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A Systematic Review Comparing Dose Response of Exercise on Cardiovascular and All-Cause Mortality

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Abstract

It is well established that exercise improves cardiovascular and all-cause mortality, although an ideal dose of exercise is not known. The physical activity guidelines currently recommend 150 minutes per week of moderate-intensity exercise or 75 minutes of vigorous-intensity activity. Most individuals do not engage in adequate exercise, although a safe upper limit does not exist and a too much exercise hypothesis has recently emerged. This review of the literature analyzes studies that have evaluated exercise dose response on all-cause and cardiovascular mortality for the purpose of determining safe and effective exercise prescriptions. Searches were performed in PubMed and CINAHL between 2010 and 2018 to identify six studies that met inclusion criteria. Moderate-intensity exercise reduced all-cause mortality in five of six studies, whereas low-dose exercise most effectively improved all-cause mortality in three studies, and cardiovascular mortality in one study. Vigorous-intensity exercise or extreme doses demonstrated variable outcomes and remain controversial; two studies found vigorous-intensity exercise beneficial to improve health, two studies discouraged vigorous exercise, and two studies had less conclusive outcomes. It is not surprising that any amount of exercise improves health compared with none at all, with the greatest benefits observed when sedentary individuals began exercising. Low-dose exercise should be recommended to everyone with a goal of meeting the minimal requirements according to guidelines for decreased all-cause and cardiovascular mortality. Additional research to more thoroughly understand exercise dose response and motivate individuals to improve exercise engagement is currently warranted.

Keywords

exercise, physical activity, dose response, cardiovascular, mortality, intensity

Introduction

Physical inactivity is a global pandemic.[1,2] The prevalence of physical inactivity has increased in the last three decades,[3] with an estimated 80% of U.S. adults currently not meeting the recommended guidelines for aerobic and muscle-strengthening activity.[4] In spite of this incidence, exercise is a known primary modifiable risk factor for cardiovascular disease[5,6] and leading risk factor for mortality.[7]

Since the early 1950s,[8,9] physical activity has been established as a predictor of longevity, with causal relationships demonstrated between improved morbidity, mortality, and metabolic profile.[10,11] The Women's Health Initiative[12] outcomes demonstrated an association between dose of exercise and cardiovascular health. The findings from the Nurse's Health Study revealed higher quantities of physical activity during midlife contributed to improved health benefits later in life (age 70 years).[13] The outcomes of the Harvard Alumni Study[14,15] revealed an inverse relationship between the health-related benefits derived from exercise intensity and quantity of exercise, at amounts equivalent to 500 to 3500 kcal/week. Intensity was observed as an essential component of fitness and strong predictor of morbidity and mortality in the Studies Targeting Risk Reduction Interventions through Defined Exercise-Aerobic Training and/or Resistance Training (STRRIDE-AT/RT) study.[16] The STRRIDE-AT/RT revealed vigorous-intensity exercise more efficiently improved fitness than moderate-intensity exercise. When exercise was performed at a fixed intensity and varied dose, a greater improvement in VO_2 peak (peak oxygen uptake) was observed than exercise performed at a varied intensity and fixed total dose, demonstrating an equivalent improvement in VO_2 peak.[16] The American Heart Association and the American College of Cardiology recommend less frequent exercise sessions (3-4 times per week) for longer durations (30-40 minutes).[17] However, since 1975, a decreased trend

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has occurred in the guidelines for exercise intensity according to the American College of Sports Medicine (ACSM)[18]—a trend paralleling the progressive increase in sedentary behavior. The ACSM recommendations to improve exercise intensity in 1975 were consistent with a maximal amount of oxygen consumed (VO_2max) of 70%.[18] By 1978, these recommendations had decreased to 50% VO_2max,[19] with a subsequent decrease to 40% to 50% VO_2max by 1990,[20] at which time the moderate-intensity exercise was considered sufficient to improve fitness.[21]

In contrast to the studies documenting the negative impact of physical inactivity on health, recent reports suggest a "too much exercise hypothesis,"[22] in which adverse cardiovascular outcomes result from exercise performed at too high of an intensity or too great of a volume.[23] Thus, various research studies pose an interesting paradox involving a simultaneous concern for individuals engaging in too much exercise versus those engaging in too little exercise. At the center of this paradox is the issue of the question of appropriate exercise dosage. Therefore, we performed a systematic review of the literature to analyze studies that have evaluated exercise dose response on all-cause and cardiovascular mortality for the purpose of determining safe and effective exercise prescriptions.

