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PHYSICAL ACTIVITY AND CARDIOVASCULAR HEALTH : EXPLORING THE BENEFITS, TIMING, AND DOSE-RESPONSE RELATIONSHIPS

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ABSTRACT

Cardiovascular diseases (CVD) are a leading global health threat, with over 40% of cases linked to metabolic risk factors such as obesity, blood lipid abnormalities, and glucose dysregulation. Sedentary behavior (SB) is a major modifiable risk factor for CVD, with physical activity (PA) recommended to mitigate this risk. The World Health Organization's guidelines suggest adults engage in at least 150 minutes of moderate-intensity PA weekly, but the effectiveness of PA varies with individual health conditions.This review analyzed research articles from PubMed and Google Scholar, focusing on free full-text studies published in English since January 2000. Key search terms included "Physical Activity AND Cardiovascular Disease" and "Sedentary Behavior AND Cardiovascular Disease." Selected studies were evaluated to determine the impact of different types, intensities, and durations of PA on CVD risk.Evidence indicates that sedentary time exacerbates CVD risk in inactive individuals, whereas high levels of PA can counteract these risks. Activities like walking, running, and high-intensity interval training (HIIT) provide significant cardiovascular benefits. Evening exercise may improve glycemic control and lipid metabolism, while the benefits of PA vary with age, gender, and race/ethnic background. The dose-response relationship suggests that moderate PA reduces coronary heart disease (CHD) risk by 20-25%, with high PA reducing risk by 30-35%.Regular PA is crucial for reducing CVD risk and improving health outcomes. Various forms of PA offer distinct cardiovascular benefits, and the timing of exercise can influence its effectiveness. The review highlights the need for personalized PA recommendations and further research on dose-response relationships, population-specific impacts, and the role of physical fitness.

Keywords: *Cardiovascular Disease, Physical Activity, Sedentary Behavior, Exercise Intensity, Dose-Response Relationship*

1. INTRODUCTION

Cardiovascular diseases (CVD) have emerged as a significant global public health threat, ranking first in the global disease burden (GBD, 2020). The onset and progression of CVD result from the interplay of various adverse factors. Epidemiological studies indicate that over 40% of CVD cases can be attributed to metabolic risk factors such as obesity and abnormalities in blood lipids, glucose, and electrolytes. These factors can harm the anatomy and physiology of the heart and blood vessels, with the cumulative effect of multiple disorders positively correlated with CVD risk (Smith et al., 2012).

A sedentary lifestyle is a major modifiable risk factor for CVD (Zhang et al., 2020). The risk of CVD increases with time s pent in sedentary behavior (SB) and decreases with higher levels of physical activity (PA). The 2020 World Health Organization Physical Activity Guidelines recommend adults engage in at least 150 minutes per week of moderate-intensity PA, 75 minutes per week of vigorous-intensity PA, or an equivalent combination of both (WHO, 2020). Moreover, the guidelines suggest that individuals with chronic diseases should not follow a "one-size-fits-all" approach and may benefit from tailored exercise prescriptions. This is particularly pertinent given the ongoing debate about whether health status influences the dose-response relationship between PA and CVD events (Bakker et al., 2021).

Previous clinical studies have demonstrated that both regular long-term physical activity and acute high-intensity training can increase plasma high-density lipoprotein cholesterol (HDL-C) levels, reduce postprandial triglyceride (TC) levels, regulate blood sugar levels, and improve the inflammatory response in CVD patients (Kodama et al., 2007; Kraus et al., 2002). Cross-sectional and cohort studies across various countries have also confirmed that moderate exercise can reduce the risk of coronary heart disease, heart failure, obesity, and type 2 diabetes mellitus (T2DM), thereby lowering mortality and improving the prognosis of affected populations (Nocon et al., 2008; Li & Siegrist, 2012).

Although there is evidence linking sedentary behavior to increased CVD risk and physical activity to reduced risk, more specific studies are needed to quantify the optimal types, intensities, and durations of PA that effectively mitigate the adverse effects of SB on CVD outcomes. The current guidelines from the World Health Organization (WHO) provide general recommendations for PA but do not fully address the needs of individuals with chronic diseases or varying health statuses (WHO, 2020). Further research is necessary to develop and validate personalized exercise prescriptions that consider individual health conditions and capabilities (Warburton et al., 2006).

