PHYSICAL ACTIVITY:

HEALTH BENEFITS, THE ROLE OF THE BUILT ENVIRONMENT AND IMPACTS OF AIR POLLUTION

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EXECUTIVE SUMMARY

Background

The health benefits of physical activity have been extensively documented throughout history. Almost 2500 years ago Plato acknowledged the positive attributes of exercise by stating that *"Lack of activity destroys the good condition of every human being, while movement and methodical physical exercise save it and preserve it."* Egyptians in 1550 BC recognized the positive treatment effect of exercise on the symptoms of a condition suspected to be diabetes, and early 20th century world heavyweight boxing champion, Gene Tunney, declared that *"Exercise should be regarded as a tribute to the heart."*

Modern scientific investigations have confirmed the anecdotal evidence of the health benefits of physical activity. Public health efforts are focused on increasing the physical activity of the general population to combat the growing prevalence of sedentary-related diseases, especially in developed nations like the United States. By 2006 the scientific literature associating physical inactivity with poor health had become so evident that the United States Secretary of Health and Human Services called for the development of federal physical activity guidelines. This mandate resulted in the *2008 Physical Activity Guidelines for Americans*. These guidelines were designed to inform policymakers, health professionals, and the public on the types and amounts of physical activity that are capable of producing significant health benefits.

This paper summarizes and updates the findings of the Physical Activity Guidelines for Americans Committee Report, commissioned by the U.S. Department of Health and Human Services. It concludes by focusing on areas of physical activity and health research which are pertinent to the California Air Resources Board's (ARB) mission to protect and promote public health by reducing air pollution exposure.

The *Sustainable Communities and Climate Protection Act of 2008* tasks ARB with setting regional targets for GHG emissions reductions from passenger vehicles. The regional plans are designed to lower pollution by reducing the dependence on individual vehicles and one strategy often included is increasing the use of walking and biking for transport. While there is overwhelming evidence that physical activity positively influences health, it is important to consider its benefits while being aware of the possible impacts of increased air pollution exposure that may occur with increased active transport, particularly in an urban setting.

The Health Benefits and Effects in At-Risk Groups

To date, there is overwhelming evidence that physical activity has wide-ranging positive health benefits related to mortality risk reduction, disease prevention, cardiorespiratory fitness, metabolic health, and cognitive function in children, adolescents, and adults of both sexes and across ethnicities. Increased physical activity has been shown to reduce the risk and improve the prognosis of 5 of the top 10 leading causes of death defined by the World Health Organization.

Regular physical activity not only reduces the risk of early death, but also is effective at preventing and treating many diseases. Researchers have reported a significant reduction in all-cause mortality risk with an average reduced risk of 20 – 40% during follow-up periods when comparing the most physically active to the least physically active study participants. The cardiovascular health benefits of physical activity can be realized by almost any subset of the population at any age, across race and sex, with recent evidence suggesting that physical activity in adolescents can reduce future cardiovascular risk. Along with its many cardiovascular benefits, physical activity has also been shown to improve metabolic health. Increased physical activity and exercise decrease the risk of developing type 2 diabetes and have been proven to be effective in treating individuals with the condition.

Physical activity not only improves muscle strength and performance in younger, healthy populations, but individuals suffering from musculoskeletal diseases or injuries and older populations can also benefit. A reduced risk of osteoporosis is seen in physically-active adult men and women, and active older individuals have improved functional health.

The health effects of physical activity extend beyond the well-known cardiovascular, metabolic, and musculoskeletal benefits. Recent work indicates that the risk of acquiring certain types of cancer is inversely associated with physical activity. Physical activity has also been shown to be effective in preventing and treating primary mental disorders, improving psychological as well as physiological health. Depression, anxiety, and age-related cognitive decline contribute significantly to morbidity and reduction in the quality of life in modern-day populations and all have been found to benefit from increased physical activity.

Summary of the Health Benefits of Physical Activity

CHILDREN AND ADOLESCENTS	ADULTS
Aerobic Fitness	Aerobic Fitness and Functional Health
Reduced Disease Risk and Symptoms	Reduced Death and Disease Rates
Healthy Weight Maintenance	Disease Treatment
Psychological Well-Being	Cognitive Health and Psychological Well-Being

The wide-ranging and robust health benefits of leading a physically active lifestyle have been so well-substantiated in the scientific literature that it led Dr. Robert Butler, an aging-research pioneer at Mount Sinai Medical Center in New York City, to state that "If exercise could be purchased in a pill, it would be the single most widely prescribed and beneficial medicine in the nation."

The Role of the Built Environment

Researchers are beginning to study how the built environment, the human-made space in which people live, work, and play on a day-to-day basis, can impact health and physical activity through changes in behavior. This rapidly expanding area of research will help determine the effectiveness of different aspects of the built environment in promoting increased physical activity of community residents.

Studies conducted in Southern California have found that children that have access to green spaces, such as parks and nature trails within their neighborhood, are more physically active.
In fact, greenness in communities incorporating access to transit and walkable, bike-friendly designs with mixed-use development (smart growth communities) seem to be more effective at encouraging physical activity in children than greenness in more sprawling, car-orientated neighborhoods. This indicates that to maximize their effectiveness, the quality, characteristics, and linking of green spaces to the surrounding neighborhood is crucial. In addition, adults who live in compact neighborhoods incorporating mixed-use designs and more street intersections exhibit higher levels of physical activity, higher usage of active transport in the form of walking and bicycling, improved cardiovascular risk factors, and lower rates of certain chronic diseases than those in more sprawling neighborhoods.

Increased access to public transportation may also influence physical activity. Many Americans meet their physical activity recommendations during their daily walk or bike to public transportation. Additionally, a novel "before and after" study conducted in Los Angeles, including funding by ARB, showed that the installation of a new light rail line can increase physical activity levels in the most sedentary individuals living close to the new stations.

A recent analysis of sustainable community research identified 5 built environment factors that appear to be most strongly associated with higher levels of residents' physical activity: (1) diverse housing types, (2) mixed land use, (3) housing density, (4) compact development patterns, and (5) levels of open space.

Health Effects of Active Transport

Planning strategies designed to increase active transport are being used as a climate change mitigation strategy to reduce greenhouse gas production from private vehicle use by substituting active transport for short trips. Research indicates that it is the overall dose of physical activity that is responsible for health benefits, regardless of the purpose of the activity (occupational, leisure, domestic, transport). Three recent international studies indicate that transport-related physical activity can lead to significant health benefits, including reductions in all-cause mortality in both male and female adults. Active transport is also associated with reduced cardiometabolic risk factors in adolescents. Children that bicycle or walk to school have higher levels of cardiorespiratory fitness, lower body mass index scores, higher aerobic power, greater flexibility, muscular strength, and endurance. Research to date indicates that adoption of active transport strategies can improve many health outcomes in male and female adults and children.

Air Pollution Impacts during Physical Activity

Although transport-related physical activity can increase an individual's overall amount of physical activity to a level that leads to significant health benefits, biking and walking to work or school may also increase exposure to air pollution compared to other modes of transportation. Short-term exposure to air pollution when exercising has been shown to have detrimental effects on lung, cardiovascular, and cognitive function in healthy and asthmatic individuals, with susceptible populations being more sensitive to exposure. A study performed in Southern California suggests that the reduced mortality risk associated with increased outdoor physical activity may be partially negated in neighborhoods with higher levels of ambient air pollution. However, the consensus of the modelling and observational literature is that the health benefits of outdoor physical activity outweigh the harms associated with increased exposure in areas with low to moderate air pollution, although this conclusion is based on a limited amount of research on the long-term combined effects of physical activity and air pollution exposure.

Future Directions

An extensive amount of high quality research has substantiated the health benefits of physical activity. However, more work is needed to define the interplay of air pollution exposure and exercise intensity and duration on health outcomes. The Air Resources Board is positioned to take a leading role in researching the health effects of sustainable community designs that promote active transportation as a way to reduce greenhouse gas emissions. Any increase in bicycling and walking for transport will have direct health implications due to increases in physical activity levels and exposure to air pollution. Research is needed to determine the effectiveness of community design at increasing healthy and sustainable behaviors such as active transport, while protecting Californians from air pollution exposure and addressing safety concerns. More work is needed to evaluate the long-term combined effect of air pollution exposure when exercising outdoors in areas with higher levels of air pollution. As public infrastructure and private development projects are incorporating sustainable community designs across the state, the need to assess the effectiveness of specific design strategies and air pollution mitigations in protecting and promoting community health will become a public health priority.

BACKGROUND

The mission of the California Air Resources Board (ARB) is to protect and promote public health. Since there is overwhelming evidence that physical activity positively influences health, it is important to consider its impact while working toward the major goal of providing safe and clean air to all Californians. Many of the innovative strategies to reduce air pollution being explored by ARB staff and other stakeholders may influence the public's physical activity patterns and exposure to air pollution. The health implications of any proposed air pollution mitigation strategies that may alter physical activity levels of the population must be considered.

A wealth of research indicates that regular physical activity results in short and long-term physiological and psychological health benefits across populations. In children, adolescents, and adults there is strong historical evidence associating regular physical activity with improved cardiorespiratory function, muscular fitness, bone health, cardiovascular and metabolic health, and maintenance of a healthy body composition. Regular physical activity has also been associated with a decreased risk of coronary artery disease (CAD), stroke, type 2 diabetes (T2D), colon and breast cancer, and hypertension. Physical activity has been linked to reduced depressive symptoms, increased cognitive function, and improved sleep quality in older adults [1]. The evidence of the health benefits of physical activity is so compelling that the U.S. Centers for Disease Control and Prevention and the World Health Organization both identify physical inactivity as one of the most important modifiable risk factors of chronic disease [2, 3].

By 2006 the scientific literature associating physical inactivity with poor health was becoming so evident that the United States Secretary of Health and Human Services called for the development of federal physical activity guidelines to promote health and wellness as a means to reduce the risk of chronic disease. This mandate resulted in the *2008 Physical Activity Guidelines for Americans (PAG)* [4]. These guidelines were constructed by a panel of over 30 experts and were designed to inform policymakers, health professionals, and the public on the types and amounts of physical activity that are capable of producing significant health benefits.

In 2013, Naci and colleagues published a novel meta-epidemiological study comparing the effectiveness of exercise to drug interventions in the prevention of coronary heart disease (CHD) and T2D, use during rehabilitation from stroke, and in the treatment of patients with heart failure. Exercise interventions appeared to be just as effective as medications in the prevention of CHD and type T2D, and more effective in the rehabilitation of stroke victims [5]. This analysis reinforces the clinical benefits of physical activity as one preventative measure and treatment modality for many diseases and conditions.

This paper summarizes the findings of the *PAG* report as well as describes recent advances in the scientific knowledge base regarding the health benefits of physical activity. This paper focuses on population association studies, controlled experimental studies, and mechanistic research projects that have investigated the effects of occupational, recreational, household, and transportation-related physical activity on health, as well as exercise intervention studies. It follows a similar structure to the *PAG* committee report [1], grouping health effects into the following categories:

- All-Cause Mortality
- Metabolic Health
- Musculoskeletal Health
- Cancer
- Cardiorespiratory Health
- Functional Health
- Mental Health

Increased physical activity by bicycling and walking for transportation (active transport) has been explored as a way to increase population health as well as reduce air pollution through reductions in vehicle miles traveled. However, walking and bicycling to work or school will also increase exposure of the population to air pollution in the near term due to increased proximity to near-roadway air pollution. With the introduction of approaches designed to increase active transport as a climate change mitigation strategy, due in part to the passage of the *Sustainable Communities and Climate Protection Act of 2008*, the range of health benefits linked with physical activity and the possible detrimental impacts of the associated increase in air pollution exposure must be considered.

This report identifies metrics commonly used to quantify the dose-response relationship between physical activity and health. Knowledge of the assumptions and limitations of these metrics will aid in the evaluation of the estimated population-wide health benefits realized when a given increase in physical activity is associated with increased active transport.

This report also examines the impact that our surrounding built environment can have on our physical activity practices, and how utilizing active forms of transportation and increasing opportunities for leisure time physical activity can lead to improved health. Also summarized are the health impacts associated with air pollution while being physically active outdoors, as well as recent work attempting to quantify the long-term overall combined effects of air pollution and physical activity on mortality and morbidity. This report concludes with suggestions for future areas of research in the general health and physical activity field, as well as specific research areas related to sustainable community design and air pollution mitigation strategies.

STUDY DESIGN METHODS

Multiple study designs have been employed to evaluate the health benefits of physical activity. The majority of studies included in the *PAG* report summary, as well as in the updated literature search, were of the four following designs (Table 1).

Table 1: Common Study Designs

- Population-based observational studies
- Prospective cohort studies
- Retrospective cohort studies
- Randomized controlled studies

Observational and cohort studies are effective at identifying relationships between physical activity and health outcomes in a real-world setting, while the randomized control studies help infer causation as well as identify possible physiologic mechanisms responsible for the health benefits of physical activity.

Various outcome measures were reported in the literature, ranging from all-cause mortality risk to clinical cardiometabolic risk factor measurements (Table 2).

Table2. Common Outcome Measures

- Mortality
    - All-cause mortality
    - Cause-specific mortality
- Morbidity
    - New disease cases (incidence)
    - Presence of disease (prevalence)
- Disease risk factors
    - Cardiometabolic
        - Blood pressure
        - Blood lipid profile
        - Blood Inflammatory markers
        - Blood glucose
        - Blood insulin
        - Glycosylated hemoglobin
    - Anthropometric measurements
        - Body mass index
        - Body composition
        - Body fat distribution
        - Waist circumference
        - Bone mineral density
- Functional capacity measurements
    - Maximal oxygen consumption (measured and estimated)
    - Musculoskeletal strength and balance
    - Walk speed/distance testing
- Cognitive function measurements

- Standardized psychological tests
- Disease symptom reduction
    - Symptom inventory surveys and questionnaires

THE HEALTH BENEFITS OF PHYSICAL ACTIVITY

Historically, exercise and physical activity have been promoted as methods to increase longevity and quality of life. An extensive body of research has associated physical activity with reductions in all-cause mortality risk. Aerobic exercise and physically-active lifestyles have been associated with decreased breast, prostate, endometrial, and lung cancer. Three major randomized intervention studies performed in the United States, Finland, and China all indicate that physical activity can prevent or delay the symptoms of T2D. Increases in physical activity have also been consistently inversely associated with coronary heart disease in studies spanning the globe [6].