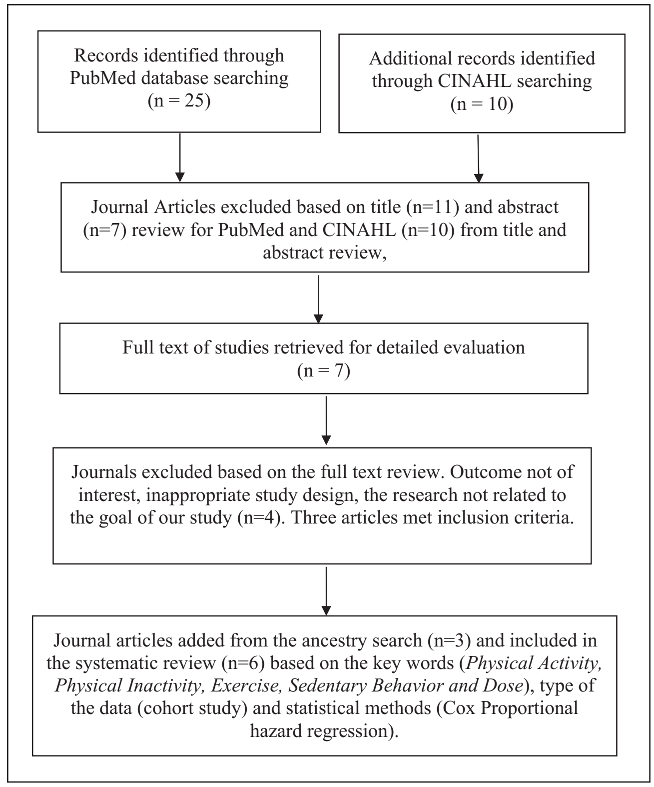

Figure 1. Study selection.

Methods

We performed a systematic review of the literature using the key words exercise, physical activity, dose response, cardiovascular, mortality. A search was performed in PubMed and CINAHL, and subject headings of key words were utilized in each database when present. Initially, 25 articles were identified in PubMed and 10 in CINAHL using these search criteria. The articles reviewed were limited to studies performed in adult participants (age 18+ years), written in English between 2010 and 2018. Two authors performed the initial screen, which included reading the abstracts of each article to determine whether the article met the inclusion criteria. The authors then collaborated for an agreed-upon consensus. Articles that met the initial screen were reviewed to determine whether the full text met the inclusion criteria. Articles were included if they used Cox proportional hazard regression models to assess the association between physical activity or exercise, and potential covariates, and the data were drawn from cohort studies. Excluded articles were those published prior to 2010 or that focused primarily on a specific age or disease, included only a single exercise intensity, or low-intensity exercise, or did not evaluate exercise intensity on exercise dose response. Following the CINAHL search, all 10 articles were excluded based on the abstract and title review. Articles that were excluded focused on a specific disease, the association of physical activity with select risk factors (i.e., cardiometabolic), screen time, or were review articles. In the PubMed search, 11 articles were excluded from the title search including nine that focused on a specific age or disease such as cancer or cognitive decline (one article matched the CINAHL search), one public health statement, and one review article. From the abstract search, seven were excluded; articles evaluated specific physiologic parameters from exercise (i.e., homocysteine), analyzed the association between a specific sport and mortality, or risk from exercise. Seven articles were then included in the full-text review, three of which did not meet inclusion criteria due to intensity (i.e., walking or nonexercise), and one study was excluded due to the methodology utilized for categorizing joggers, precluding comparison of the outcomes with other studies included in this review. The references of the three selected articles that met inclusion criteria were reviewed and one additional article was found in the reference list of two articles. Two additional articles were found in the references of the other articles. Six articles ultimately met the inclusion criteria and were utilized in the final evaluation (Figure 1).

The methodological quality of article selection included only those articles involving original research designs that utilized well-designed case-control or cohort studies.