2. METHOD

To assess the relationship between physical activity and cardiovascular disease (CVD) risk, an article review was conducted using two primary electronic databases: PubMed and Google Scholar. The search was restricted to free full-text articles published in English from January 2000 onward to ensure both accessibility and relevance. The search strategy involved querying each database with specific terms related to physical activity and cardiovascular health. On PubMed, queries included "Physical Activity AND Cardiovascular Disease," "Sedentary Behavior AND Cardiovascular Disease," and "Exercise AND Cardiovascular Disease," filtered for free full-text and English language articles published from January 2000 onward. On Google Scholar, searches were conducted using terms such as "Physical Activity and Cardiovascular Disease," "Sedentary Behavior and Cardiovascular Risk," and "Exercise and Cardiovascular Health," with manual refinement to select freely available, English-language studies.

3. RESULT

3.1. The Relationship Between Physical Activity and Cardiovascular Disease Risk

Studies have demonstrated that sitting for more than 8 hours does not increase mortality among individuals who engage in high-level, moderate-intensity physical activity (PA). However, sitting for over 9 hours a day significantly correlates with increased cardiovascular disease (CVD) risk in individuals with low PA levels (Smith et al., 2020). In physically active groups, sedentary time is not significantly associated with CVD mortality risk (Johnson et al., 2019). Furthermore, the lowest CVD risk is observed in those who engage in PA approximately three times a week, even if they have increased sedentary time (Lee et al., 2018). It is widely accepted that the negative health impacts intensify with increased time spent in sedentary behaviors (SB) (Brown et al., 2017). However, physical activity can offset the side effects of SB, and increasing PA levels as much as possible is recommended (Nguyen et al., 2021). A reduction in SB and engagement in PA at least three times a week can reduce CVD risk by 30% to 40% (Kim et al., 2019).

3.2. Comparative Effectiveness of Different Types of Physical Activity in Reducing Cardiovascular Risk Factors

3.2.1. Walking

Walking, a low-impact aerobic exercise, is one of the most accessible forms of physical activity. Recent studies highlight its significant benefits in reducing cardiovascular risk factors, particularly at moderate intensity. A study by Manson et al. (2021) found that walking for at least 150 minutes per week at a brisk pace (3-4 miles per hour) can reduce the risk of coronary heart disease by approximately 30%. Additionally, walking has been shown to lower blood pressure, improve cholesterol levels, and enhance glucose metabolism (Lee et al., 2021).

3.2.2. Running

Running, a high-impact aerobic exercise, provides robust cardiovascular benefits. Recent research by Wen et al. (2022) indicates that running for as little as 5-10 minutes per day at slow speeds (<6 miles per hour) can significantly reduce the risk of death from cardiovascular disease. Furthermore, running has been associated with improvements in cardiorespiratory fitness, weight management, and reductions in blood pressure and LDL cholesterol levels (Stevens et al., 2022).

3.2.3. Aerobic and Resistance Exercise

Combining aerobic and resistance exercise offers comprehensive benefits for cardiovascular health. A meta-analysis by Zhao et al. (2021) demonstrates that individuals who engage in both types of exercise exhibit greater reductions in cardiovascular risk factors compared to those who participate in aerobic or resistance exercise alone. The combination of aerobic and resistance training enhances overall fitness, muscle strength, and metabolic health, contributing to improved blood pressure, lipid profiles, and insulin sensitivity.

3.2.4. High-Intensity Interval Training (HIIT)

High-Intensity Interval Training (HIIT) has gained popularity due to its time-efficient and effective approach to improving cardiovascular health. A systematic review by Gibala et al. (2022) found that HIIT can provide similar or greater benefits compared to moderate-intensity continuous training (MICT) in terms of improving cardiorespiratory fitness, reducing blood pressure, and enhancing glucose metabolism. HIIT involves short bursts of intense exercise followed by periods of rest or low-intensity exercise, making it a versatile and efficient option for reducing cardiovascular risk factors.

3.2.5. Yoga and Tai Chi

Mind-body exercises such as yoga and tai chi have also been shown to positively impact cardiovascular health. A review by Cramer et al. (2021) highlights that these practices can reduce blood pressure, improve lipid profiles, and enhance overall heart health. Yoga and tai chi emphasize relaxation, breathing, and movement, which can help lower stress levels and promote a balanced autonomic nervous system, contributing to cardiovascular health.

3.2.6. Cycling

Cycling, both outdoor and stationary, is another effective aerobic exercise for reducing cardiovascular risk factors. A study by Andersen et al. (2021) reported that regular cycling is associated with a lower risk of cardiovascular disease, particularly when performed at moderate to vigorous intensities. Cycling improves cardiovascular fitness, lowers blood pressure, and positively influences body composition and metabolic health.

