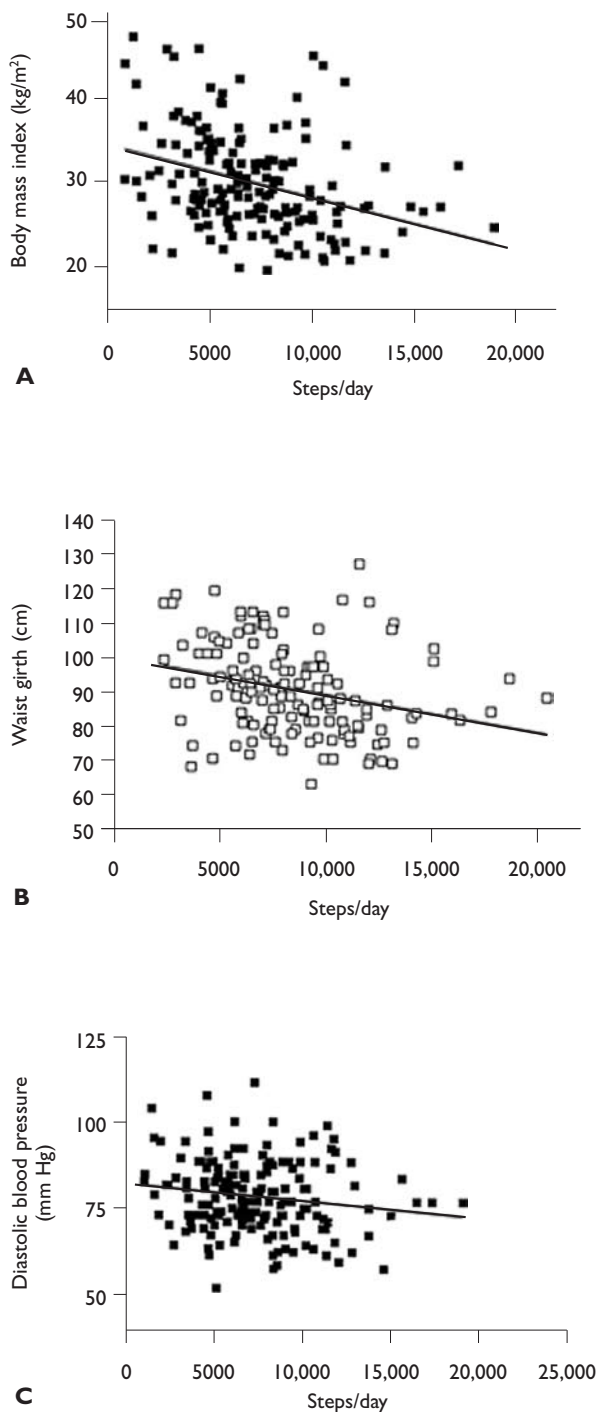


Figure 5. Correlation analysis of body mass index (A), waist circumference (B), and diastolic blood pressure (C) with total daily activity (steps/day) for 173 subjects. (Adapted with permission from Chan CB, Spangler E, Valcour J, Tudor-Locke C. Cross-sectional relationship of pedometer-determined ambulatory activity to indicators of health. *Obes Res* 2003;11:1566.)

SUMMARY

In the United States, physical inactivity is prevalent among women and men. Physical activity is inversely related to age, smoking, hypertension, body mass index (BMI), waist-to-hip ratio, total and non-high-density lipoprotein cholesterol, and triglycerides, whereas these factors are directly related to C-reactive protein concentrations. Although exercise acutely increases oxidative metabolism and thereby induces oxidative stress, there is evidence that long-term physical activity increases antioxidant defenses through the upregulation of endothelial nitric oxide synthase and antioxidant enzymes. Physical training has been shown to reduce skeletal muscle lipid levels and insulin resistance, regardless of BMI. Strategies that target the underlying risk factors of obesity, physical inactivity, and atherogenic diet are the most efficacious treatments and the only effective prevention of the metabolic syndrome. Greater cardiorespiratory fitness is associated with primary prevention of metabolic syndrome, especially among patients who have already begun to develop components of the metabolic syndrome. Patients with metabolic syndrome who exercise show a statistically significant reduction in markers of inflammation as compared to those who do not exercise. Measuring ambulatory activity with an inexpensive, precise, accurate, and objective monitoring device such as a pedometer can be used to support and encourage patients to achieve their goals of daily activity. Individuals who take more than 9000 steps per day are more likely to be within the normal weight range, whereas those who take fewer than 5000 steps per day are more likely to be classified as obese. Increasing activity levels using a pedometer-based program or lifestyle changes that include exercise counseling can lower blood pressure in hypertensive individuals and protect against type 2 diabetes. **HP**

ACKNOWLEDGMENT

This review was supported by grant HL-079156 from the National Heart, Lung, and Blood Institute.