Key Terminology Used to Define Physical Activity

Before discussing the health benefits of physical activity, it is critical to agree on certain operational definitions to avoid confusion and assess the consistency between studies. Although there are variations within the literature, table 3 and table 4 below summarize the most widely accepted definitions of common terms used in physical activity research. It is universally accepted that physical activity is any bodily movement that requires contraction of skeletal musculature resulting in increased energy expenditure above a resting level. Physical activity can then be divided into 4 main categories, depending on its setting and purpose. Physical activity can occur at work, for leisure or transportation, as well as around the home when performing chores. Studies cited in this report may measure or estimate total physical activity of the participants, stratify physical activity by specific categories, or capture one or a subset of the physical activity categories (Table 3).

Table 3. Physical Activity Definitions

Physical Activity	Any bodily movement that requires contraction of skeletal musculature resulting in increased energy expenditure above a resting level.
Physical Activity Categories	Physical activity is classified into specific domains, such as leisure-time, occupational, transport, and household activity.
Exercise	Physical activity that is planned and structured with the objective of improving health, fitness, or performance.
Physical Fitness	The ability to perform physical tasks that can be measured with specific tests.

Many health effects appear to be most closely linked to an individual's total physical activity amount (i.e. dose), regardless of the setting or purpose. To estimate the amount of physical activity performed by an individual, the intensity, duration, and frequency of physical activity must be quantified (Table 4.)

Table 4. Quantification of Physical Activity

Metabolic Equivalent Task (MET)	Expression of intensity in multiples of an individual's resting energy expenditure.
Moderate to vigorous physical activity (MVPA)	Activity requiring between 3 – 6 METS, while vigorous physical activity corresponds with activity requiring over 6 METS.
Duration	Amount of time an individual spends participating in one session of physical activity.
Frequency	Number of physical activity sessions during a specific time period (e.g. one week).
Volume(Dose)	The total physical activity dose associated with an activity. It is based on the intensity, duration, and frequency with which the activity is performed.

Some researchers may express the intensity of an activity in more qualitative terms, such as "light", "moderate" or "vigorous" physical activity. Even though these terms indicate ranges of physical activity intensity, their values still correspond to METS (Table 5).

Table 5. Physical Activity Intensity Categories

Vigorous Physical Activity	7+ METS
Moderate to Vigorous Physical Activity (MVPA)	3 – 6 METS
Light Physical Activity	1.5 – 3 METS
Sedentary Activity	1 – 1.5 METS
Resting	1 MET

As an example of a volume calculation, commuting to work via bicycle at a self-selected pace is estimated to require an intensity of 6 METS [7], which is equivalent to an energy expenditure six times that of resting in a seated position. If the duration of an individual's bike commute is known, as well as the number of trips the individual performs over a set time period (week), it is possible to estimate his or her commuting physical activity volume in MET-minutes per week (METS x duration x frequency).

Physical Activity and All-Cause Mortality

The *2008 Physical Activity Guidelines for Americans Advisory Committee Report* concluded that a large body of evidence consistently indicated an inverse relationship between an individual's level of physical activity and all-cause mortality [1]. This inverse relationship was seen in both males and females, older individuals, and in white and non-white populations. The report found that the dose-response curve relating physical activity to disease risk is curvilinear, with approximately a 20% reduction in mortality risk occurring when an individual performs 1.5 hours of moderate to vigorous physical activity (MVPA) a week.

Substantial benefits occur with at least 2.5 hours a week of MVPA. Below this threshold volume, any amount of physical activity, even one exercise session a month, reduces all-cause mortality risk. As the duration and intensity of physical activity increase, risk is further reduced, but at lower magnitudes (fig. 1).

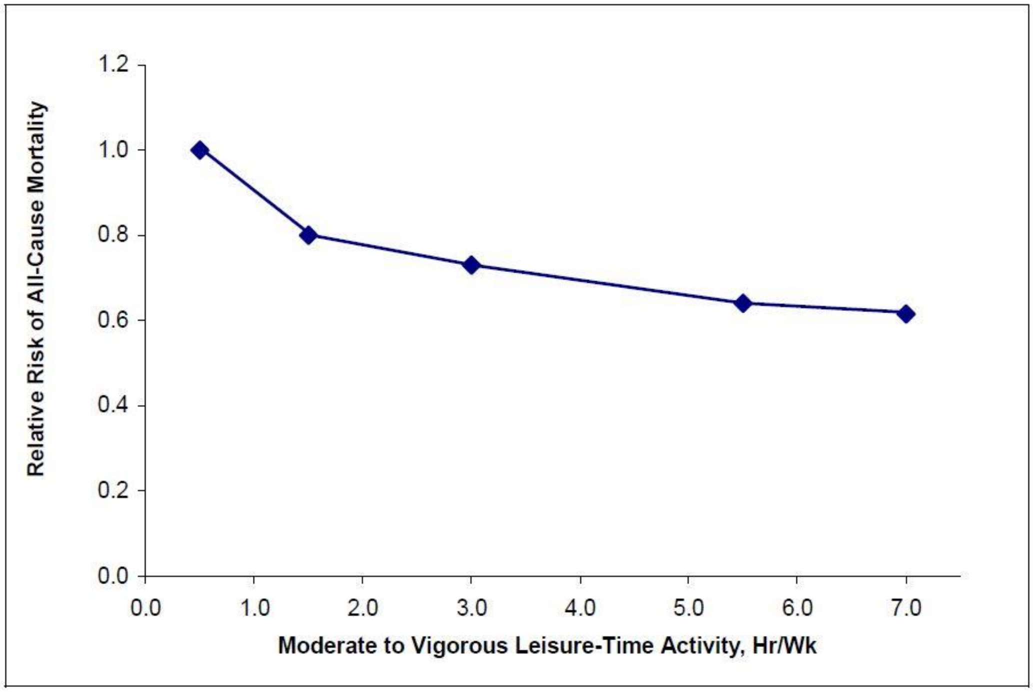


Figure 1. Median Shape of Dose-Response Curve for Physical Activity and Relative Risk of All-Cause Mortality. *Adopted from 2008 Physical Activity Guidelines for Americans Advisory Committee Report,* Page G1-20.

A recent meta-analysis of international studies utilizing mortality data from the World Health Organization identified a 21 – 32% decrease in mortality risk in moderately active individuals aged 40 – 79 when compared to those in the lowest activity category. It was estimated that if all individuals could achieve a moderate level of physical activity, approximately 5.3 million lives would be saved annually worldwide. The health risk of physical inactivity was comparable in magnitude to the established health risks of smoking and obesity [8].

Physical activity has also been shown to improve longevity in sedentary adults who increase their activity levels later in life. In a well-controlled study following a cohort of men aged 50 for 35 years, physical activity status was updated at regular intervals during the study period. Sedentary individuals that increased their physical activity between 50 and 60 years of age experienced similar relative mortality risk reductions as individuals who were physically active throughout the study period. The magnitude of mortality risk reduction was similar to that of study participants who quit smoking, which is one of the most substantiated modifiable mortality risk factors. In contrast, the mortality risk of individuals who were physically active at study enrollment but became sedentary returned to a level similar to that of individuals who were classified as sedentary throughout the entire study period [9]. These results indicate that the adoption of a physically active lifestyle can be of benefit at any age, but routine physical activity is necessary to maintain reductions in all-cause mortality risk.

All-Cause Mortality in Older Adults

Reinforcing the concept that physical activity imparts health benefits across age groups, researchers have identified significant reductions in mortality in older populations that remain physically active. Aged adults (70+ years old) - who were the most active based on objective accelerometer step counts had a mortality risk that was reduced 11-fold during the 50 month follow-up period when compared to the least active third of the participants [10]. A long-term follow-up study of males found that high leisure-time physical activity was associated with higher survival rates up to 85 years of age [11]. With over 1.4 million person-years of follow-up, a 34% reduced risk of mortality was seen in older male and female adults who achieved over 300 minutes/week of MVPA [12].

All-Cause Mortality and the Influence of Sex

Historically, male participants have formed a disproportionate size of the study populations in physical activity research. Recently, an increasing body of research has been performed to confirm that these mortality benefits are also seen in women. In a large prospective study of 40-70 year-old Chinese women, higher levels of non-exercise physical activity were associated with a 35% reduction in all-cause mortality risk, indicating that participation in multiple forms of leisure and work-related physical activity can produce health benefits in women as well as men [13]. Regardless of whether physical activity was related to exercise, transportation, or household activities, reductions in all-cause mortality risk were similar at equivalent levels of energy expenditure (hazard ratio; 0.61 – 0.86).

Nocon and colleagues performed a large meta-analysis of over 33 studies including 883,372 male and female participants from around the globe. The pooled risk reduction for all-cause mortality between the most active and least active participants was 33% after adjustment for known risk factors such as blood pressure, blood cholesterol, smoking, and family medical history. There was no significant difference in the risk reduction observed between males and females. The results of this meta-analysis confirm the pooled all-cause mortality risk reduction reported in the *PAG* report, further substantiating the robust and consistent beneficial effect of physical activity on life expectancy across populations [14].

All-Cause Mortality in Individuals with Co-Morbidities

Recommended amounts of physical activity have not only been shown to decrease mortality risk in a healthy population, but are also associated with decreased mortality risk in individuals already diagnosed with certain chronic medical conditions. Research in hypertensive patients found that running or walking for an average of 11.5 miles per week lowered all-cause mortality risk by 29% compared to sedentary hypertensive controls [15]. As long as energy expenditure was equivalent, hypertensive walkers and runners achieved similar levels of risk reduction. Measuring physical activity in patients with peripheral arterial disease (PAD) is a valuable assessment of mortality risk. Chang and colleagues reported that physically active PAD patients had an 85% reduced mortality risk compared to sedentary patients [16]. Currie and colleagues showed that exercise improves vascular function in healthy males, indicating that exercise may mitigate the progression of PAD [17].

Physical activity also mitigates the deleterious effects of hyperglycemia associated with T2D. Sluik and colleagues observed a prospective cohort of male and female diabetics aged 35 – 70 years old to investigate the association between physical activity and mortality. Both total physical activity and leisure-time physical activity time were associated with reduced all-cause mortality risk in males and females [18, 19]. Recent work indicates that participating in leisure-time physical activity at least once a week, regardless of mode (swimming, biking, hiking, etc.), reduced all-cause mortality risk across all levels of glycemic control [20]. Physically-active subjects with very poor glycemic control, an indication of a diabetic metabolic condition, did not show an increased-risk of all-cause mortality compared to sedentary controls with normal glycemic control. This implies that being physically-active can ameliorate the increased mortality risk due to metabolic dysfunction associated with T2D. Even if physically-active diabetics were unable to improve their blood glucose control, their mortality risk improved with exercise. These results indicate that physical activity is capable of increasing life expectancy in addition to treating symptoms in a diabetic population as well as those suffering from high blood pressure and other vascular diseases.

Physical Activity and Cardiovascular Health

Cardiovascular Mortality

Consistent with studies on all-cause mortality, the *PAG* report showed that cardiovascular mortality risk was greatly reduced by physical activity, with moderately active individuals exhibiting a 20% lower risk than sedentary controls [1]. There also appeared to be a dose-response effect, with more active individuals showing a 30% reduction in risk. Women and men who on average performed 60 minutes of brisk walking a week (or other physical activity of a comparable intensity and duration) presented with fewer clinical events for cardiovascular disease than sedentary controls. In many of the studies reviewed, multivariate analyses were employed to control for variables such as obesity, cigarette smoking, blood pressure, and blood lipid concentrations. This may have resulted in an underestimation of the health benefit of physical activity, because some of the benefits related to increased physical activity may also be mediated through these variables.

A recent prospective study that examined the association between occupational physical activity and CVD mortality reinforces the *PAG* report findings that higher levels of physical activity at work decrease the risk of CVD mortality in males and females [21]. Exercise volume appears to be the most critical parameter relating physical activity and health outcomes, and the purpose of the physical activity is of minimal importance.

Acute Cardiovascular Risk

The *PAG* report determined that the specific risk of fatal and non-fatal coronary heart disease (CHD) episodes is decreased with physical activity in a dose-dependent manner. A large body of evidence indicated that both males and females respond similarly, with reported relative risks (RR) between 0.61 – 0.81 for light-moderate physical activity and 0.48 – 0.62 for higher amounts of activity, compared to sedentary controls [1].

Although there is substantial evidence that physical activity can reduce the risk of myocardial infarction (MI) in males and females, recent work has shed some light on the mechanisms through which physical activity may reduce the risk of heart attack. Exercise can modulate signaling pathways involved in cardiac remodeling, leading to increased heart efficiency [22]. In a case-control study comparing men that had suffered a MI to a matched control group, 3 hours a week of vigorous physical activity (over 6 METS) was associated with a 22% lower risk of suffering a MI. This relationship was partially explained by the beneficial effects of physical activity on blood cholesterol levels, vitamin D balance, and glucose homeostasis [23].

In the report, stroke risk was also found to be decreased with increased physical activity. More active individuals exhibited a 25% – 30% lower risk of stroke than sedentary controls. Moderately-active women showed a RR for stroke of 0.82 and highly-active females a RR of 0.72 when compared to sedentary controls. Men showed a similar reduction in risk, with a median RR of 0.65 for moderate-intensity and 0.72 for high-intensity [1]. A recent study indicates that physical activity as part of a healthy lifestyle drastically reduced the risk of a fatal stroke in high risk adult males over a 10 year follow-up period [24]. Men and women respond similarly to exercise at all studied age ranges, indicating that physical activity mitigates stroke risk to a comparable degree across the sexes [1, 5, 25-27].