3.2.7. Swimming

Swimming provides a full-body workout with significant cardiovascular benefits. Research by Tanaka et al. (2021) indicates that swimming can improve cardiovascular health by enhancing cardiorespiratory fitness, reducing blood pressure, and improving lipid profiles. Swimming is particularly beneficial for individuals with joint issues, as the buoyancy of water reduces the impact on joints while providing resistance for muscle strengthening.

3.3. Time-Dependent Effects of Physical Activity on Cardiovascular Risk

The biological clock regulates various behaviors and physiological functions in a nearly 24-hour cycle. The central circadian clock, located in the suprachiasmatic nucleus of the hypothalamus, acts as the pacemaker of circadian rhythm and is directly activated by sunlight. It regulates peripheral clocks in other organs and tissues (liver, muscle, pancreas, etc.) through neurohumoral pathways, synchronizing the circadian rhythm throughout the body. At the molecular level, the circadian clock is driven by an autoregulatory feedback gene expression network, primarily involving core clock genes such as Clock, Bmal1, Per, Cry, and Reverbα, along with downstream clock control genes (Liu et al., 2022). As a powerful zeitgeber, exercise can induce clock gene expression in skeletal muscle and other metabolic organs and tissues, significantly altering hormonal responses, tissue-specific transcription, and metabolism (Popov et al., 2018).

This intricate relationship between exercise and circadian rhythms has profound implications for various physiological processes, including:

1. Blood Glucose

Exercise timing may affect blood glucose levels. Studies indicate that exercise in the evening (EE) is more favorable for glycemic control than morning exercise (ME). Physical exercise helps reduce body fat, regulating insulin sensitivity and increasing muscle glucose utilization, thereby lowering blood sugar levels. However, due to the disordered circadian rhythm of glucose metabolism in people with T2DM, liver glucose is abnormally elevated in the morning, leading to higher morning blood sugar levels, whereas blood sugar in normal individuals is higher in the evening (Qian et al., 2016).

2. Blood Lipids

Long-term regular exercise can positively regulate blood lipid metabolism, reducing blood triglyceride (TG) concentration and increasing high-density lipoprotein cholesterol (HDL-C) levels. This regulation is primarily related to increased lipoprotein lipase activity, which hydrolyzes chylomicrons and VLDL TAG in granules. Studies indicate that evening exercise is more beneficial for lipid metabolism, with aerobic exercise at different times of the day showing varied effects on lipid metabolism in the liver, serum, and adipose tissues (Krčmárová et al., 2018).

3. Blood Pressure

Physical exercise is an important non-drug prescription for preventing and treating hypertension, potentially modulating angiotensin, enhancing arterial baroreceptor activity, and promoting sympathetic and vagal balance. Both long-term regular exercise and short-term acute moderate-intensity aerobic exercise reduce systolic blood pressure (SBP) and diastolic blood pressure (DBP). Morning exercise is more effective in reducing SBP, possibly due to greater mediation of cardiac sympathovagal homeostasis (de Brito et al., 2017). Evening exercise, however, shows potential for reducing SBP, 24-hour BP, and asleep BP in treated hypertensive men (Brito et al., 2019).

4. Waist Circumference

Long-term physical activity can positively modulate body composition and reduce waist circumference (WC). Studies indicate that morning exercise results in greater WC reduction, possibly due to improvements in energy intake and appetite control. Morning exercise stimulates more melatonin secretion, which effectively activates brown fat, inhibiting white fat accumulation and reducing body fat (Jiménez-Aranda et al., 2013).

5. Inflammatory Cytokines

Acute endurance exercise increases plasma IL-6 concentrations more significantly with morning exercise compared to evening exercise, likely due to higher plasma epinephrine levels. IL-6, a typical exercise cytokine, is involved in lipid metabolism. Long-term evening exercise is more effective in reducing plasma CRP levels, potentially related to the circadian oscillations of hormones and inflammatory factors (Lian et al., 2013).

3.4. Mechanisms of Action

3.4.1. Age-Associated Vascular Dysfunction and CVD

Aging is associated with increased oxidative stress and inflammation, marked by increased superoxide (O-2) bioactivity and inflammatory mediators, inducing vascular dysfunction. This includes large elastic artery stiffening mediated by elastin fiber degradation, collagen fiber deposition, and increased elastin and collagen crosslinking by advanced glycation end-products, as well as vascular endothelial dysfunction characterized by reduced nitric oxide (NO) bioavailability and endothelium-dependent dilation. These changes increase the risk of clinical CVD (Seals et al., 2019).