REFERENCES

1. Thom T, Haase N, Rosamond W, et al. Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2006;113(6):85–151.
2. Schulz LO, Schoeller DA. A compilation of total daily energy expenditures and body weights in healthy adults. *Am J Clin Nutr* 1994;60:676–81.
3. Halcox J, Quyyumi AA. Metabolic syndrome: overview

- and current guidelines. *Hosp Physician*. Available at www.turner-white.com/pdf/hp_jun06_overview.pdf.
4. Vaccarino V, Bremner JD. Stress response and the metabolic syndrome. *Hosp Physician*. Available at www.turner-white.com/pdf/hp_jun06_stress.pdf
 5. Dunbar SN, Kacharava AG. Obesity and the metabolic syndrome. *Hosp Physician*. Available at www.turner-white.com/pdf/hp_jun06_obesity.pdf.
 6. Phillips LS, Rhee MK. The metabolic syndrome and glucose intolerance. *Hosp Physician* 2006;42(7):26–38, 71.
 7. Khan QA, Sola S, Khan BV. The metabolic syndrome: inflammation and endothelial dysfunction. *Hosp Physician* 2006;42(8):26–35.
 8. Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of overweight and obesity In the United States, 1999–2004. *JAMA* 2006;295:1549–55.
 9. Adult participation in recommended levels of physical activity—United States, 2001 and 2003. Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep* 2005;54:1208–12.
 10. Kronenberg F, Pereira MA, Schmitz MK, et al. Influence of leisure time physical activity and television watching on atherosclerosis risk factors in the NHLBI Family Heart Study. *Atherosclerosis* 2000;153:433–43.
 11. Manson JE, Greenland P, LaCroix AZ, et al. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *N Engl J Med* 2002;347:716–25.
 12. Paffenbarger RS Jr, Hyde RT, Wing AL, Hsieh CC. Physical activity, all-cause mortality, and longevity of college alumni. *N Engl J Med* 1986;314:605–13.
 13. Stampfer MJ, Hu FB, Manson JE, et al. Primary prevention of coronary heart disease in women through diet and lifestyle. *N Engl J Med* 2000;343:16–22.
 14. Mittleman MA, Siscovick DS. Physical exertion as a trigger of myocardial infarction and sudden cardiac death. *Cardiol Clin* 1996;14:263–70.
 15. Ross R. Atherosclerosis—an inflammatory disease. *N Engl J Med* 1999;340:115–26.
 16. Alexander RW. Theodore Cooper Memorial Lecture. Hypertension and the pathogenesis of atherosclerosis. Oxidative stress and the mediation of arterial inflammatory response: a new perspective. *Hypertension* 1995;25:155–61.
 17. Pearson TA, Mensah GA, Alexander RW, et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: a statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation* 2003;107:499–511.
 18. Fletcher GF, Balady GJ, Amsterdam EA, et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation* 2001;104:1694–740.
 19. Kasapis C, Thompson PD. The effects of physical activity on serum C-reactive protein and inflammatory markers: a systematic review. *J Am Coll Cardiol* 2005;45:1563–9.
 20. Wannamethee SG, Lowe GD, Whincup PH, et al. Physical activity and hemostatic and inflammatory variables in elderly men. *Circulation* 2002;105:1785–90.
 21. Ford ES. Does exercise reduce inflammation? Physical activity and C-reactive protein among U.S. adults. *Epidemiology* 2002;13:561–8.
 22. Aronson D, Sheikh-Ahmad M, Avizohar O, et al. C-Reactive protein is inversely related to physical fitness in middle-aged subjects. *Atherosclerosis* 2004;176:173–9.
 23. Adamopoulos S, Parissis J, Kroupis C, et al. Physical training reduces peripheral markers of inflammation in patients with chronic heart failure. *Eur Heart J* 2001;22:791–7.
 24. Taddei S, Galetta F, Virdis A, et al. Physical activity prevents age-related impairment in nitric oxide availability in elderly athletes. *Circulation* 2000;101:2896–901.
 25. Zafari AM, Harrison DG, Griendling KK. Vascular oxidant stress and nitric oxide bioactivity. In: Panza JA, Cannon RO 3rd, editors. *Endothelium, nitric oxide, and atherosclerosis*. Armonk (NY): Futura Publishing Company; 1999:133–44.
 26. Powers SK, Ji LL, Leeuwenburgh C. Exercise training induced alterations in skeletal muscle antioxidant capacity: a brief review. *Med Sci Sports Exerc* 1999;31:987–97.
 27. Thompson PD, Buchner D, Pina IL, et al. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation* 2003;107:3109–16.
 28. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C. Physical activity/exercise and type 2 diabetes. *Diabetes Care* 2004;27:2518–39.
 29. Shern-Brewer R, Santanam N, Wetzstein C, et al. Exercise and cardiovascular disease: a new perspective. *Arterioscler Thromb Vasc Biol* 1998;18:1181–7.
 30. Klein S, Sheard NF, Pi-Sunyer X, et al. Weight management through lifestyle modification for the prevention and management of type 2 diabetes: rationale and strategies: a statement of the American Diabetes Association, the North American Association for the Study of Obesity, and the American Society for Clinical Nutrition. *Diabetes Care* 2004;27:2067–73.
 31. LaMonte MJ, Barlow CE, Jurca R, et al. Cardiorespiratory fitness is inversely associated with the incidence of metabolic syndrome. *Circulation* 2005;112:505–12.
 32. van Loon LJ, Goodpaster BH. Increased intramuscular lipid storage in the insulin-resistant and endurance-trained state. *Pflugers Arch* 2005;451:606–16.
 33. van Loon LJ, Manders RJF, Koopman R, et al. Inhibition of adipose tissue lipolysis increases intramuscular lipid use in type 2 diabetes patients. *Diabetologia* 2005;48:2097–107.
 34. van Loon LJ. Use of intramuscular triacylglycerol as a substrate source during exercise in humans. *J Appl*