Definitions of Physical Activity, Physical Inactivity, Exercise, Sedentary Behavior, and Dose Response

For the purposes of this review, it was important to define and, in certain cases, compare the terminologies such as physical activity, physical inactivity, exercise, sedentary behavior, and dose response. Physical activity has been defined as skeletal muscle movement resulting in energy expenditure, whereas exercise is a subcategory of physical activity to improve fitness.[24] Dose response refers to the relationship between physical activity and a specific health parameter, such as cardiovascular disease.[24] Physical inactivity refers to situations when less activity is performed than recommended in the guidelines,[24] whereas sedentary behavior is activity performed at a low energy expenditure (e.g., resting metabolic rate, typically ≤1.5 metabolic equivalents [METs]).[4,24,25]

Recommended Exercise Guidelines and Dose Components

The physical activity guidelines recommend a minimum of 150 minutes of weekly moderate-intensity (3-5.9 METs) or 75 minutes of vigorous-intensity activity (>6 METs).[4,21] During an exercise session, efficiency in exercise may be improved by adjusting an individual dose component such as *frequency, intensity*, or *time*.[21,26,27] The exercise dose components such frequency, intensity, time, type, total volume, and progression have been customized according to the FITT-VP principle,[21] where *frequency* involves the number of exercise sessions in a specific time period, *intensity* refers to exertion during exercise and is a reflection of energy expenditure, *time* is the duration of each exercise session, *type* refers to the mode or method of exercise, and *volume* refers to the product of frequency, intensity, and time.

Intensity may be measured in absolute or relative terms.[26,27] The unit of METs[24] is a measure for absolute intensity and reflects energy expenditure, that is, 1 MET is equivalent to the energy expenditure during rest[24]; therefore, an activity requiring 10 METs is equivalent to 10 times the energy required at rest. Relative intensity is measured subjectively based on individual fitness level. Relative intensity may be measured by using maximal heart rate, aerobic capacity by using a percentage of the VO_2max during exercise,[21] or according to perceived exertion using a Borg rating (Table 1).[28] In this analysis of study outcomes, intensity is measured in METs, percent of VO_2max, percent of maximum heart rate, and rating of perceived exertion (Borg scale = 6-20).[28]

Examples of common everyday activities are categorized according to intensity in METs and presented in Table 2. These categories may be defined as low-intensity, moderate-intensity, or vigorous-intensity activity. Low intensity includes very light to light exercise such as walking at a pace of less than 2.0 miles per hour or 1 mile in 30 minutes. Moderate intensity is equivalent to walking 3.5 miles per hour or at a pace of 1 mile in 17 minutes. Vigorous-intensity activity is equivalent to running 1 mile in 10 minutes,[4] or extreme-intensity exercise which qualifies as near-maximum exercise. One minute of vigorous-intensity exercise is considered analogous to 2 minutes of moderate-intensity exercise.[4]

Table 1. Measures of Exercise Intensity.[21]

Absolute-METs	Relative	Relative	Relative
Rest 1 MET = 3.5 mL O_2	Percentage of VO_2max	Percentage of maximum heart rate	Rating of perceived exertion (Borg scale = 6-20)
Very light 1.5 METs	<37	<57	<9
Light 2 to <3 METs	37 to 45	57 to <63	9 to 11
Moderate 3 to 6.0 METs	46 to 63	64 to <76	12 to 13
Vigorous 6.0 to 8.8 METs	64 to 90	77 to <95	14 to 17
Near maximal-maximal ≥8.8 METs	91	≥96	≥18

Note. MET = metabolic equivalent; VO_2max = maximal amount of oxygen consumed.

Exercise Dose Classification in the Studies

Each of the studies in this review involved sample cohorts from prospective longitudinal studies, and all six evaluated the outcomes of light and moderate exercise interventions.[29,30] Only five studies[29,31] evaluated vigorous-intensity exercise and two studies[31,32] included extreme exercise in their analyses. Six of the studies evaluated all-cause mortality outcomes, and two studies[31,33] evaluated cardiovascular mortality in addition to all-cause mortality outcomes.