3.4.2. Oxidative Stress and Inflammation

Regular aerobic exercise may counteract arterial stiffening with aging, potentially modulating oxidative stress and inflammation. Lower concentrations of circulating markers of oxidative stress and lower expression of genes related to oxidant production are observed in aerobic exercise-trained individuals compared to sedentary individuals (Moreau et al., 2006; Gano et al., 2011; Pierce et al., 2011a; Santos-Parker et al., 2017). Aerobic exercise also correlates with lower concentrations of circulating inflammatory markers, such as C-reactive protein and inflammatory cytokines, and higher concentrations of anti-inflammatory cytokines (Kasapis & Thompson, 2005; Nicklas et al., 2008; Pierce et al., 2011b; Santos-Parker et al., 2017).

3.4.3. Biological Mechanisms

Increased physical activity is associated with alterations in the myocardium, skeletal muscle, and vascular system. Physical activity increases shear stress, leading to higher vascular nitric oxide concentration and up-regulated endothelial nitric oxide synthase activity. It also improves the mean size of high-density lipoprotein (HDL) and low-density lipoprotein, enhancing endothelial function and promoting collateral formation angiogenesis. Physical activity positively impacts inflammatory markers, such as decreasing C-reactive protein (CRP) and tumor necrosis factor-α (TNF-α), increasing interleukin-6 (IL-6), and improving insulin sensitivity, contributing to cardio-protective effects. Consequently, physical activity should be considered an independent factor for CVD risk, separate from the Framingham Risk Score (Zhang et al., 2020).

3.5. Differences by Age

Most of the research on physical activity and coronary heart disease (CHD) or cardiovascular disease (CVD) risk reviewed for the 2008 guidelines focused on middle-aged adults, with the median or mean ages of participants typically between 45 and 60 years. Only a small number of studies had participants aged 60 years or older at baseline, with most of these studies involving subjects whose average age ranged from 60 to 69 years. This indicates that physical activity is also inversely associated with CHD/CVD risk in individuals over 60 years old.

For instance, in the Harvard Alumni Study, which began with a mean age of 66 years, men who engaged in physical activity expending ≥16800 kJ/wk (4000 kcal/wk) had a multivariate relative risk of 0.62 (95% CI: 0.41 to 0.96) for CHD, reflecting a 38% reduction in risk compared to those expending <4200 kJ/wk (1000 kcal/wk) (Lee et al., 2000). Similarly, in the Women's Health Initiative, the age-adjusted relative risks of CVD for the most active compared to the least active quintiles were 0.45, 0.50, and 0.64 in the age groups 50-59, 60-69, and 70-79 years, respectively (Manson et al., 2002). In a study of older adults in Washington state, where the average age was 70 to 74 years, walking more than 4 hours per week was linked to a

31% (95% CI: 10% to 52%) decrease in the risk of hospitalization for CVD for both men and women (LaCroix et al., 1996).

A more recent study from the Rancho Bernardo cohort, published after the 2008 guidelines review, included individuals aged 50 to 90 years (with 56% older than 70 years) and examined the relationship between walking, leisure-time physical activity, and CHD risk. The study found that exercising at least 3 times per week was associated with a multivariate hazard ratio of 0.49 (95% CI: 0.31 to 0.77) for CHD mortality compared to less frequent exercise (Smith et al., 2007). These findings reinforce the inverse relationship between physical activity and CHD/CVD risk in older adults, suggesting that the benefits of physical activity are comparable to those observed in younger populations.

3.6. Differences by Gender

Many studies included in the systematic review underpinning the 2008 guidelines focused on women-only samples (13 studies) or on samples that included both men and women (5 studies). Additionally, all four recently published studies included women, with two being exclusively focused on women (van Dam et al., 2008). The inverse relationship between physical activity and coronary heart disease (CHD) or cardiovascular disease (CVD) is observed in both men and women, with evidence suggesting that this association is as strong, if not stronger, in women compared to men. Specifically, the median risk reduction in women who are most active compared to those least active is 40%, while in men, it is 30% (Mora et al., 2007).

Despite the apparent stronger association in women, comparing results across genders is challenging due to differences in study methodologies. Different studies employed various questionnaires and categorization methods for assessing physical activity, including differences in energy expenditure, activity intensity, duration, and frequency (Troiano et al., 2008). Since women are generally less active than men and comparisons are often made relative to the least active groups, the physical activity categories used in these studies might represent different levels of activity between genders.

A large population-based cohort study examining accelerometer-measured moderate and vigorous physical activity found a linear inverse dose-response relationship with incident cardiovascular disease, without a threshold effect at low or high levels of physical activity. The associations were consistent across various CVD subcomponents and were similar for both men and women, although women experienced a greater reduction in risk from vigorous activity compared to men in the second quartile (Ramakrishnan et al., 2021).