Markers of Cardiovascular Risk

In addition to the decreases in the relative risk of cardiovascular disease (CVD), studies summarized in the *PAG* report found that increased physical activity was associated with significant improvement of two strong risk factors, high blood pressure and elevated levels of triglycerides and cholesterol in the blood. Physical activity and structured exercise were shown to produce clinically-significant reductions in resting blood pressure as well as increased high-density lipoprotein (HDL) cholesterol, and to a lesser extent, reduced low-density lipoprotein (LDL) cholesterol and very low-density lipoproteins (VLDL), all of which are beneficial changes in these CVD risk factors. A range of 600 – 720 MET-minutes per week was shown to increase HDL cholesterol levels in the blood, while to achieve significant reductions in LDL cholesterol, exceeding 720 MET-minutes of physical activity per week was indicated [1]. A recent epidemiological study in elderly non-Hispanic white males found an inverse association between physical activity level and arterial stiffness, which is a risk factor for CVD and acute cardiovascular events [28].

The beneficial effects of physical activity on blood pressure seem to be similar in men and women and both respond in a dose-dependent fashion, as well as individuals who are overweight or obese. Physical activity was shown to significantly reduce systolic and diastolic resting blood pressure in normotensive as well as hypertensive individuals, with hypertensive patients showing a greater reduction: hypertensive individuals experienced a 6.9 mmHg drop in systolic pressure and a 4.9 mmHg reduction in diastolic pressure. These reductions were reproducible when the volume of physical activity exceeded 800 MET-minutes per week, which falls within the committee's physical activity recommendations for adults of 500 – 1000 MET-minutes per week [1].

Historically many of the beneficial cardiovascular health effects of physical activity have been thought to be mediated through its ability to balance energy intake and expenditure, induce weight loss, and aid in weight maintenance. In a recent randomized control study, sedentary diabetic patients were split into two groups, a control group and a structured exercise group. Following the exercise protocol, the exercise group showed significant improvements in various cardiometabolic risk factors. Interestingly, this decrease in CVD risk was independent of weight loss, indicating that participating in physical activity can improve strength and fitness and induce beneficial changes in cardiometabolic risk factors even without losing weight [29].

Sex Differences

The benefits of physical activity on cardiovascular health have been shown to be of a similar magnitude in males and females. The magnitude of risk reduction appeared to be slightly lower in women than men, although comparing risk reduction between the sexes has proven challenging [1]. There is some evidence that the least-active females perform less physical activity than the least-active males. Age distributions differ between the studies included in many of the meta-analyses, and cardiac event rates differ by age in males and females. Since the number of cardiac events is lower in women, the reliability of the calculated risk reduction in many studies is questionable. Regardless of these limitations, physically-active men and women both exhibit significant reduced cardiovascular risk compared to their sedentary counterparts [30].

Cardiovascular Health and Ethnicity

Until 2007, few studies in the United States of adequate power had evaluated the relationship between physical activity and cardiovascular health in race or ethnic groups other than non-Hispanic whites. A similar magnitude of risk reduction that has been reported in studies with white males and females has also been seen in the populations of Japan, China, and India. This indicates that the benefits of physical activity on cardiovascular health documented in non-Hispanic white males and females occurs in individuals of other races, ethnicities, and nationalities [1].

Recent work has documented cardiovascular disease to be higher among the African-American population compared to non-Hispanic whites in the United States [27]. Because disease incidence and prevalence rates differ between race and ethnic subpopulations in the United States, there has been some debate if the extent of physical activity benefits differs among these subgroups. Using a group comparison design, recent evidence suggests that physical activity is associated with reduced CVD incidence in both African-American and non-Hispanic white males, with no between-group differences in risk reduction [26]. In a large, ethnically-diverse cohort, Reddigan and colleagues found similar results, indicating that individuals of varying ethnic and racial backgrounds can realize the cardiorespiratory benefits of physical activity [31].

Genetic Risk of Cardiovascular Disease

Recent work has indicated that higher levels of physical activity may attenuate increased genetic risk for cardiovascular disease. In a study of non-Hispanic white women who participated in the Women's Genome Health Study, 21,674 women were genotyped for the presence of the FTO gene risk allele which has been associated with higher incidence of cardiometabolic disease. Only those women who had the risk allele and were also inactive showed a higher risk of developing CVD disease. Physically-active women who were carriers of the risk allele did not show any increased risk over a control group of women who did not carry the FTO gene risk allele, suggesting that physical activity was able to counteract increased genetic risk in these individuals [32]. In a similar cohort of women with and without common gene variants associated with dysregulated cholesterol homeostasis and increased risk of myocardial infarction, women with the high-risk gene variants who were physically active significantly attenuated their risk of suffering a heart attack by 30% – 50% when compared to genetically at-risk sedentary cohort members [33]. Also, in males and females, the increased cardiometabolic risk associated with a gene polymorphism that affects lipid metabolism is significantly attenuated with increased physical activity based on regression models accounting for age, smoking status, sex, and education [34].

Age Differences

Increased physical activity was consistently shown in the *PAG* report to improve cardiovascular health across three well-studied adult age groups (50 – 59, 60 – 69, and 70 – 79) [1]. A recent study of adult men and women over the age of 50 identified a significant reduction in CVD mortality at moderate levels of physical activity, with a greater risk reduction at higher levels. The robust CVD risk reduction was still present when only including individuals over 70 years of age in the analysis [30]. A recent study published in 2014 indicates that physical activity is associated with reduced mortality risk in older individuals aged well into their 80's [10]. The body of literature to date indicates that moderate levels of physical activity improve cardiovascular health and reduces mortality risk in adults of all ages.

Data regarding cardiovascular morbidity or mortality in younger populations was not readily available, due to the infrequency of cardiovascular events in people under 40 years of age. However, recent studies in children and adolescents have examined the effects of physical activity on the risk of future disease.

Cardiovascular Risk in Children and Adolescents

Although the primary negative health outcomes related to many chronic cardiovascular diseases (premature death, incidence, disability) are not realized until later in life, there is autopsy evidence of cardiovascular damage consistent with coronary artery disease in children as young as 15 years old [35] and recently research has been conducted to assess risk factors for cardiovascular disease in adolescents. Walking and bicycling to school have been associated with greater laboratory-measured cardiorespiratory fitness in male and female children and adolescents [36]. A prescribed bicycling exercise protocol has been shown to increase vascular function in young males, which could help prevent future vascular complications [17]. Males and females aged 8-18 who were placed into a "low-fit" group based on a treadmill fitness test had the most adverse scores on a metabolic syndrome risk assessment, which is used to predict future cardiovascular risk [37]. A recent study found that frequent breaks in sedentary time in adolescent males and females aged 8-11 were associated with reductions in cardiovascular risk factors. In this same study, the specific sedentary activities of television viewing and computer time were positively associated with increased cardiovascular risk [38]. In a group of 13-17 year old adolescents, high levels of adiposity and sedentary time were linked to the most adverse cardiovascular risk factor scores, based on 11 laboratory measurements [39]. These recent reports add to the body of evidence substantiating that the cardiovascular benefits of physical activity are not only seen in older adults, but are also seen in young individuals.

Physical Activity and Metabolic Health

Reduced Risk and Treatment

T2D and metabolic syndrome (a constellation of clinical signs including, central obesity, impaired glucose metabolism, high blood pressure, insulin resistance, high blood triglycerides and cholesterol) are two conditions that are highly associated with obesity and a sedentary lifestyle. It is understood that there are both genetic and environmental influences on the development of T2D and metabolic syndrome, but the literature summarized in the *PAG* report and research carried out since its publication indicate that both clinical symptoms of T2D and metabolic syndrome respond positively to increased physical activity. It appears that physical activity and exercise can aid in the prevention and treatment of both conditions.

The *PAG* committee concluded that increased physical activity, structured exercise, and reduced sedentary behavior can all improve metabolic syndrome symptoms, reduce associated risk factors, and prevent the onset of symptoms. Cross-sectional studies with male and female participants have regularly shown a lower risk of acquiring metabolic syndrome in more physically-active individuals. All 9 of the studies presented in the *PAG* report found an inverse, dose-dependent relationship between the amount of physical activity and metabolic syndrome (fig. 2). The *PAG* committee concluded that men and women experienced similar physical activity-related benefits in regards to metabolic syndrome risk [1].

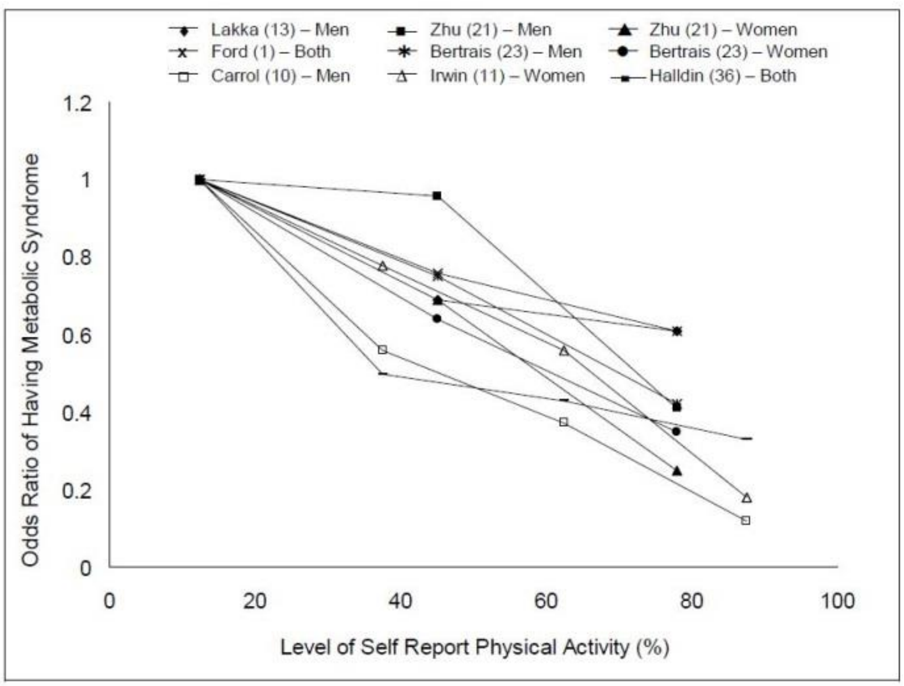


Figure 2. Summary of Cross-Sectional Physical Activity and Metabolic Syndrome Studies Using Categories of Physical Activity That Could Be Used To Examine Dose-Response. *Adopted from 2008 Physical Activity Guidelines for Americans Advisory Committee Report, page G3-4.*

Within the scientific literature regarding T2D, the *PAG* committee found consistent and substantial evidence that increased physical activity reduces the risk of a T2D diagnosis, as well as being an effective treatment. Physical activity and structured exercise programs were also seen as viable options to prevent and mitigate many of the vascular and neural complications associated with T2D. However, the *PAG* committee found it challenging to evaluate the results of many of the randomized controlled trials because diet interventions were included with exercise in many of the treatment groups, making it difficult to distinguish the individual benefits of increased physical activity.

At the time of publication of the *PAG* report, it appeared that both men and women suffering T2D could benefit from increased physical activity and there was limited data available on the influence of race and ethnicity. When looking at national and international studies including participants of various races, ethnicities, and countries of origin published over the last 10 years, no strong evidence counters the idea that all individuals, regardless of sex, age, and race/ethnicity can metabolically benefit from physical activity [8, 40-51].

Since 2008, due to the overwhelming amount of data supporting an association between low levels of physical activity and the presence of metabolic conditions, research has focused on randomized controlled studies implementing physical activity as a way to reduce the incidence of metabolic conditions as well as treat patients already diagnosed with T2D or metabolic syndrome.

Metabolic Risk

In individuals that are predisposed to a metabolic condition or are showing early clinical signs of disease, physical activity can reduce the risk of disease and improve clinical signs and symptoms of disease. In 2009, Kallings and colleagues performed a study of 101 sixty-eight year-old sedentary male and female overweight individuals who were randomized to participate in a 6-month physical activity intervention program or a minimal intervention control group. The exercise group experienced improvements in many cardiometabolic risk factors. On average, the physical activity intervention group saw reductions in body fat, waist and neck circumference, resting blood glucose, glycated hemoglobin levels and total blood cholesterol, all of which indicate a reduced risk of acquiring metabolic syndrome or T2D [52].

Physical activity has also been shown to resolve current cases and prevent the onset of diabetes and metabolic syndrome in at-risk individuals in the United States and abroad [53-55]. The metabolic benefits of physical activity appear to have long-lasting effects, with a 34% reduction in diabetes incidence seen in an intervention group, compared to controls, over a 10 year follow-up period [48].

Intervention in Metabolic Disorders

Physical activity as an intervention in individuals diagnosed with T2D or metabolic syndrome has been shown to be an effective treatment in many randomized controlled studies, with improved symptomology and attenuation of cardiometabolic risk factors. These results have been reproduced in middle-aged and older adults, males and females, and in studies conducted internationally [47, 50, 55-59]. The long-term benefits of physical activity interventions have been confirmed in other studies, with follow-up periods ranging from 13 to 20 years [46, 47]. These results were also validated in the Italian Diabetes Study, which indicated that a 12-month physical activity intervention program improves cardiovascular fitness and reduces insulin resistance, glycated hemoglobin, blood pressure, total cholesterol, inflammatory markers, and cardiometabolic risk scores in adult type 2 diabetics [60]. The effect of physical activity can be so great that in a study of men diagnosed with metabolic syndrome, after completion of a 20-week exercise intervention program, 30% were no longer classified as having metabolic syndrome [61].