Exercise dose classification according to intensity. Studies were categorized according to the ACSM[21] definitions for exercise intensity as presented in Table 1. The methodology used in each of the studies to classify exercise intensity did not consistently align with the ACSM definitions. Study methodology varied with respect to the population and computations for exercise intensity. The methodology in each study for determining light, moderate, and vigorous exercise intensity was, therefore, analyzed, and in situations where a discrepancy with the guidelines existed,[21] was recalculated for the purpose of accurate comparison among study findings. The measurements utilized for calculating light, moderate, and vigorous doses of exercise in each study are summarized and presented in Table 3. For example, Schnor et al[31] computed exercise according to the following: light activity is performed at a slow or average pace, approximately 5 mph, <0.5 hours of jogging, ≤3 times per week, or ~6 METs/week; moderate exercise involved jogging at a slow or average pace ≥2.5 hours per week, ≤3 times per week at a fast pace, or ≤4 hours, ≤3 times per week; and vigorous exercise involved at least 12 METs (fast-pace jogging > 7 mph), >4 hours per week or ≥2.5 hours per week, ≥3 times per week.

Gebel et al[34] classified exercise according to the percentage of vigorous intensity as per the categories: none

Table 2. METs of Common Activities as Very Light, Light, Moderate, or Vigorous Intensity.[21]

Very light 1.5 METs	Light 2 to <3 METs	Moderate 3 to 6.0 METs	Vigorous 6.0 to 8.8 METs	Maximum (extreme) ≥8.8 METs
Sitting, using the computer or light hand tools = 1.5	Washing dishes, making bed, ironing, cooking = 2.5	Walking at 3 mph = 3.0 Walking at a very brisk pace = 5.0	Walking at a very, very brisk pace (4.5 mph) = 6.3 Hiking = 7.0-8.0	Jog 5 mph = 8 Jog 6 mph = 10 Run 7 mph = 11.5 Competitive soccer = 10.0
Arts and crafts, playing cards = 1.5	Billiards, croquet, darts = 2.5	Carpentry = 3.6 Carrying wood = 5.5	Shoveling sand, coal = 7.0 Heavy farming = 8.0	Ski cross country skiing; slow = 7.0, fast = 9.0
Walking slowly around home or office = 2	Fishing, power boating = 2.5 Sail boating, wind surfing = 3.0	Shooting baskets = 4.5 Fast dancing = 4.5	Bicycling on a flat surface—moderate effort (12-14 mph) = 6.0	Bicycle race or all-out sprint (14-16 mph) = 10
Playing most musical instruments = 2.0-2.5	Slow dancing = 3.0	Golf, walking with clubs = 4.3	Leisurely swimming = 6.0	Moderate-hard swimming = 8.0-11.0

Note. MET = metabolic equivalents.

(0 to <30%), some (<30%), or ≥30%—categories that were different than the ACSM guidelines. Light activity involved a duration of 10 to 149 min/week; moderate activity was <30% vigorous for a duration of 15 to 299 min/week, such as gentle swimming or social tennis; and >30% vigorous activity at least 300 min/week, for example, jogging, was considered vigorous. As these classifications of exercise intensity were not consistent with the ACSM[21] categories for intensity (Table 1), we considered low-dose exercise as 30% vigorous activity for 10 to 149 minutes.

Arem et al[29] classified exercise as light, moderate, vigorous, and extremely vigorous. Light activity was 0.1 to <7.5 MET hr/week (less than recommendations); moderate exercise was 7.5 to <15.0 MET hr/week (1-2× recommendations); vigorous activity 15.0 to <22 MET hr/week (2-3× recommendations); and extremely vigorous at least a 30% vigorous intensity (3-5 times the exercise recommendations).

Statistical Analysis

Cox proportional hazard regressions were used to assess the risk of cardiovascular mortality and all-cause mortality in each of the six studies, and to assess the results of the original studies from the Cox hazard regression models, as well as for the adjustment of potential confounders, that is, age, smoking, and intensity. These confounding variables are presented in Table 3. A systematic comparison for dose of exercise was compared among studies according to intensity, "light," "moderate," and "vigorous," and illustrated using Forest plots (Figures 2-4). An estimate each of the study results of combined is also illustrated using Forest plots as presented in Figures 2 to 4. Forest plots provide a simple illustration of the risk reduction of exercise at a glance by summarizing the hazard ratio (HR) data across each study.[35] The Quade test (a nonparametric method, more powerful between a small number of groups)[36] compared the differences among the studies across dose of exercise (light to vigorous).