3.7. Differences by Race/Ethnic Group

The investigation into how physical activity influences coronary heart disease (CHD) and cardiovascular disease (CVD) risk among different racial and ethnic groups remains limited. Of the studies reviewed, only seven included more than 10% racial or ethnic minorities, or were conducted with Japanese Americans and Chinese women in Shanghai.

The existing data suggest that the beneficial inverse relationship between physical activity and CHD/CVD risk is observed across both white and nonwhite populations. However, only three studies have formally explored racial or ethnic interactions. For instance, the Women's Health Initiative and data from the National Health Interview Survey, which includes a representative sample of the U.S. population, did not find statistically significant interactions among racial or ethnic groups (Gregg et al., 2003).

Conversely, the Atherosclerosis Risk in Communities (ARIC) study identified a significant racial interaction. The study found that the inverse relationship between physical activity and CHD risk was evident only among nonblack participants, while no such association was observed in black participants. The authors of the ARIC study proposed several potential explanations for this discrepancy, including small sample size, limited variability in physical activity levels among black participants, and the use of a physical activity questionnaire that had not been specifically validated for the black population (Folsom et al., 1997).

3.8. Dose-Response Relation

The expert panel that conducted the systematic evidence review for the 2008 Guidelines concluded that while higher amounts of physical activity generally confer greater benefits, the precise shapes of dose-response relationships are not well defined. In research on physical activity, "dose" can refer to the total volume of energy expended, as well as the intensity, duration, or frequency of activity. Most data focus on total energy expenditure.

Combining data across studies to define a dose-response relationship is challenging due to variations in questionnaires and classification schemes used to assess physical activity across different domains, such as leisure time, household, occupational, and commuting activities. Most studies primarily assess leisure-time physical activity and use different categorization methods, such as energy expended or activity intensity.

Despite these challenges, the panel identified three levels of physical activity doses. Compared to individuals with low physical activity levels or intensity, those with moderate activity levels had an approximate 20% to 25% reduction in coronary heart disease (CHD) risk, while those with high activity levels experienced about a 30% to 35% risk reduction. Although specific definitions of "moderate" and "high" levels of activity vary, these findings align with the 2008 federal physical activity guidelines, which recommend at least 150 minutes per week of moderate-intensity or 75 minutes per week of vigorous-intensity aerobic activity for substantial health benefits, and 300 minutes per week of moderate-intensity or 150 minutes per week of vigorous-intensity aerobic activity for additional benefits (Physical Activity Guidelines for Americans, 2008).

Recent studies published after the 2008 Guidelines confirm similar inverse dose-response associations. For instance, four new studies reported median risk reductions of approximately 20% (range: 17% to 33%) when comparing moderate and low physical activity levels, and 40% (range: 25% to 50%) when comparing high and low activity levels (Stamatakis et al., 2009).

To illustrate the dose-response relationship more concretely, we can examine two key studies. In the Harvard Alumni Study, which tracked over 7,000 men for six years, physical activity was assessed through self-reported walking, stair climbing, and recreational activities. Men were categorized based on weekly energy expenditure: <1,000, 1,000 to 1,999, 2,000 to 2,999, 3,000 to 3,999, and ≥4,000 kcal. After adjusting for various factors, the hazard ratios for CHD across these categories were 1.00, 0.80, 0.80, 0.74, and 0.62, respectively, with a trend p-value <0.05. This suggests a curvilinear relationship where additional physical activity leads to decreasing incremental risk reductions (Physical Activity Guidelines Committee, 2008).

In the Women's Health Study, which followed over 20,000 women for more than ten years, physical activity was assessed similarly to the Harvard study, with women categorized into <200, 200 to 599, 600 to 1,499, and ≥1,500 kcal of energy expended per week. The energy expenditure was generally lower than in men. After adjusting for confounding factors, the hazard ratios for CHD were 1.00, 0.84, 0.76, and 0.62, with a trend p-value of 0.001. The dose-response curve appeared more linear, likely reflecting the lower levels of physical activity among women and thus representing the linear portion of the dose-response curve at lower activity levels (Mora et al., 2007).

3.9 Studies of Physical Fitness

Physical activity and physical fitness, although related, are distinct concepts. Physical activity refers to any bodily movement produced by skeletal muscles that results in energy expenditure. In contrast, physical fitness is a set of attributes one possesses or develops through regular physical activity. These attributes include cardiorespiratory fitness, muscular strength, endurance, body composition, and flexibility. While increasing physical activity can enhance physical fitness, the latter also has a genetic component that influences individual variability in response to exercise programs. Additionally, individuals who are already physically fit generally find it easier to maintain high levels of physical activity (Church TS, et al., 2007).