Intervention in Metabolic Disorders and Ethnicity

Prevalence rates of metabolic conditions, such as T2D and metabolic syndrome, vary by ethnicity, but physical activity interventions have been shown to improve risk factors and symptomology across ethnic and racial groups, with all ethnic populations studied benefiting from increased physical activity [40, 42, 45, 49, 51, 62]. Two large studies (NHANES and CARDIA) contained a large number of non-Hispanic white and African American participants, and there was no indication that race influenced the ability of physical activity to reduce metabolic syndrome risk and symptom progression [54, 63]. These studies indicate that regardless of the social, behavioral, and environmental variables or physiological mechanisms that may contribute to racial disparities in the prevalence of metabolic conditions, increasing physical activity is an effective intervention strategy across ethnic groups.

Obesity and Overweight

Excess weight gain and obesity, which aren't diseases in themselves, are considered strong risk factors for metabolic morbidity. Obese individuals have been shown to have an increased risk of coronary artery disease (CAD), T2D, and some forms of cancer. Research has also shown a strong association between obesity and CAD in the absence of other risk factors, such as hypertension and high cholesterol [64, 65].

The *PAG* committee identified a large body of evidence indicating an inverse dose-response relationship of physical activity and body weight or body mass index (BMI). Study periods ranged from short-term clinical trials to over six years of follow-up in prospective cohorts. Although the evidence is not as strong as for the short-term intervention studies, the report does indicate that physical activity is associated with weight loss and weight maintenance over long periods of time. At the time of publication, randomized trials evaluating the dose-response relationship between physical activity and body weight indicated that at least 780 MET-minutes of weekly activity is necessary to lose or maintain body weight. The *PAG* committee recognized that physical activity is a critical component of a weight-maintenance program following weight loss, although at the time of publication there were only 8 randomized controlled studies addressing the role of physical activity and weight maintenance.

Physical activity was also identified as a strategy to reduce the presence of other obesity-related disease risk factors, such as abdominal obesity, intra-abdominal fat, and total body fat. Regular physical activity was shown to improve body composition, with reduced body fat and increases in lean mass. Physical activity achieved these changes without caloric restriction, although the synergistic effect of dietary changes and increased physical activity were shown to be more effective at inducing weight loss and maintenance than either strategy implemented alone. Despite some evidence that men and women and different race/ethnic groups may require different amounts of physical activity to lose or maintain weight, results have consistently shown physical activity as an effective weight loss and maintenance modality. Based on this gap in the literature, the *PAG* committee elected to forgo sex and race-specific physical activity recommendations regarding weight maintenance.

Obesity-Related Disease and Genetics

The variation in the amount of physical activity needed to maintain a healthy weight may be related to individual genetic differences. With the recent advent of cost-efficient, large-scale genome wide association studies, a group of genetic polymorphisms has been linked to an increased risk of obesity and obesity-related disease [66]. There has been specific interest in the fat mass and obesity-associated gene (FTO) and its correlation with increased obesity, diabetes, and cardiovascular disease risk. Many recent studies have indicated a strong correlation between specific polymorphisms of the FTO gene and obesity-related disease in a wide range of age groups and ethnicities [67-72].

Due to the ability of physical activity to reduce the symptoms and risk of many obesity-related diseases, researchers have investigated whether physical activity can modify the risk of obesity-related genetic variations. Studies in Sweden, Britain, and the United States have found that the genetic risk of FTO gene polymorphisms is attenuated in physically-active adults when compared to sedentary subjects [73-75].

Physical Activity and Musculoskeletal Health

The musculoskeletal system is composed of the body's bones, muscles, cartilage, tendons, ligaments, joints and connective tissue. The musculoskeletal system provides support, stability, and locomotive functions to the body. The *PAG* committee focused on specific health and fitness outcomes to assess the benefits of physical activity on musculoskeletal health including fracture risk, osteoporosis, osteoarthritis, and muscle quantity and quality.

Fracture Risk

Physical activity was shown to be inversely associated with fracture risk based on prospective and retrospective cohort studies, cross-sectional studies, and small randomized controlled studies. A large majority of the case-control and cross-sectional studies indicated that physical activity can reduce fracture risk in adult populations. One randomized control study identified by the *PAG* committee showed that a back strengthening program initiated over a 2-year period significantly reduced the incidence of vertebral fractures in women. A definitive dose-response relationship between physical activity and fracture risk was difficult to establish with the data available. Due in part to the different parameters used to quantify physical activity between studies and site-specific fracture risk, there was no discernable difference in risk reduction between men and women shown in the literature [1].

Osteoporosis

Exercise training and physical activity appear to mitigate the risk of osteoporosis through an increase, or a reduction in the rate of decrease, of bone mineral density (BMD) in adult women and men. The vast majority of bone mineral density studies focus on the lower lumbar vertebrae, hip, and femoral neck due to the clinical significance of fractures in these anatomical areas. In a review of 15 meta-analyses looking at exercise and lumbar spine BMD, 13 found significant increases in BMD across sex and adult age groups. Studies focused on femoral neck and hip BMD were not as consistent, with some indicting an increase in BMD, and other not showing any change. It was unclear to the committee the degree to which physical activity can attenuate age-related decreases in BMD, but one study showed that increases in BMD can be maintained for up to 4 years with regular physical activity and calcium supplementation in post-menopausal women [76].

Arthritis

Osteoarthritis, the most common form of arthritis, is a degenerative disorder in which the articular cartilage at joints wears away, causing pain with joint movement and compression. The *PAG* committee did not uncover any evidence that regular exercise within the recommendations of health providers increases the risk of osteoarthritis. A body of observational and animal research implies that moderate amounts of physical activity may prevent the onset of osteoarthritis at weight-bearing joints and increase bone density and articular cartilage thickness [77-79]. Although at the time of the *PAG* committee report publication there was a lack of case-control studies looking at the protective effect of physical activity against osteoarthritis, a large body of evidence did indicate that certain types of exercise were beneficial for individuals suffering from osteoarthritic conditions. Out of 17 interventional exercise studies, all the exercise programs were shown to effectively reduce pain and improve function. Recent randomized controlled studies indicate that exercise interventions in patients with osteoarthritis are effective at reducing pain and increasing function through improved lower extremity strength and coordination [80-82]. Long-term participation in high-impact sports (competitive basketball, volleyball) may increase the risk of developing osteoarthritis later in life [83, 84].

Muscle Function

Most of the studies examining the effects of physical activity and muscle function reviewed in the *PAG* report, and found in the interim, focus on randomized controlled intervention designs, with none looking at non-exercise physical activity (occupational, active transport, etc.). At the time of the *PAG* report publication, exercise and physical activity were shown to increase muscle mass, strength, and functional capacity in many intervention studies. The greatest gains were seen with resistance exercises at moderate to high loads. The strength and mass benefits are seen across sex and age groups, but the beneficial effects of resistance training on muscle mass and function may be attenuated in advanced age groups, although recent evidence indicates that older individuals can increase strength, muscle mass, flexibility, minimize osteoarthritic symptoms, and improve bone density through exercise [85, 86]. One study has indicated that exercise can reduce oxidant-induced DNA damage associated with muscle loss in the elderly [87]. Even though aged adults have been shown to have lower muscle protein synthesis rates than young adults, resistance exercise has been shown to increase muscle protein synthesis in 62-90 year olds to a magnitude that is similar to that seen in men and women aged 20-32, indicating that the potential of muscle tissue to respond positively to exercise is present late into life [88]. Increases in muscle mass due to resistance exercise in 72 year-old men were accompanied by increases in muscle fiber progenitor cells, similar to that seen in younger populations [89]. After a short, 10-week exercise program, elderly males showed improvements in strength and power [90]. Following a single bout of resistance exercise, elderly males aged (69 +/- 5 years) also show acute increases in testosterone and growth hormone levels comparable to 23 year-old males [91]. These recent studies indicate that exercise can have beneficial effects on musculoskeletal physiology and function in adult males and females of all ages.

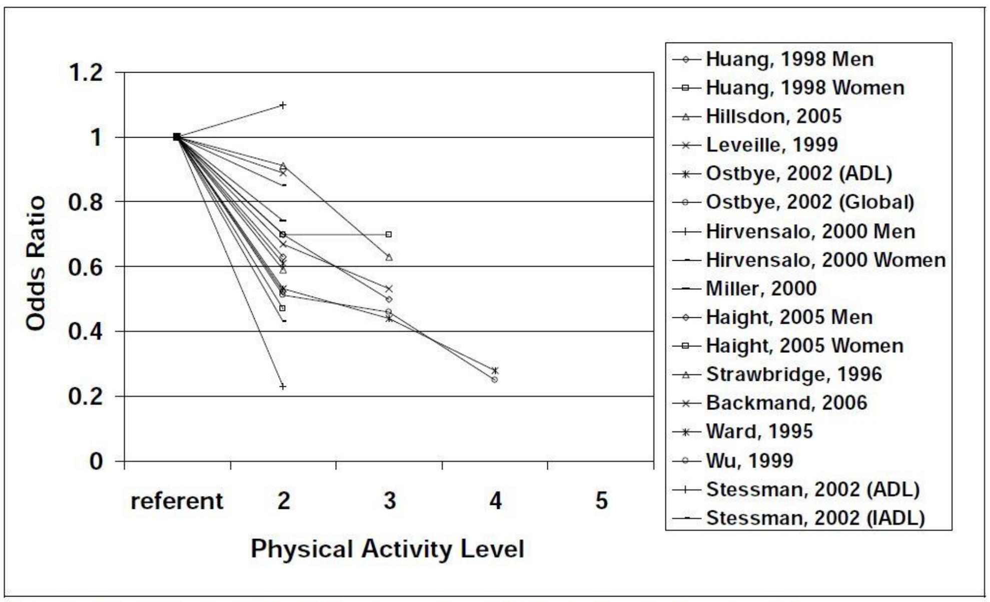
Musculoskeletal Health and Ethnicity

Results of studies which included individuals of varying race and ethnic backgrounds indicate that all individuals respond similarly to resistance training of equal intensity and volume [1]. In regards to osteoarthritis risk, there are conflicting reports of ethnic differences specifically between non-Hispanic whites and African-Americans, which also vary by anatomic site, with African-Americans exhibiting lower rates of hip osteoarthritis, but higher rates at the knee joint [92, 93]. Interestingly, there is some evidence that blood levels of potential biomarkers of osteoarthritis vary by sex and ethnicity, with women and African-Americans exhibiting higher levels than non-Hispanic white males [94]. This finding is consistent with epidemiological work indicating that osteoarthritis prevalence tends to be higher in these subgroups. Regardless of varying risk, physical activity seems to be a viable intervention in the treatment of a variety of musculoskeletal conditions across subpopulations with differences in age, sex, and ethnicity.

Physical Activity and Functional Health

The functional health of an individual is determined by his or her physiologic and functional capacities. Limitations may impair an individual's ability to adequately perform daily activities of an occupational, leisure, or domestic nature. A large body of observational studies indicates that physically active mid-life and older males and females have on average a 30% reduced risk of developing a moderate or severe functional limitation when compared to inactive individuals. Many long-term longitudinal studies have found that participants who increased activity over the study period saw a risk reduction comparable to those that remained active, indicating that increases in physical activity at almost any age will deliver some benefit.

All but one of the prospective cohort studies examined in the *PAG* report indicated a strong dose-response relationship between physical activity and functional health. Six of the studies reported a significant statistical trend across physical activity categories, ranging from the least active to the most active participants (fig. 3). The methods used for assessing physical activity and defining functional impairment were very heterogeneous among studies, not allowing the *PAG* committee to determine the specific amount of risk reduction for a given amount of physical activity.



Legend: ADL, activities of daily living; IADL, instrumental activities of daily living. The figure shows the reported odds ratio for each category of physical activity, with the lowest category of physical activity assigned as the referent category. For example, the Huang study had three categories of physical activity, with category 1 (the referent) assigned to those with the lowest level of physical activity, category 3 assigned to those with the highest activity level, with all categories forming an ordinal scale.

Figure 3. Prospective Cohort Studies with Measurements of ADL, IADL, and Global Outcomes. ADL (activities of daily living) comprise basic self-care tasks; the skills that people usually learn in early childhood including feeding, toileting, dressing, grooming, bathing, walking and transferring (ex. moving from a bed to wheelchair). IADL (instrumental activities of daily living) are more complex skills needed to successfully live independently, such as managing finances, shopping, handling transportation, preparing meals, managing medications, performing housework and basic home maintenance. *Adopted from 2008 Physical Activity Guidelines for Americans Advisory Committee Report*, page G6-9.

Although the evidence was modest, the *PAG* report highlights two intervention studies in older men and women (aged 70 – 85 years of age) with moderate functional impairment that showed improvement in mobility scores and walk speeds with a structured exercise program, indicating that physical activity can improve functional health in older populations with existing disability. Studies also indicated that exercise interventions that focused on balance and strength exercises combined with walking were successful at reducing the risk of falls in older, at-risk populations. In many cases, the clinical intervention studies looking at fall reduction include multiple interventions, making it a challenge to assess the impact of physical activity alone [1]. In 70 to 80 year old women, a recent study demonstrated that an exercise intervention increased objectively-assessed strength and balance and reduced the rate of fall-associated injuries [95].

Physical Activity and Cancer

Cancer accounts for almost 25% of reported deaths in the United States and is the leading cause of death in high-income countries [96]. Any intervention that reduces the prevalence or incidence of cancer or improves the prognosis of cancer patients will have a positive health impact on the general population. Physical activity has been shown to have a positive impact on the diagnosis, prognosis, and symptomology of certain cancers. In a large prospective cohort study of almost 80,000 residents of Japan, daily physical activity was strongly inversely correlated to total cancer risk in males and females. Each 10-MET/day increase in activity was associated with a decreased incidence risk of 7% in males and 10% in females for any form of cancer while accounting for age, smoking status, medical history, alcohol use, and diet. In men, the most significant decreases in risk were observed for colon, liver, and pancreatic cancer. Women saw the greatest improvement in risk for stomach cancer, followed by cancer of the colon [97]. Table 6 summarizes the strength of the evidence supporting physical activity's association with reduced incidence risk of specific types of cancer from the *PAG* report and subsequent research findings.