- Physiol 2004;97:1170-87.
35. Krssak M, Petersen KF, Bergeron R, et al. Intramuscular glycogen and intramyocellular lipid utilization during prolonged exercise and recovery in man: a ¹³C and ¹H nuclear magnetic resonance spectroscopy study. *J Clin Endocrinol Metab* 2000;85:748-54.
 36. Wojtaszewski JF, Hansen BF, Gade J, et al. Insulin signaling and insulin sensitivity after exercise in human skeletal muscle. *Diabetes* 2000;49:325-31.
 37. Gordon NF. The exercise prescription. In: Ruderman N, Devlin JT, Schneider SH, editors. *Handbook of exercise in diabetes*. Alexandria (VA): American Diabetes Association; 2002:269-309.
 38. NHLBI Obesity Education Initiative. The practical guide: identification, evaluation, and treatment of overweight and obesity in adults. National Institutes of Health, National Heart, Lung, and Blood Institute, North American Association for the Study of Obesity. Available at www.nhlbi.nih.gov/guidelines/obesity/prctgd_c.pdf. Accessed 31 Jul 2006.
 39. Vanhees L, Lefevre J, Philippaerts R, et al. How to assess physical activity? How to assess physical fitness? *Eur J Cardiovasc Prev Rehabil* 2005;12:102-14.
 40. Fletcher GF, Balady GJ, Amsterdam EA, et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation* 2001;104:1694-740.
 41. Tudor-Locke CE, Myers AM. Challenges and opportunities for measuring physical activity in sedentary adults. *Sports Med* 2001;31:91-100.
 42. Shepard RJ. Limits to the measurement of habitual physical activity by questionnaires. *Br J Sports Med* 2003;37:197-206.
 43. Raven PB, Perrel AW, Robertson DM, et al. Measurement of moderate physical activity: advances in assessment techniques. *Med Sci Sports Exerc* 2000;33:S439-516.
 44. Tudor-Locke C, Ainsworth BE, Whitt MC, et al. The relationship between pedometer-determined ambulatory activity and body composition variables. *Int J Obes Relat Metab Disord* 2001;25:1571-8.
 45. Zhang JG, Ohta T, Ishikawa-Takata K, et al. Effects of daily activity recorded by pedometer on peak oxygen consumption (V_O₂ peak), ventilatory threshold and leg extension power in 30- to 69-year-old Japanese without exercise habit. *Eur J Appl Physiol* 2003;90:109-13.
 46. Fukuoka Y, Nakagawa Y, Ogoh K, et al. Dynamics of the heart rate response to sinusoidal work in humans: influence of physical activity and age. *Clin Sci (Lond)* 2002;102:31-8.
 47. Chan CB, Spangler E, Valcour J, Tudor-Locke C. Cross-sectional relationship of pedometer-determined ambulatory activity to indicators of health. *Obes Res* 2003;11:1563-70.
 48. Iwane M, Arita M, Tomimoto S, et al. Walking 10,000 steps/day or more reduces blood pressure and sympathetic nerve activity in mild essential hypertension. *Hypertens Res* 2000;23:573-80.
 49. Hirsch IB. The prevention of type 2 diabetes: are we ready for the challenge [editorial]? *Clin Diabetes* 2002;20:106-8.
 50. Sequeira MM, Rickenbach M, Wietlisbach V, et al. Physical activity assessment using a pedometer and its comparison with a questionnaire in a large population survey. *Am J Epidemiol* 1995;142:989-99.

Copyright 2006 by Turner White Communications Inc., Wayne, PA. All rights reserved.

Call for Submissions

CLINICAL REVIEW ARTICLES

The editors of *Hospital Physician* are currently seeking Clinical Review Article submissions. These articles summarize basic strategies to facilitate the physician's approach to diagnosis and treatment or highlight emerging diagnostic and therapeutic modalities. Length is 2500 to 4500 words. Manuscripts should include at least 25 current references and appropriate illustrative material. Please send an e-mail to hp@turner-white.com stating your topic of interest before submission to confirm that the topic has not been covered recently. All manuscripts will undergo peer review. Author guidelines can be obtained at:

<http://www.turner-white.com/hp/authorhp01.htm>.