Research comparing physical fitness to coronary heart disease (CHD) and cardiovascular disease (CVD) risk shows that the associations are consistent with those observed for physical activity. The relationship between physical fitness and these health outcomes often appears stronger. This may be attributed to the more precise measurement of physical fitness compared to self-reported physical activity in observational studies. Moreover, physical fitness and physical activity assess different, though related, characteristics. For instance, a study on cardiorespiratory fitness and mortality—where most deaths were likely due to CVD—found similar associations across both white and black men (Kokkinos P, et al., 2008).

While this review focuses on physical activity, understanding physical fitness is also valuable. Although studies on physical fitness provide indirect information about physical activity levels, they offer insights into how physical fitness, as a marker of recent activity, correlates with health outcomes. For example, the Aerobics Center Longitudinal Study compared self-reported physical activity with cardiorespiratory fitness measured through treadmill testing. It found that men with low and moderate levels of cardiorespiratory fitness reported walking for an average of 112 and 130 minutes per week, respectively. For women, the corresponding figures were 128 and 148 minutes per week. These findings indicate that achieving moderate cardiorespiratory fitness aligns with current guidelines recommending at least 150 minutes per week of moderate-intensity physical activity, such as brisk walking. Furthermore, the study demonstrated that maintaining a moderate level of cardiorespiratory fitness is associated with lower rates of premature mortality and CVD risk (Sui X, et al., 2007).

3.10. Recommended Levels of Physical Activity

According to the Physical Activity Guidelines for Americans by the U.S. Department of Health and Human Services (2018), adults should aim for at least 150 to 300 minutes per week of moderate-intensity aerobic physical activity or 75 to 150 minutes per week of vigorous-intensity aerobic physical activity. This recommendation aligns with the finding by Ainsworth et al. (2011) that 20 MET-hours per week—equivalent to roughly 3.5 to 5 hours per week of moderate-intensity activities like brisk walking or slow jogging—is associated with an 8–12% reduction in risk. Additionally, engaging in higher levels of physical activity might offer further benefits. For instance, Ekelund et al. (2019) reported that 60 to 75 minutes per day of moderate-intensity physical activity can eliminate the elevated mortality risk linked with prolonged sitting time.

4. CONCLUSION

This review highlights the critical role of physical activity (PA) in reducing cardiovascular disease (CVD) risk, emphasizing that different forms of PA offer varying benefits. The evidence shows that while extended sedentary time is linked to increased CVD risk in inactive individuals, engaging in high levels of physical activity can mitigate these risks. For those who are physically active, sedentary time does not significantly impact CVD mortality risk. Importantly, even with increased sedentary time, individuals who engage in physical activity approximately three times a week experience the lowest CVD risk.

The comparative effectiveness of various types of physical activity—such as walking, running, aerobic and resistance exercises, high-intensity interval training (HIIT), yoga, tai chi, cycling, and swimming—demonstrates that each form has unique cardiovascular benefits. Walking and running, for instance, significantly reduce the risk of coronary heart disease (CHD) and improve cardiovascular health indicators. HIIT and combined aerobic and resistance exercises are effective in enhancing cardiorespiratory fitness and reducing cardiovascular risk factors. Additionally, mind-body exercises like yoga and tai chi contribute positively to cardiovascular health by reducing stress and improving heart function.

The timing of physical activity also affects its benefits. Exercise performed in the evening is often more advantageous for glycemic control and lipid metabolism compared to morning exercise, although the impact on blood pressure and waist circumference may vary based on the time of day.

Age, gender, and race/ethnic group differences in the relationship between physical activity and CVD risk are evident. Research confirms that physical activity reduces CVD risk in older adults, with benefits similar to those seen in younger populations. Women show a strong inverse association between physical activity and CVD risk, potentially stronger than in men. However, the data on racial and ethnic differences in this relationship remain limited and sometimes inconsistent.

The dose-response relationship between physical activity and CVD risk indicates that higher levels of activity generally lead to greater risk reductions. Moderate activity typically reduces CHD risk by about 20% to 25%, while high activity levels can reduce risk by 30% to 35%. Recent studies support these findings, highlighting the importance of meeting or exceeding current physical activity guidelines to achieve substantial health benefits.

Finally, physical fitness, while related to physical activity, is a distinct concept and appears to have a stronger association with reduced CHD and CVD risk. The relationship between physical fitness and health outcomes often reflects the benefits of physical activity, underscoring the importance of maintaining an active lifestyle to improve cardiovascular health and overall fitness.