Table 6. Cancer Incidence Risk Reduction Associated with Physical Activity

STRONG EVIDENCE
• Lower risk of colon cancer [64, 98-103]
• Lower risk of breast cancer [103-113]
MODERATE EVIDENCE
• Lower risk of lung cancer[114-117]
• Lower risk of endometrial cancer[118, 119]
• Lower risk of ovarian cancer [120-122]
WEAK EVIDENCE
• Lower risk of pancreatic cancer [123, 124]
CONFLICTING EVIDENCE
• Prostate cancer [125-129]

Adapted from 2008 Physical Activity Guidelines for Americans Advisory Committee Report, Part G, Section 7. Selected references for specific cancer incidence risk shown in "[ ]."

Colon Cancer

A large body of observational studies showed a strong, consistent, inverse relationship between physical activity and colon cancer. On average, studies assessed by the *PAG* committee indicated that individuals engaging in aerobic physical activity for 3 to 4 hours per week have a 30% reduced risk of colon cancer. Prospective cohort and case-control studies published from 1995-2008 consistently show an inverse relationship between physical activity and colon cancer incidence. Across all the studies included in the *PAG* committee review, an average RR of 0.7 was seen between the most physically active and least physically active participants. In general, the study designs were thorough in controlling for confounding factors such as BMI, smoking, alcohol use, diet, and medication use (including hormone replacement therapy in postmenopausal women). Many of the studies included at least three levels of physical activity in the analysis, and results indicate the presence of a dose-response relationship, although the various methods used to measure physical activity made it difficult for the *PAG* committee to quantify or describe the shape of the dose-response relationship between physical activity and colon cancer [1].

Recent research supports a strong association between physical activity, obesity, and colorectal cancer risk. In an extensive review, Mehta and colleagues uncovered a strong association between physical activity and a high fiber diet with a reduced incidence of colorectal cancer in males and females [101]. In 2014, an additional review of colon cancer incidence found a strong relationship between leisure-time and occupational physical activity and reduced incidence rates [130]. After adjustment for several confounders including sex, age, and an extensive list of lifestyle factors in a large cohort of close to 350,000 individuals, high physical activity was strongly associated with a reduction in colon cancer risk among males and females. In a recent meta-analysis of 21 studies looking at physical activity and colon cancer rates, there was an approximately 27% decrease in proximal and distal colon cancer incidence seen in males and females, adding to the large body of research associating physical activity with reduced colon cancer risk [100].

A recent animal study has shed some light on one possible mechanism responsible for the reduction in colon cancer risk seen in physically-active individuals. In mice fed a high fat diet, those that performed exercise reduced colon inflammatory markers and experienced an increase in anti-inflammatory mediators [131].

Breast Cancer

Population-based case-control studies and cohort studies have consistently shown a 20 –70% decrease in breast cancer risk in the most active individuals compared to the most sedentary. The results of over 60 observational studies led the *PAG* committee to state that the relationship between breast cancer risk and physical activity is strong. A recent review article found an average 25% reduction in breast cancer risk comparing the most active to the least active women.

Also, a dose-response relationship was evident in the majority of studies that assessed breast cancer incidence at multiple levels of physical activity [107]. In addition, a pilot study has indicated that physical activity can increase the production of the protein product of a normal copy of the BRCA gene in females. Women who carry a BRCA mutation have a high risk of developing breast cancer, so any intervention that can increase the expression of the normal BRCA gene may reduce this risk, and physical activity appears to be a promising modality, although more research is needed [105]. Also, it appears that physical activity may modulate breast cancer risk in females through hormonal signaling pathways. Steindorf and colleagues noticed that the inverse association between physical activity and invasive breast cancer risk was modulated by the specific hormone receptor status of the cancer, with growth of tumors exhibiting progesterone and estrogen receptors being inversely associated with physical activity, unlike tumors lacking both receptors [106].

The *PAG* committee also found that the benefits of physical activity on breast cancer risk are seen across racial and ethnic sub-populations with large cohorts of black, Hispanic, and Asian-American women present in many of studies. Studies performed internationally have also shown breast cancer risk reduction similar to those that were performed in the United States [1].

There is also recent evidence that physical activity can increase survival times after a diagnosis of invasive breast cancer. Women diagnosed with breast cancer that performed more than 21 MET-hours/week of physical activity experienced a 64% reduction in all-cause mortality at 6 years of follow-up compared to the least active subgroup [104]. Many studies indicate that physically active women during adolescence and childhood have a reduced lifetime breast cancer risk independent of their adult activity level, although recent work failed to find a reduced risk of breast cancer in post-menopausal women associated with physical activity at various life stages [111-113]. More research into the cumulative benefit of physical activity on breast cancer risk is needed.

Lung Cancer

The *PAG* committee report evaluated 11 cohort and case-control studies looking at the influence of physical activity on lung cancer. The median lung cancer risk reduction was 24% from the most active to the least active individuals across the studies. This is similar to a previous review that saw a median risk reduction of 20% [132]. Because the lung cancer risk reduction associated with smoking cessation is so large, confounding from changes in smoking activity becomes a problem when looking at physical activity and lung cancer incidence. Also, different types of lung cancer (adenocarcinoma, small cell, squamous cell) may respond differently to physical activity.

A recent study looked at the association between objectively-measured cardiorespiratory fitness, self-reported leisure-time physical activity, and lung cancer incidence in middle-aged males [115]. Higher levels of cardiorespiratory fitness, measured as maximal oxygen consumption via gas exchange techniques, were associated with reduced lung cancer incidence in a dose-dependent fashion, although self-reported leisure time physical activity was not. It appears that unlike other forms of cancer, objective cardiorespiratory function, such as maximal oxygen consumption measured in a laboratory, is associated with reduced risk of lung cancer. Leading a physically active lifestyle may not be enough to reduce lung cancer risk if the intensity and frequency of the activity is not adequate to improve cardiovascular function. Like colon cancer discussed above, animal models of lung cancer are shedding some light on the possible mechanism associated with the benefits of physical activity and lung cancer prognosis. Exercising mice with lung cancer have shown suppressed tumor growth when compared to sedentary control animals. These exercising mice also exhibited increased levels of tumor suppression proteins, which may have been responsible for the slowed tumor growth [116].

Ovarian and Endometrial Cancer

Physical activity appears to have a modest effect on the relative risk of both ovarian and endometrial cancer incidence. The 15 studies examining ovarian cancer risk published prior to the writing of the *PAG* report had a median RR of 0.7 when comparing the most active to least active participants. This RR appeared to be robust, and was not significantly altered when controlling for BMI or hormone replacement therapy. Oral contraceptive use or BMI did not impact the calculated RRs, indicating that physical activity may act independently of both.

Since 2008, the literature on the epidemiological link between ovarian or endometrial cancer risk and physical activity remains equivocal. In a large meta-analysis of 33 studies, recreational, occupational, and transport-related physical activity was only associated with reduced endometrial cancer risk in women who were overweight or obese, with no significant relationship seen in normal weight females [118]. Regarding ovarian cancer, an extensive review of the literature found a consistent association between increased physical activity and reduced risk in the case-control studies, but only half of the cohort studies indicated a positive benefit [120]. One meta-analysis including 730,000 participants looking at the association between non-occupational physical activity and ovarian cancer produced similar results with a strong, statistically-significant association only present among case-control studies, but not in prospective cohort designs [121].

Pancreatic Cancer

There have been limited studies looking at the influence of physical activity on pancreatic cancer incidence prior to 2008. Two case-control studies and 8 cohort studies were included in the *PAG* committee analysis. The RRs of the studies ranged from 0.78 – 1.21. The inconsistent results in the published literature at the time the report was released led the *PAG* committee to rate the association between pancreatic cancer and physical activity as “weak.” Subsequently, a large cohort study of over 560,000 individuals aged 50 – 71 did not find any association between self-reported physical activity and pancreatic cancer, although there were strong associations between pancreatic cancer risk and obesity [124]. A very recent meta-analysis of 32 studies containing 10,501 pancreatic cancer cases looking at the association between physical activity and pancreatic cancer identified a small, but highly variable association [123]. This meta-analysis found a 7% – 22% reduction in pancreatic cancer risk associated with long-term physical activity when adjusting for BMI, smoking status, and sex. Care needs to be taken when interpreting the results due to the large difference in risk estimates between cohort and case-control studies included in the meta-analysis, which led the authors to state that the evidence indicates a weak relationship between physical activity and pancreatic cancer incidence. More current research supports the *PAG* committee position that there is not enough information available to strongly support an association between physical activity and pancreatic cancer risk [123, 133-135].

Prostate Cancer

The *PAG* committee evaluated 37 studies looking at the relationship between prostate cancer and physical activity and noted that 51% of the studies found an inverse relationship between prostate cancer risk and physical activity, while 38% found no association. The remaining 4 studies saw an increase in prostate cancer risk with increasing levels of physical activity [1]. The equivocal results regarding prostate cancer risk reduction and physical activity led the *PAG* committee to conclude that there was not an adequate body of evidence to indicate any benefit of physical activity when considering prostate cancer mortality risk. An updated review in 2012 found similar results, with 22 out of 40 studies showing a decrease in prostate cancer incidence [129]. A recent case-control study of individuals with prostate cancer saw an increase in risk associated with family history of prostate cancer, high fat diet, red meat consumption, and obesity. There was also a modest inverse association of prostate cancer incidence with high fruit and vegetable consumption, as well as higher levels of self-reported activity [136]. It has been suggested that the enhancement of an exercising individual's antioxidant defense mechanisms may indicate a plausible mechanism through which physical activity can have a beneficial effect on prostate cancer risk and prognosis [128]. A recent mechanistic study of 71 men with low-risk prostate cancer found that cell cycling and DNA repair pathways were enhanced in men that participated in greater than 3 hours a week of moderate to vigorous physical activity [126]. Thus, although the epidemiological data regarding the benefits of physical activity on prostate cancer risk and prognosis are equivocal, recent work indicates that it is mechanistically plausible for physical activity to reduce prostate cancer risk and impede its progression.

Mechanisms Linking Physical Activity to Reduced Cancer Risk

Recent work has focused on the mechanisms responsible for reductions in general cancer risk with increased physical activity. Excess body weight is associated with increased risk of many types of cancers, so physical activity may mediate its effects through reductions in adiposity, resulting in changes in blood adipokines and cytokines, improving insulin sensitivity, and altering hormone production [64]. Physical activity also results in reduced skeletal muscle insulin resistance and reduced high blood insulin levels even in the absence of weight loss.

Physical activity also decreases transit time in the colon through increased motility, which may reduce carcinogen exposure. Physical activity may also reduce oxidative damage and improve DNA repair mechanisms [137]. Future work should further examine these mechanisms using randomized controlled study designs whenever possible.

Physical Activity and Mental Health

The US Centers for Disease Control and Prevention defines mental health as "a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community [138]." Higher amounts of physical activity have been associated with beneficial effects on many of the symptoms and disorders associated with poor mental health, such as depression, anxiety, and declining cognitive function. The *PAG* committee determined from literature published from 1995-2007 that there is moderate to strong evidence that physical activity can reduce the incidence and beneficially treat the symptoms of many mental health disorders, including those listed above. Physical activity has also been indicated as a promising treatment in other mental disorders outside of depression, anxiety, and dementia, with a recent meta-analysis indicating that exercise interventions consistently reduce psychiatric symptoms and improve neuro-cognition in schizophrenic patients [139].

Depression

Twenty-eight studies from 11 nations using a prospective cohort design found that the risk of adults developing physician-diagnosed depression was 25% – 40% lower in the most active individuals compared to the least active. These results, combined with over 100 observational studies associating higher levels of physical activity with lower incidence and prevalence of depression led the *PAG* committee to conclude that there is strong evidence indicating that physical activity can reduce the risk of developing physician-diagnosed depression and depressive symptoms. In the intervening years, there has been a large body of research confirming the association between physical activity and depressive symptoms. In addition, studies have illustrated exercise's effectiveness in reducing the risk of the development of depression in healthy individuals as well as mitigating symptoms in patients suffering from depression.

A prospective study of 701 elderly individuals followed for 5 years found a strong association between increased physical activity and reduced risk and persistence of depression, confirming previous work in younger adults [140]. Over the past decade, there has been an explosion of research using randomized controlled studies that indicate exercise is a successful treatment intervention in young, adult, and elderly populations with mild and major depression [141-145]. Trivedi and colleagues identified a dose-response relationship in their study, in which a high and low exercise group both demonstrated improvements in depressive symptoms and cognitive function, with the high exercise volume group exhibited greater improvements [146]. Exercise interventions have also proved successful in depressed patients with cognitive dysfunction who were unresponsive to antidepressant medication. Patients with major depressive disorder in the high-dose exercise group saw improvements in psychomotor speed, attention, visual memory, and spatial learning compared to a low-dose control group [147].

Increased physical activity has also been shown to be effective at alleviating depressive symptoms in patients with co-morbidities. In lung, colon, and breast cancer patients, exercise programs have been shown to improve sleep and quality of life as well as lessen depressive symptoms, fatigue, and anxiety [148-151]. Randomized control studies have also shown exercise to be effective at reducing symptoms associated with depression and anxiety in patients with chronic fatigue syndrome, fibromyalgia, rheumatoid arthritis, and lupus [152, 153].

A recent review article highlighted the effects of physical activity on symptoms and biomarkers of depression [154]. Through an extensive analysis of available primary research and meta-analyses, Archer et. al. concluded that physical activity is effective at improving cognitive, emotional, motivational, and somatic symptoms of depression. The authors also found evidence that exercise has anti-neurodegenerative effects, improves neurotransmitter and neuro-immune function, shedding light on the neural mechanisms behind the documented improvement in depressive symptoms.

There has also been some mechanistic work on depression and physical activity in animal models. In humans, serotonin is an important chemical messenger influencing functions related to mood, appetite, sleep, memory and learning, and some social behaviors. In a model of depression in mice, 8 weeks of treadmill running improved maze and swim test scores (surrogates for depressive symptoms), as well as altered serotonin receptor density in the hippocampus, indicating that exercise may improve serotonin signaling in regions of the depressed brain [155].

Anxiety

Although fewer studies have looked at anxiety diagnosis and symptoms as compared to depression, there is strong evidence that physical activity and exercise reduces anxiety incidence and can reduce the frequency and severity of symptoms of individuals diagnosed with an anxiety disorder. The *PAG* committee highlighted four population-based prospective cohort studies that reported an average 28% reduction in the relative risk of developing anxiety in physically active individuals compared to the least active sub-group, even after controlling for sociodemographic and comorbidity confounders. A recent study indicated that the risk of anxiety and depression in children with a familial history of these two disorders is partially mitigated by keeping these at-risk children physically active [156].

Cognitive Disorders

There has been much interest on the possibility that physical activity and exercise could be an effective intervention and preventative measure to reduce the risk of cognitive disorders and age-related cognitive decline. Four prospective cohort studies reviewed by the *PAG* committee showed that physical activity and exercise had a protective effect against cognitive decline. The report found that 64% of prospective studies looking at dementia incidence indicated that increased physical activity reduces the relative risk, specifically in regards to Alzheimer's disease (fig. 4). Current, early and late-life exercise/physical activity participation was all shown to delay the onset of dementia symptoms. In addition to the prospective cohort studies, 20 randomized control studies consistently showed improvements in sub-categories of cognitive function and Alzheimer's symptoms in older adults who participate in exercise programs, lending more evidence to the positive cognitive benefits of increased physical activity.

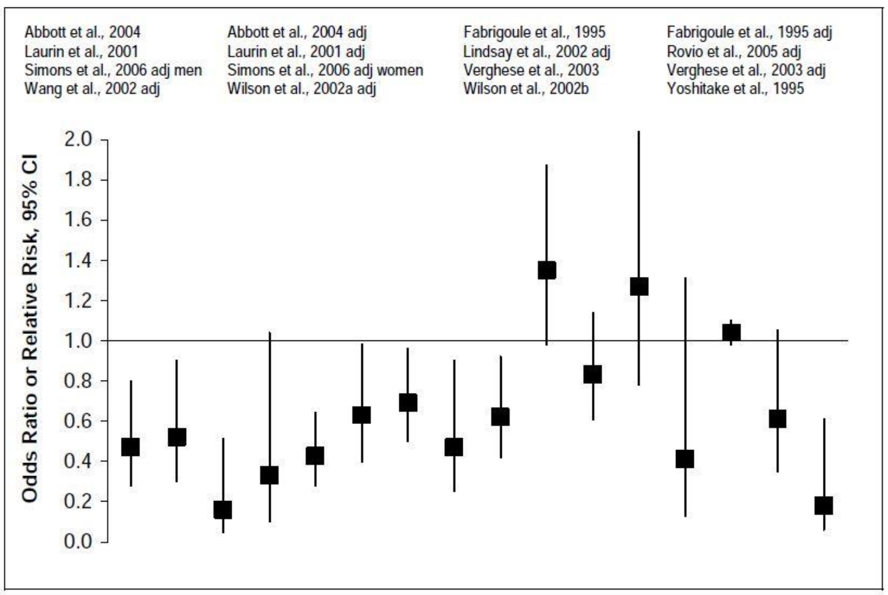


Figure 4. Incident Total Dementia or Alzheimer's Disease: Prospective Cohort Studies, 1995 through 2007**.** *Adopted from 2008 Physical Activity Guidelines for Americans Advisory Committee Report, page G8-29.*

Due to the multitude of methods used to assess cognitive function and the variety of exercise interventions, it was not possible for the *PAG* committee to define a dose-response relationship between physical activity and depression, anxiety, or dementia. However, a handful of studies included 3 or more levels of activity, and it seems that higher levels of physical activity may impart a greater health benefit. In a recent review article of randomized controlled studies looking at cognitive function in individuals over 55, exercise that improved cardiorespiratory function also improved motor function, auditory attention, and delayed memory function [157]. In Norway, self-reported leisure physical activity in men and women aged 65 – 80 was associated with decreased dementia-related mortality risk after controlling for known covariates associated with dementia [158]. A case-control study in Beijing, China indicated that there was a 60% reduction in the risk of suffering from mild cognitive impairment in men and women over

60 years old that participated in regular physical activity [159]. A randomized controlled study of 86 women 70 – 80 years old showed that 6 months of aerobic exercise increased brain hippocampal volumes, improved processing speed, conflict resolution, and verbal fluency, indicating that exercise interventions can improve performance in certain cognitive tasks, and linked these improvements with structural neural changes [160].

The possibility for sex or race/ethnic differences in the cognitive health benefits of physical activity and exercise has not been adequately studied [157], although many studies performed outside of the United States corroborate the cognitive health benefits of physical activity, indicating that country of origin does not influence an individual's cognitive response to physical activity or an exercise intervention [140, 158, 161, 162].

Sedentary Time as an Independent Risk Factor

Mortality, Disease Risk, and Sedentary Time

Sedentary activities, requiring between 1 and 1.5 METS, are now a major component of modern society, underscored by a consistent shift to sedentary occupations and leisure activities (TV viewing, computer games) in the United States. Recent studies have indicated that the average person spends over half of their day performing sedentary activities involving prolonged sitting. Sedentary activity time has been shown to be weakly correlated with MVPA (3-6 METS) time, but is highly inversely correlated to light activity time (1.5-3 METS) [163]. This indicates that being sedentary is not the same as being physically inactive, and may discount the health benefits of light activities that require less than 3 METS, which are not captured in most study designs that evaluate the health benefits of physical activity. These circumstances have lead researchers to view "sedentary time" as an independent risk factor for disease and morbidly, exclusive of physical activity. Some of these studies have found that prolonged sitting attenuated the health benefits in individuals who were otherwise meeting physical activity guidelines [164]. In most developed countries, like the United States, the majority of the population exhibits high sitting times and very little MVPA. Also it is important to realize that high levels of MVPA and high sedentary time can coexist within the same individual. An example would be an office worker who exercises before or after work. Healy and colleagues defined this type of individual as an "active couch potato [165]."

In a large meta-analysis focused on adult populations, overall sitting time was associated with increased cardiovascular and all-cause mortality, cardiovascular disease and type 2 diabetes incidence, as well as increase incidence of colon, colorectal, endometrial and ovarian cancer [164]. These risk estimates were adjusted only slightly when MVPA was controlled for, reinforcing the concept that MVPA and sedentary time are independent risk factors for mortality and many diseases. This meta-analysis confirmed the results of a previous study that included over 790,000 participants, which estimated a 49% increase risk of all-cause mortality and a 90% increased risk of type 2 diabetes in the most sedentary individuals, independent of MVPA [166].

A meta-analysis of 10 cross-sectional studies found that higher sedentary time increased the risk for metabolic syndrome by 73% when compared to less sedentary individuals [167]. A study of 929 male autoworkers associated sedentary time with many of the risk factors for cardiometabolic disease, such as elevated blood pressure, triglycerides and cholesterol, as well poor glucose homeostasis and increased inflammatory markers [168].

Objective Assessment of Sedentary Behavior

Higher levels of accelerometer-derived sedentary time in women have been associated with coronary artery calcification, a risk factor for coronary artery disease, independently of MVPA. This indicates that excessive sedentary time can lead to the progression of sub-clinical heart disease [169]. Thorp and colleagues also found consistent increases in mortality risk and incidence of certain types of cancer, type 2 diabetes, obesity, and multiple cardiometabolic risk factors in a meta-analysis of 48 papers that used self-reported sedentary measures as well as accelerometer-derived measurements. The researchers saw a consistently higher risk of disease associated with prolonged sitting times, regardless of MVPA level [163].

Risk of Sedentary Behavior in Children and Adolescents

With cardiovascular disease still ranking as the leading cause of death worldwide and the increase in obesity-related diseases in children and adolescents, the influence of sedentary time on cardiometabolic risk factors in younger populations has become a growing area of interest. High accelerometer-derived sedentary time in 13 – 17 year olds was associated with a worse cardiovascular risk factor index score based on blood pressure, body composition, blood lipid, blood cholesterol, and blood glucose measurements. This association was present in both girls and boys, and although it was attenuated, was still present when controlling for adiposity [39]. These results were corroborated in a slightly younger cohort of 8 – 11 year olds who also exhibited increased cardiometabolic risk with increased objectively-measured sedentary time [38]. Saunders and colleagues assessed metabolic risk in a group of school-aged children with a family history of obesity. Elevated cardiometabolic risk scores were strongly associated with more prolonged siting time. This association was independent of sex, sexual maturation stage, and family income level. Interestingly, the association between prolonged sitting time and cardiometabolic risk was also independent of physical activity and total sitting time, indicating that long, uninterrupted bouts of sedentary activity are more closely associated with risk than the total daily amount of sedentary time. This reinforces the concept that frequent short breaks in sedentary activities, such as walking, standing, or stretching, can mitigate the deleterious effects of being sedentary.

Prolonged sitting and sedentary activity has been shown to increase cardiometabolic morbidity and mortality in adults, as well as increase the risk of cardiometabolic conditions in children and adolescents. In addition to the epidemiological work referenced above, there is a substantial body of mechanistic evidence indicating that sedentary activities can lead to dysregulated glucose and lipid metabolism, independently of obtaining the recommended amount of MVPA. This documented metabolic dysfunction seen in sedentary individuals may be a causative factor in the increased risk of cardiovascular morbidity and mortality [170].

Health Effects of Active Transport

Mortality

As previously highlighted, a large body of research indicates that it is the dose of physical activity that is responsible for any beneficial health effects, regardless of the purpose or goal of the activity (occupational, leisure, domestic, transport). Active commuting by walking or riding a bike is considered a practical way to incorporate physical activity into an individual’s daily routine. Recently, there has been interest in focusing on the specific health benefits associated with active transportation via walking or cycling and to determine if there is an independent association between health and commuting to work/school via bike or foot, rather than using a car.

A large study in Denmark reported a 28% decrease in all-cause mortality associated with cycling to work. Stratified by age, females and males both saw a significant reduction in mortality risk with greater than 3 hours of bicycling commute time a week, after controlling for other forms of physical activity [171]. Two studies in Finland and one in China also confirmed a reduction in all-cause mortality in adult females who spent at least 15 minutes a day walking or cycling to work [13, 172]. In the Shanghai Women’s Study a decrease in mortality associated with active transport was also seen in individuals with clinically-diagnosed chronic diseases, such as diabetes, respiratory disease, and chronic hepatitis. The reduction in mortality was independent of time spent exercising [13]. Interestingly, although males were included in both Finish studies, no statically-significant decrease in all-cause mortality was associated with active commuting in men, although men who reported a high level of occupational or leisure time physical activity (LTPA) reduced their risk of CVD-related and all-cause mortality [172]. Kelly and colleagues recently published the largest meta-analysis on the association between mortality and walking and cycling, and found an overall 10% reduction in all-cause mortality after controlling for other forms of exercise across age and gender [173].

Health Risk

Walking and cycling have not only been linked with reduced mortality in adults, but also with positive health indicators, lower disease incidence, and improved risk factor profiles. In a large meta-analysis looking at the association between active commuting and cardiovascular disease, active transport was associated with decreased heart attack and stroke incidence and a lower risk of coronary artery disease and diabetes in both males and females [25]. Moderate and high levels of physical activity during commuting has been associated with a significantly reduced risk of acquiring T2D in both males and females, even after controlling for occupational and leisure time physical activity [174]. A strong inverse association between active commuting and CHD in women aged 25 – 64 has been identified over a 19 year follow-up period [175]. Walking or cycling to work can also positively impact body composition and contribute to healthy weight maintenance. In a cohort study that followed over 8500 middle-aged males, participants that walked or biked to work had smaller waist circumferences, lower body mass index scores, and less increases in body mass index scores over a 5 year period [176]. This body of research indicates that the substitution of car trips with walking and bicycling in a sedentary population can significantly improve health.

Impact on Child and Adolescent Health

In addition to the evidence associating cycling and walking for transport to reduced mortality risk in adults, active transport has also been linked to improved cardiometabolic profiles and cardiorespiratory fitness in children and adolescents. Among 9 – 15 year olds enrolled in the European Youth Heart Study, those that bicycled to school had higher laboratory-assessed aerobic fitness than those who traveled by car or bus [36]. In addition, a 6-year long longitudinal study found that adolescents who traveled by car or bus to school at the study's initiation, but switched to an active transport mode during the study period, had higher cardiovascular fitness than those who continued using passive transport [177]. A study in Denmark found that boys and girls 15-19 years old had higher aerobic power, flexibility, and dynamic and isometric muscular endurance compared to students who traveled to school using passive transport, reinforcing that multiple health and functional benefits are associated with physical activity [178]. These findings were confirmed in a cross-sectional analysis of randomly selected students from 40 schools across Norway [179]. In 7^{th} – 9^{th} graders, cycling to school was also found to be associated with a lower risk of being obese or overweight, two adolescent risk factors linked to cardiometabolic disorders later in life [180].

In light of the positive health benefits associated with biking and walking to school, encouraging active transport in young individuals gains even more import considering that there is evidence that the percentage of children walking and biking to school has been declining. A Canadian study that analyzed national transport data found that the percentage of kids that walked or biked to school dropped from 51% in 2001 to 24% in 2010 [181].

PHYSICAL ACTIVITY AND THE BUILT ENVIRONMENT

Influence of the Built Environment

Our built environment, the human-made space in which people live, work, and recreate on a day-to-day basis, can significantly influence our physical activity patterns. Health and transportation professionals have become concerned that many communities have been designed in a way that discourages active transport by making it difficult, or possibly even dangerous, to walk and ride a bike [182]. In contrast, neighborhoods with compact, mixed-use designs and highly interconnected streets are consistently associated with higher active transport measured as the number of total walking and cycling trips [183-185]. A review of transportation studies showed that the number of trips taken by foot or bicycle was approximately 5 times higher in the highest versus lowest density areas [186]. Current research is exploring not only the relationship between the built environment and physical activity, but also assessing the health benefits associated with these differences in physical activity patterns.