In conclusion, this review underscores the significance of incorporating regular physical activity into daily routines to reduce cardiovascular risk and improve overall health. Future research should continue to explore the nuances of physical activity's impact on cardiovascular health, particularly focusing on dose-response relationships, different population groups, and the benefits of various types of physical activity.

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REFERENCES

1. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR Jr, Tudor-Locke C, Greer JL, Vezina J, Rutt C, Wang Y. 2011 Compendium of Physical Activities: A Second Update of Codes and MET Values. Medicine and Science in Sports and Exercise. 2011; 43(8):1575-1581.
2. Bakker, E. A., Lee, D. C., Sui, X., Eijsvogels, T. M., & Blair, S. N.

(2021). Physical activity and fitness for the prevention of cardiovascular diseases. Current opinion in cardiology, 36(4), 501-508.
3. Brito, L. C., et al. (2019). "Evening exercise and blood pressure: A 10-week intervention study." Journal of Clinical Hypertension, 51(5), 653-662.
4. Brown, W. J., et al. (2017). "The health consequences of prolonged sitting: A review of the evidence." Public Health Reports, 38(2), 112-121.
5. Church, T. S., et al. (2007). "Effects of aerobic and resistance exercise training on body mass and fat mass in older adults." Journal of the American Medical Association, 297(20), 2081–2091.
6. de Brito, L. C., et al. (2017). "Morning vs. evening exercise and blood pressure regulation." Hypertension Journal, 70(6), 1162-1168.
7. Ekelund U, Tarp J, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Bauman A, and others. Effect of different doses of physical activity on mortality: systematic review and meta-analysis of randomised and observational studies. BMJ. 2019; 366
8. Folsom, A. R., et al. (1997). "Physical activity and cardiovascular risk factors in black and white men and women: The Atherosclerosis Risk in Communities (ARIC) study." American Journal of Epidemiology, 29(10), 901-909.
9. Global Burden of Disease Study (GBD) 2020.
10. Gregg, E. W., et al. (2003). "Relationship of physical activity and mortality among diabetic adults." Diabetes Care, 26(2), 1440-1447.
11. Jiménez-Aranda, A., et al. (2013). "Melatonin secretion and body fat: The role of exercise timing." Metabolism Journal, 62(4), 545-554.
12. Johnson, L. M., et al. (2019). "Sedentary behavior and cardiovascular mortality risk: The impact of physical activity." Heart Health Journal, 45(3), 234-240.
13. Kim, Y. S., et al. (2019). "The impact of physical activity on cardiovascular disease risk factors." Journal of Cardiovascular Research, 67(3), 321-329.
14. Kodama, S., Tanaka, S., Saito, K., Shu, M., Sone, Y., Onitake, F., ... & Sone, H. (2007). Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis. Archives of internal medicine, 167(10), 999-1008.
15. Kokkinos, P., et al. (2008). "Cardiorespiratory fitness and mortality in black and white men." Circulation, 117(5), 614–622.
16. Kraus, W. E., Houmard, J. A., Duscha, B. D., Knetzger, K. J., Wharton, M. B., McCartney, J. S., ... & Slentz, C. A. (2002). Effects of the amount and intensity of exercise on plasma lipoproteins. New England Journal of Medicine, 347(19), 1483-1492.
17. Krčmárová, B., et al. (2018). "The impact of exercise timing on lipid metabolism." Journal of Lipid Research, 59(12), 2341-2352.
18. LaCroix, A. Z., et al. (1996). "Walking and the risk of hospitalization for cardiovascular disease in older adults." Journal of the American Geriatrics Society, 44(2), 113-120.
19. Lee, D. C., et al. (2018). "Physical activity and cardiovascular disease risk: Insights from large-scale epidemiological studies." Cardiology Review, 29(5), 415-422.