In a cross-sectional study of almost 5000 adults ranging from 18-90 years old living in Texas, longer work commuting distances were associated with decreased energy expenditure, lower cardiorespiratory fitness and a higher prevalence of metabolic syndrome [187]. Commuting distances greater than 15 miles were associated with lower odds of meeting MVPA recommendations and achieving high levels of fitness and with greater odds of obesity and central adiposity. The authors postulated that these longer commute distances displaced walking and bicycling for motorized transport, leading to sedentary behavior-related adverse health effects.

Durand and colleagues performed a systematic review of the literature focusing on studies that evaluated the effects of the 10 smart growth principles outlined by the Smart Growth Network, a partnership of government, business, and civic organizations that support smart growth [188]. The review of over 517 analyses identified 5 built environment principles that appeared to be most strongly associated with higher levels of physical activity: (1) providing a range of housing types within a neighborhood to ensure that residents at different life stages are provided for, which attracts a diverse range of people to a location; (2) blending a combination of residential, commercial, cultural, institutional, or industrial uses, where those uses are physically and functionally integrated through public transport and pedestrian connections; (3) increasing the number of dwellings per acre to create more compact neighborhoods enabling more walking and bicycling, as well as more opportunities for social interaction; (4) emphasizing compact development around transit stations and transit corridors in existing districts to promote a pedestrian-friendly environment; (5) preserving areas of urban open space for recreation, ecological conservation, and aesthetic appeal.

Walkable Neighborhoods

Increasing the walkability of our neighborhoods presents opportunities for realizing environmental and health benefits. In a study of individuals aged 20 – 65 living in King County, WA, participants living in neighborhoods that were rated as highly walkable with many transit and recreational options (parks, swimming pools, play grounds, golf courses) participated in 17.1 more minutes a day of MVPA and 58.2 more minutes per week of leisure-time physical activity than those residing in neighborhoods with low walkability and recreation scores [189]. In a meta-analysis including research on adults from 11 countries, the built environment's aesthetics and land-use mixes were positively associated ($p \leq 0.05$) with activity levels and meeting physical activity guidelines, with perceived neighborhood walkability accounting for 16% of the site variance in MVPA minutes [190]. This last study also points out the influence of multiple factors in increasing physical activity in a neighborhood, including the appearance of the neighborhood.

In an analysis of walking patterns in Stockholm, Sweden individuals living in highly walkable neighborhoods walked on average 3.1 minutes/day more than those that lived in less walkable communities, after accounting for confounding variables. This study agrees with research conducted in the U.S., Belgium, Germany, and Australia, indicating that regardless of social, cultural, economic, and political differences between countries, the walkability of a neighborhood is positively associated with higher levels of physical activity [191, 192].

A longitudinal study in Portland, OR examined built environment characteristics, health behaviors, and changes in blood pressure of 1100 residents aged 50 – 75 across 120 neighborhoods. Over one year of follow-up, low neighborhood walkability scores were associated with increases in systolic and diastolic blood pressures, which is a strong risk factor for cardiovascular disease. Individuals in highly walkable neighborhoods had on average systolic blood pressures 4 mmHg lower and diastolic blood pressures 3.9 mmHg lower than those living in low walkable neighborhoods [193]. In an analysis of travel behavior in King County, WA, researchers used linear regression techniques to predict BMI and active transport use from neighborhood walkability scores. Their results indicated that individuals living in more walkable environments walked and biked more, used their cars less, and had lower body mass index scores when compared to individuals residing in less walkable communities. A 5% increase in a neighborhood's walkability score was associated with a 32% increase in minutes devoted to active transport and about a one-quarter point lower BMI score [194]. Sturm and colleagues used U.S. nationwide household data and examined the association between chronic health conditions and a calculated citywide "sprawl index." After adjusting for many confounders such as age, race, household income and education, a significant relationship between the number of chronic medical conditions and more sprawling (less walkable) built environments was reported [195]. One standard deviation decrease in Sturm and colleagues' sprawl index predicted 96 fewer chronic medical conditions per 1000 residents. These studies highlight the potential of the built environment to affect cardiovascular risk factors, such as blood pressure and BMI, as well as influence the prevalence of chronic disease.

Child and Adolescent Health

Children as well as adults can benefit from certain built environment features. Neighborhood greenness has been associated with MVPA in children and adolescents. In a novel study comparing children's exposure to green spaces (parks, nature trails, and playgrounds), Almanza and colleagues determined that the more a young individual is exposed to these green spaces, the more active they are. Children who experienced more than 20 minutes of daily greenness exposure performed 4.7 times more MVPA than those below 20 minutes of exposure. Researchers also compared the GPS and accelerometer-derived data between a "smart growth" community and surrounding neighborhoods [196]. Children and adolescents in the smart growth community were exposed to green spaces significantly more on a daily average than those residing in traditional neighborhoods, and the association between exposure to greenness and MVPA was slightly stronger in 8 – 14 year olds residing in the smart growth neighborhood (39% increase in odds of performing MVPA compared to 34%) [197].

Public Transportation

Researchers have also discovered that not only is high neighborhood walkability associated with increased physical activity, but that easy access to public transportation can also lead to population-wide improvements. In a meta-analysis of research on transportation trends, it was shown that individuals who take public transportation spend 8 – 33 more minutes a day walking than those that use cars, indicating that some adults meet the recommended amount of physical activity just by walking to and from transit stops [198]. Investigation into the effect of a newly-opened rail line in Los Angeles revealed that operation of the new rail line led to 8 – 10 minutes of increased physical activity in the most sedentary individuals living within ½ mile of a rail station [199]. This unique study corroborated earlier work showing that over 30% of individuals who used a combination of walking and public transit to commute walk for at least 30 minutes a day, which meets the minimum physical activity level recommended by the US Department of Health and Human Services and the World Health Organization [200]. These studies indicate that improving access to public transportation may also lead to increased active transport and daily physical activity levels.

AIR POLLUTION IMPACTS DURING PHYSICAL ACTIVITY

Health Effects of Exposure to Air Pollution while Exercising

The health benefits of increasing physical activity have been well documented. However, when individuals exercise outdoors they can potentially increase their exposure to air pollution. Exposure to outdoor air pollution has been associated with many negative health effects, including increased risk of all-cause, cardiovascular, and diabetes-related mortality. Many air pollutants exacerbate respiratory symptoms and reduce lung and cardiac function, particularly in asthmatics [201-211]. Acute exposure to air pollution is also associated with increased cardiovascular and respiratory-related emergency department visits and hospitalizations for males and females of all ages [212-219]. Being active outdoors elevates the air pollution exposure of an individual not only by increasing the duration of exposure to ambient air, but also by increasing the inhaled dose of air pollution due to the higher breathing rates associated with physical activity.

Controlled and environmental air pollution exposure studies have shown that sensitive populations, such as asthmatics or individuals with other cardiopulmonary conditions, are more impacted by air pollution during physical activity. Short-term exposure of asthmatics to diesel exhaust during a 2-hour walking program resulted in reduced lung function documented` as a 6.1% drop in the forced expiratory volume achieved in one second and a 5.4% drop in forced vital capacity compared to the same individuals performing the identical program in an environment with significantly lower levels of PM2.5 (28.3 vs. 11.9 $\mu g/m^3$) [220]. Asthmatics seem to experience greater lung inflammation than non-asthmatics following ozone exposure during exercise, exhibiting significant increases in lung inflammatory markers that were not seen in non-asthmatic controls subjects [221].

Over the past decade, a research group in Belgium has been investigating the effects of air pollution exposure during aerobic exercise on cognitive function and markers of blood inflammation and neuroprotective proteins. As previously stated, physical activity has been shown to increase cognition and delay the onset of neurodegenerative diseases (see section on Cognitive Disorders). Bos and colleagues compared cognitive function and inflammatory, immune, and neuroprotective blood markers between volunteers exercising in a rural area versus those exercising in an urban environment [222]. After 12 weeks of training the volunteers exercising in the urban setting had raised levels of inflammatory markers compared to the rural group. Also, the rural group showed improvements on cognitive performance tests that were absent in the urban group. Both groups saw similar levels of increases in cardiorespiratory fitness, and it was confirmed that the urban setting had significantly higher levels of ultrafine particulate matter (UFPM) present during exercise sessions (7244 vs. 5625 particles/cm^3), suggesting that exercising regularly in urban areas with high levels of air pollution increases systemic inflammation and attenuates exercise-induced cognitive benefits [223]. Bos and colleagues also performed an experiment in rats showing that the increase in brain-derived neurotrophic factor, thought to be the key mediator of the cognitive improvements seen with physical activity, was attenuated when the rats were exposed to UFPM, identifying a possible mechanism responsible for the cognitive findings in human participants [224].

There is also evidence that physical activity performed in higher levels of ambient traffic-related air pollution (TRAP) can negatively impact neural control of the heart. In a cross-over study examining the acute effects of ambient air pollution exposure, healthy volunteers performed a cycling exercise protocol along both a higher exposure and lower exposure route [225]. Deleterious changes in heart rate variability, which describes the electrical activity of the heart, were present only when the volunteers bicycled on the high exposure route. Personal monitoring equipment and estimations from central site monitors confirmed that exposure was greater on the more traffic-dense route. These results suggest that short-term exposure to TRAP while exercising may negatively impact heart function in healthy adults. The long-term health ramifications of these results are unclear, because it is possible that the cardiovascular health benefits (see Physical Activity and Cardiovascular Health) of cycling may outweigh the negative influence of air pollution exposure on heart rate variability.

Lundback and colleagues measured increases in blood vessel stiffness, a risk factor for CVD, in 12 healthy volunteers when exposed to 350ug/m^3 of diesel exhaust while exercising [210]. In young healthy volunteers exercising outdoors, a statistically significant association was seen between increases in the ambient concentration of particulate matter and an increase in the fraction of exhaled nitric oxide, a marker of lung inflammation. These studies indicate that the entire population is susceptible to the effects of air pollution to some extent, not just sensitive groups [209].

Physical Activity Benefits in Populations Exposed to Air Pollution

Physical Activity and Air Pollution Exposure Studies

Even though air pollution poses some risk to health evidenced by the scientific literature, does this threat warrant reducing or eliminating physical activity outdoors? There are a handful of studies available that have attempted to examine this question.

A few international studies have reported on the combined health effect of air pollution and physical activity. Rojas-Rueda and colleagues took advantage of the implementation of a new bicycle sharing program in Barcelona, Spain. Utilizing travel data, surveys obtained from members of the bike sharing service, and relative risk functions calculated from the entire Barcelona population aged 16 – 64, it was estimated that approximately 12 deaths among the 28,251 regular participants in the bike share program would be avoided annually due to increased physical activity through biking while taking into consideration air pollution exposure and traffic accidents [226].

A study in Hong-Kong that retrospectively assessed the physical activity habits of the recently deceased found that short-term elevated air pollution measures were associated with mortality in the non-exercisers, but not in the individuals categorized as moderate exercisers, indicating that physical activity may have a protective effect on the harms associated with acute air pollution exposure [227]. When compared to the exercise group, non-exercisers had a 4.3%, 1.75%, and 3.06% increased mortality risk from nitrogen dioxide, ozone, and particulate matter, respectively. Although these results were encouraging, the protective effect of exercise was not seen in those individuals who were very physically-active ($\geq$ 4 days/week), indicating that the "more is better" mentality may not apply to physical activity in areas with higher levels of outdoor air pollution.

A recent study conducted in Denmark has also demonstrated that the health benefits of physical activity can outweigh the negative health impacts of air pollution using individual air pollution exposure and activity assessments [228]. Andersen and colleagues collected physical activity data and modelled traffic-related air pollution at each participant's residence. Higher levels of physical activity were associated with a substantial reduction of 22% in all-cause mortality risk, regardless of whether the individual resided in a higher or lower air pollution environment. Although the results of this study indicate that the benefits of outdoor physical activity may outweigh the air pollution exposure risk, even the "high" exposure neighborhoods in the Andersen study had annual average NO_2 levels well below the U.S. national ambient air quality standard. It remains to be seen if the physical activity benefit would outweigh the negative effects of air pollution in areas with higher ambient levels.

Only one similar study was conducted in California. Researchers utilized regional travel surveys to estimate physical activity and residential exposure to air pollution and compared the influence of physical activity and air pollution on heart disease mortality in higher and lower walkable communities in Southern California [229]. Overall, residents of both types of neighborhoods were relatively inactive, although those in higher walkable neighborhoods were comparatively more active and this was associated with 7 fewer IHD deaths per 100,000 persons/year. Unfortunately, these higher walkable neighborhoods also had higher levels of air pollution, specifically PM2.5, which was attributed to being responsible for 6 more IHD-related deaths per 100,000 persons/year, almost cancelling out the benefit of being more physically active. This suggests that the health benefits of living in a highly walkable environment like those surveyed in the study may be offset by increased exposure to air pollution.

In a paper published in 2016, Tainio and colleagues modeled the net health impact on all cause mortality along a wide range of physical activity levels and ambient air pollution levels [230]. The authors' conclusion was that in general, the benefits of active travel outweigh the health risk of air pollution exposure. As an example, the model predicted that an individual living in an area with an outdoor PM2.5 concentration of 50 $\mu g/m^3$ would have to bicycle for approximately 300 minutes per day before the health benefits of physical activity would start being outweighed by the health harms due to increased exposure to PM2.5. Even in a location with a high background PM2.5 concentration of 100 $\mu g/m^3$, it would require 75 minutes of cycling and over 10 hours of walking before a net increase in all cause mortality risk would be seen (fig. 5).