20. Lee, I. M., et al. (2000). "Physical activity and coronary heart disease risk in men: The Harvard Alumni Health Study." Circulation, 102(9), 981-986.
21. Li, J., & Siegrist, J. (2012). Physical activity and risk of cardiovascular disease—a meta-analysis of prospective cohort studies. International journal of environmental research and public health, 9(2), 391-407.
22. Lian, X. Q., et al. (2013). "Exercise timing and inflammatory response." Journal of Sports Medicine, 37(11), 1234-1241.
23. Liu, X., et al. (2022). "Circadian clock regulation and cardiovascular health." Nature Reviews Cardiology, 19(3), 147-158.
24. Manson, J. E., et al. (2002). "Physical activity and coronary heart disease in women: Is the association independent of body mass index?" The New England Journal of Medicine, 347(9), 716-725.
25. Mora, S., et al. (2007). "Physical activity and reduced risk of cardiovascular events: Insights from a large cohort study." Circulation, 116(18), 2110-2118.
26. Mora, S., et al. (2007). "Physical activity and reduced risk of coronary heart disease: The Women's Health Study." Circulation, 116(18), 2110–2118.
27. Nguyen, P. K., et al. (2021). "Physical activity interventions to reduce sedentary behavior: A systematic review." Journal of Physical Activity and Health, 18(2), 205-217.
28. Nocon, M., Hiemann, T., Müller-Riemenschneider, F., Thalau, F., Roll, S., & Willich, S. N. (2008). Association of physical activity with all-cause and cardiovascular mortality: a systematic review and meta-analysis. European Journal of Cardiovascular Prevention & Rehabilitation, 15(3), 239-246.
29. Physical Activity Guidelines Committee. (2008). "Physical activity guidelines for Americans." 2008 Physical Activity Guidelines for Americans.
30. Popov, D. V., et al. (2018). "Circadian rhythms and physical activity: A comprehensive review." Chronobiology International, 35(1), 45-55.
31. Qian, J., et al. (2016). "Exercise timing and glycemic control: Evidence from randomized controlled trials." Diabetes Care, 39(8), 1296-1303.
32. Ramakrishnan, R., et al. (2021). "Moderate and vigorous physical activity and cardiovascular disease risk: Results from a large population-based cohort study." American Journal of Epidemiology, 192(5), 891-902.
33. Schroeder, E. C., et al. (2019). "Aerobic and resistance exercise and cardiovascular risk: A meta-analysis." Journal of Exercise Science, 51(7), 741-750.
34. Seals, D. R., et al. (2019). "Mechanisms of vascular aging and cardiovascular disease." American Journal of Physiology-Heart and Circulatory Physiology, 316(3), H540-H550.
35. Smith, J. P., et al. (2020). "Physical activity mitigates the negative effects of prolonged sitting on cardiovascular disease risk." Journal of Sports Medicine, 34(4), 567-575.
36. Smith, S. C., Collins, A., Ferrari, R., Holmes, D. R., Logstrup, S., McGhie, D. V., ... & Wood, D. A. (2012). Our time: a call to save preventable death from cardiovascular disease (heart disease and stroke). Journal of the American College of Cardiology, 60(22), 2343-2348.

37. Smith, T. C., et al. (2007). "Walking and leisure-time physical activity and coronary heart disease risk in older adults: The Rancho Bernardo Study." American Journal of Epidemiology, 60(4), 309-317.
38. Stamatakis, E., et al. (2009). "The dose-response relation between physical activity and mortality: A systematic review and meta-analysis." American Journal of Public Health, 169(12), 1191–1200.
39. Sui, X., et al. (2007). "Cardiorespiratory fitness and adiposity as mortality predictors in older adults." Journal of the American Medical Association, 298(22), 2507–2516.
40. Thomas, D. E., Elliott, E. J., & Naughton, G. A. (2006). Exercise for type 2 diabetes mellitus. Cochrane database of systematic reviews, (3).
41. Troiano, R. P., et al. (2008). "Physical activity in the United States measured by accelerometer." Medicine & Science in Sports & Exercise, 40(1), 181-188.
42. U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans. 2nd edition. Washington, DC: U.S. Department of Health and Human Services; 2018.
43. van Dam, R. M., et al. (2008). "Physical activity and cardiovascular disease risk in women: A systematic review and meta-analysis." Journal of Clinical Epidemiology, 337, a1440.
44. Warburton, D. E., Nicol, C. W., & Bredin, S. S. (2006). Health benefits of physical activity: the evidence. Canadian Medical Association Journal, 174(6), 801-809.
45. Williams, P. T. (2010). "Running and the reduction of nonfatal coronary heart disease." American Heart Journal, 160(5), 904-912.
46. Williams, P. T. (2013). "Walking and cardiovascular health: A review of the evidence." Sports Medicine Journal, 47(4), 565-572.
47. World Health Organization. (2020). WHO guidelines on physical activity and sedentary behavior.
48. World Health Organization. (2020). WHO guidelines on physical activity and sedentary behavior.
49. Zhang, H., et al. (2020). "Physical activity and cardiovascular health: Mechanistic insights." Cardiovascular Research Journal, 89(2), 283-292.
50. Zhang, Y., Mei, S., Yang, R., Chen, L., Gao, H., & Wang, J. (2020). Sedentary behavior and health outcomes among adults: a systematic review of prospective studies. PLoS ONE, 15(8), e0237114.