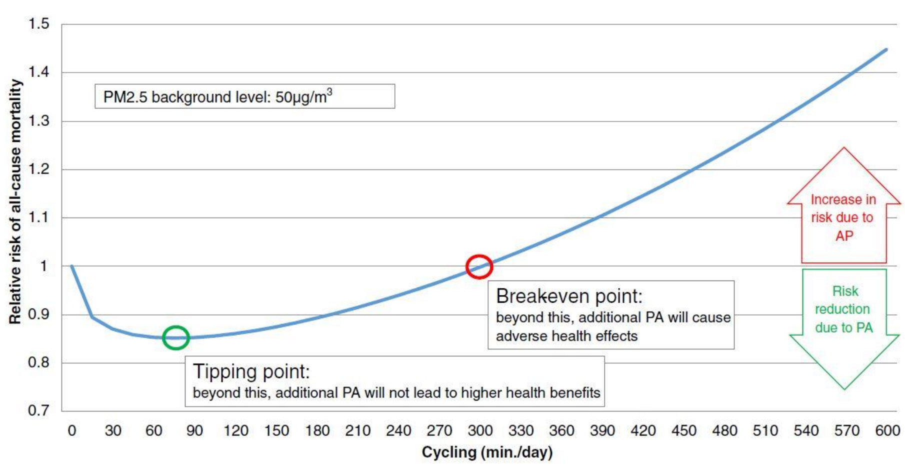


Figure 5. Illustration of tipping point and break-even point of relative risk of all-cause mortality combining the effects of physical activity and air pollution (PM2.5 = 50 $\mu g/m^3$). AP = air pollution, PA = physical activity. *Adopted from Tainio, M., et al., Can air pollution negate the health benefits of cycling and walking?, Prev. Med. (2016).*

Modeling the Combined Effects of Physical Activity, Air Pollution, and Traffic Injuries

A few researchers have recently attempted to address the interaction between physical activity, air pollution exposure, and traffic injuries utilizing modelling techniques [231-235]. These studies use transportation survey data, mortality and morbidity relative risk assessments, traffic injury statistics, and air pollution emissions and exposure models to compare the combined population health risk between alternate scenarios of active transport utilization. In many of the studies, the health outcomes associated with changes in transportation-related physical activity, air pollution, and traffic accident exposure are compared between a baseline scenario and hypothetical alternatives. These modeling studies consistently estimate that the health benefits of increases in physical activity due to a population shift to active transport from personal automobile use outweigh the negative health consequences of increased air pollution exposure and traffic accident risk. One study in England using the Integrated Transport and Health Impact Modelling Tool (ITHIM) [236] estimated that with significant but achievable reductions in car use and driving speeds coupled with increases in bicycling and walking that there would be a 1.8% – 4.1% decrease in total population disease burden when considering air pollution exposure, physical activity, and traffic accidents [233]. Specific to California, one modelling study customized ITHIM for use in the Bay Area, and taking into account mortality and morbidity risks, found that the adoption of active transport strategies in the Bay Area could lead to significant public health gains with approximately 2,200 fewer premature deaths and 17,000 fewer years lost to disability annually, as well as aid in the attainment of greenhouse gas emission reduction goals [231].

At this time, developers of other health modeling tools designed for widespread application are incorporating air pollution assessment components, such as the *Health Economic Assessment Tool for Cycling and Walking (HEAT)* designed by the World Health Organization [237]. Also, developers of a land-use scenario planning tool, UrbanFootprint, are working on a health module to estimate the health benefits of physical activity while considering air pollution exposure [238].

Although it is encouraging that the results of these modeling studies indicate increases in active transport use can lead to significant health benefits, the limitations and assumptions of such models need to be addressed. ITHIM and HEAT models fail to take into account the increased ventilation rates associated with physical activity, although some study-specific modeling efforts, such as those performed in Barcelona, attempt to control for changes in ventilation [226, 234]. The exposure to air pollution may be similar for pedestrians/cyclists and vehicle occupants, but the increased ventilation rates of those bicycling and walking would result in higher air pollution doses in this active population [239]. Also, most of the modeling studies focus on the health effects of exposure to fine particulate matter to determine the health impact of increased air pollution exposure, and fail to model health outcomes associated with other traffic-related pollutants, such as ozone, UFP, and NO_2. Ozone has been linked to increased health system utilization and the exacerbation of respiratory and cardiovascular symptoms in sensitive populations, contributing significantly to the overall disease burden associated with air pollution [213, 214, 240-242]. Some research suggests that chronic ozone exposure may also lead to the onset of respiratory disease [207, 243]. In addition, research indicates that exposure to the many constituents of traffic-related air pollution has significant health impacts [209, 212, 244-248]. The inability to include the risks associated with the full spectrum of air pollutants most likely underestimates the disease burden attributed to air pollution exposure in these models.

The majority of these studies assumes that if individuals adopt active transportation, their non-transportation physical activity levels (leisure, occupational, domestic) will remain the same, and no substitution will take place. If, in practice, individuals do “substitute” leisure-time physical activity with transport-related activity, the health gains from increased adoption of active transport may be overestimated. Also, many of the health gains detailed in these studies are dependent on older age groups (50 +) adopting active transport. Individuals over 50 are at a higher risk for chronic disease, but also less likely to adopt active transport strategies than younger individuals. If older individuals do not take up bicycling and walking for transportation in sufficient numbers as the models assume, the overall health benefits predicted by the models will be overestimated. These models predict health benefits based on published studies that attempt to quantify the relationships between physical activity, pollution exposure and selected health outcomes. Because the models rely on the results of epidemiological studies, the inherent uncertainty of these source studies is carried over into the model predictions, limiting their predicative ability; a model can only be as certain as its data inputs are.

Regardless of the assumptions and limitations inherent in modelling studies of this nature, sensitivity analyses have indicated that most of the models are fairly robust. Even when considering the worst-case scenario utilizing the most conservative relative risk estimates for the health benefits of physical activity and the most aggressive health harms associated with air pollution and traffic injury exposure, the overall benefit of active transportation outweighs the risks in all of the models found in the literature to date [226, 231-235, 249-251].

Although research techniques designed to look at the combined effects of physical activity and air pollution exposure are in their infancy, the consistent finding in the research is that the health benefits of increased physical activity outweigh any harms related to increased air pollution exposure, especially at the levels of air pollution seen in countries such as the United States, Canada, and many European nations [4, 164, 166, 201, 203, 231, 233, 250, 252, 253]. More work in this area is needed to fully address the concern of increased air pollution exposure during outdoor activity in healthy children and adults, as well as sensitive populations.

FUTURE DIRECTIONS

Gaps and limitations of current body of research

Over the last 25 years the health effects of physical activity have been extensively investigated. The association between physical activity and a myriad of health outcomes has been established in males and females, adolescents and the elderly, and in populations from varying ethnic backgrounds and countries of origin. The epidemiological literature is unequivocal in suggesting that highly-active populations dramatically reduce their mortality and morbidity risks regarding many chronic non-communicable diseases to a magnitude similar to that seen with quitting smoking.

In spite of the overwhelming amount of epidemiological and experimental data supporting the health benefits of exercise, there are some areas that are in need of further exploration. Future research should:

- Investigate the effect of varying intensities and durations of activity on health outcomes.
- Further investigate the possible negative health outcomes associated with intense, vigorous physical activity in older individuals.
- Develop valid and reliable objective measurements of individual activity levels.
- Examine the influence of genetic/epigenetic modifiers on the health benefits of physical activity.

Previous studies have indicated that the total volume of exercise is the key metric linked to the health benefits of physical activity, but will this relationship hold when comparing multiple short bouts of exercise to longer sessions of the same total duration? Research has shown that 3, 10-minutes exercise sessions are just as effective at controlling weight and increasing fitness as one 30-minute session of a similar intensity [254, 255]. Further research comparing activities of varying duration while controlling for intensity should be performed to see if the similarity in health benefits is also extended to other endpoints, such as reduced incidence of cancer, metabolic disorders, cardiovascular disease, and mental disorders. If short sessions of physical activity are just as effective at increasing and maintaining health and reducing risk as longer sessions, changes in occupational activity may be a very effective way to battle the harms associated with sedentary behavior and inactivity, as well as incentivize sedentary individuals to exercise, even if there are limitations on the duration of the activity that can be performed.

Researchers have historically focused on moderate to vigorous intensity activities (3 to 6 METS) and have not distinguished between the health benefits of this level of activity and more intense exercise. Some recent work suggests that high volumes of vigorous activity, even in fit older adults, may mitigate the mortality benefits seen at lower levels of exercise. Data from the Copenhagen City Heart Study saw the greatest reduction of mortality risk in adults over 50 in the light jogging group, and reported that strenuous joggers experienced a mortality risk greater than the light and moderate groups, seeing no improvement over sedentary controls. This indicates that there may be a U-shaped relationship between physical activity and all-cause mortality in older populations [256]. Further research should investigate the benefits/harms of high intensity physical activity in older and diseased populations.

A common limitation of observational research examining the interaction between physical activity and health is the reliance on self-reported metrics of physical activity, acquired in the form of surveys, questionnaires, or activity diaries. Due to advances in individual tracking technology that offer detailed dynamic spatial information and the proliferation of smart phones, there has been a surge in the interest of leveraging cutting edge hardware and software to develop reliable and valid objective measurements of physical activity. New technologies have proven successful at tracking the physical activity characteristics of individuals over time [257]. Future research should continue to refine GPS-enabled activity tracking to reduce misclassification of individual physical activity volume and identify barriers or enablers that may influence physical activity patterns.

Epigenetics is the study of heritable phenotypes that result from modifications to DNA, resulting in changes in gene expression without a direct alteration of the DNA base sequence. There are many mechanisms by which epigenetic modifications can be induced, and the performance of physical activity and exercise has been shown to stimulate some of these mechanisms. Chronic physical activity and exercise have been linked to reduced inflammatory biomarkers, which may be responsible for the myriad health benefits associated with physical activity. Recent work has shown that exercise interventions and highly physically-active lifestyles can result in genetic alterations that have been associated with reduced inflammation. Further research is needed to corroborate these initial findings and detail all of the confounding variables regarding how physical activity can influence epigenetic modifications [258].

Future research avenues pertinent to the mission of the ARB

In California, with the passage of the *Sustainable Communities and Climate Protection Act of 2008*, the transportation planning and land-use sectors have been increasingly focused on strategies to reduce transportation-related greenhouse gas emissions (GHGE) and the reliance on fossil fuels for transportation. Along with increases in public transportation use and more compact urban design, increases in active transport utilization (biking, walking) have been suggested as ways to decrease GHGE. Many co-benefits have been associated with sustainable community designs focused on reducing GHGE, two of these being reduced criteria air pollutant exposure and increased physical activity due to utilization of active transport. These two co-benefits of increased active transport present a rapidly-advancing area of research pertinent to the mission of the ARB. Some specific areas regarding the built environment that the ARB may be interested in pursuing are outlined below:

- Take advantage of planned infrastructure changes to observe the before and after effects of the alteration of the built environment on air pollution exposure and physical activity levels for communities and individuals, including active transportation. These types of studies have the potential to infer causality to a greater extent than the current cross-sectional studies that are only able to indicate an association between built environment characteristics and physical activity levels.
- Leverage planned and completed infrastructure changes to assess the effectiveness of different air pollution mitigations strategies, such as barriers, bike route selection, and pedestrian paths offset from roadways.
- Continue to explore specific community design strategies' effectiveness at minimizing air pollution exposure of individuals while being physically active in urban environments.
- Create an outreach strategy to inform the public on the health benefits of physical activity in the context of air pollution exposure, as well as the health and environmental advantages of shifting from fossil fuel-based transportation to active transport.

In the long-term, increased active transport use may help reduce ambient levels of many of the air pollutants that the ARB is charged with evaluating and regulating. But in the short-term, early-adopters of active transport may be subject to an increased exposure to air pollution and possible increases in their risk of injury due to traffic accidents by bicycling and walking in areas high in automotive traffic. It is important for ARB to continue research evaluating the health effects of air pollution exposure and to begin considering physical activity levels as an important covariate in overall health outcome analyses. Listed below are some suggested areas of research regarding exposure while being physically-active:

- Continue to assess and review the progress of research into modeling the combined health effects of increased outdoor physical activity and air pollution exposure related to the adoption of active transportation.
- Encourage model developers to expand the air pollution assessment component to include other pollutants that are well-substantiated to contribute to morbidity and mortality, like ozone and TRAP.
- Focus research to identify the constituents of TRAP that are responsible for the association between TRAP exposure and cardiovascular and respiratory morbidity.
- Create updated and improved time-activity data leveraging new mobile technology to better assess personal exposure to air pollution and physical activity.
- Evaluate the safety of increased outdoor physical activity in populations sensitive to air pollution, such as children, asthmatics, the elderly, and those individuals with cardiopulmonary comorbidities.
- Include physical activity level as a covariate in future analyses of the association between air pollution and mortality/morbidity whenever possible.

Conclusion

ARB is in a position to take a leading role in the analysis of the combined health impacts of air pollution exposure and increased physical activity related to the adoption of public transportation and active transport strategies. A large body of research regarding this interaction is in the theoretical modeling and forecasting stages. As smart growth and sustainable community designs are implemented across the state, the need to assess the effectiveness of those designs and their impact on air pollution exposure and community health will become increasingly apparent. In particular, studies that evaluate the real world effects of these community designs should prove useful to multiple public and private stakeholders. Considering the technical skills of its staff and the regulatory duties of ARB, it is organizationally positioned to be a valuable contributor to this emerging field.

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APPENDIX: LIST OF ABBREVIATIONS

BMD	Bone mineral density
BMI	Body mass index
CAD	Coronary artery disease
CHD	Coronary heart disease
CVD	Cardiovascular disease
FTO	Fat mass and obesity-associated gene
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
MET	Metabolic Equivalent Task
MI	Myocardial infarction
MVPA	Moderate to vigorous physical activity
OR	Odds ratio
PAD	Peripheral arterial disease
PAG	Physical Activity Guidelines for Americans
RR	Relative risk
T2D	Type 2 diabetes mellitus
TRAP	Traffic-related air pollution
UFPM	Ultra-fine particulate matter
VLDL	Very low-density lipoprotein