Results

The findings from our analysis of dose-response exercise trends on cardiovascular and all-cause mortality in the outcomes of six epidemiological studies in this systematic review suggest low-intensity exercise provides a similar benefit for all-cause and cardiovascular mortality compared with moderate-intensity exercise. We initially identified 36 articles from our search, 30 of which were excluded for a variety of reasons. From our analysis of the outcomes of the six articles that met inclusion criteria and were utilized in the final evaluation (Figure 1), we did not identify an *ideal* exercise dose suitable for all individuals.

Low-Dose Exercise

Low-dose exercise demonstrated a significant reduction in all-cause mortality[29,30,33] and cardiovascular mortality[31] (Figure 2). On average, a 27% lower mortality risk and estimated combined average benefit from 8.6% to 38% (HR) was observed (Figure 2; Table 3) in the studies. Compared with sedentary activity, low-dose exercise resulted in a lower adjusted HR ranging from 14% to 78%; the lowest was 14% observed by Wen et al,[30] followed by Arem et al, 20%[29]; Williams and Thompson, 25%[31]; Lee et al, 30%[33]; and Schnor et al, 78%.[32] Schnor et al[32] observed a risk of death that was 4 to 5 times higher in sedentary individuals compared with light joggers (HR = 0.22, 95% confidence interval [CI] = 0.10-0.47), with an *ideal* dose of approximately 1 to 2.4 hours of walking 2 to 3 times per week at a slow to average pace.[32] Only Gebel et al[34] did not find significant mortality benefits (HR = 1.09; CI = 0.84-1.42) from low-dose exercise.

Moderate-Dose Exercise

The majority of studies demonstrated a reduction in all-cause mortality from moderate-dose exercise,[29,30,33] with a combined average effect of 26% lower mortality risk and an estimated combined average benefit between 4% and 42%

Table 3. Studies Evaluating the Relationship Between All-Cause and/or Cardiovascular Mortality and Exercise Dose Response.

Study characteristics	Exercise dose	Mortality	Key findings
Gebel et al[34]	Sedentary reference	*All-Cause Mortality*	*Curvilinear* dose-response trend
Australian adults		HR = 1	
≥45 years	Light		
Cohort study	10-149 min/wk	1.09 (0.84-1.42)	• No significant health benefits
• n = 204,542	≤30% vigorous activity		
• Follow-up: 8 years			• No significant health benefits
	Moderate	0.83 (0.67-1.03)	
Adjusted for age, sex, education, marital status, smoking weight, alcohol, fruit/vegetable intake, and total MVPA volume	150-299 min/wk ≤30% vigorous activity		• Decreased risk of mortality, 8% to 22% compared with sedentary group
	Vigorous ≥300 min/wk	0.85 (0.78-0.92)	• Performing vigorous activity may increase longevity in middle-aged and older adults
	≥30% vigorous activity		
Schnor et al[31]	Sedentary nonjogger reference group	*All-Cause Mortality*	*U-shaped* dose-response trend
Copenhagen Heart Study Danish	Based on quantity of jogging (p. 415)	HR = 1	
• Cohort study			• Lower all-cause mortality light joggers than nonjoggers (53%-90%)
• Joggers, n = 1,098	Light: <2.5 hr/wk and frequency of <3 times per week	0.22 (0.10-0.47)	
• Nonjogger, n = 3950			
• Follow-up: 12 years	Moderate: >2.5 hr/wk and frequency of <3 times per week	0.66 (0.32-1.38)	• Moderate joggers not significantly different than nonjoggers
• Quantity, frequency, and pace of jogging related to all-cause mortality			• Strenuous joggers not statistically different from nonjoggers
Adjusted for age and sex, smoking, alcohol, education, diabetes	Vigorous: >2.5-4 hr/wk frequency of >3 times per week	1.97 (0.48-8.14)*	
Arem et al[29]	Sedentary nonjogger reference group	*All-Cause Mortality*	*J-shaped* dose-response trend
National Cancer Institute		HR = 1	
• Cohort study	Light: 0.1 to <7.5 MET hr/wk	0.80 (0.78-0.82)	• Significant decreased mortality at doses below recommendations; 18% to 22% lower than inactive group
• n = 661,137 adults	(less than recommendations)		
• Follow-up: 14 years	Moderate: 7.5 to <15.0 MET hr/wk	0.69 (0.67-0.70)	• Significant decreased mortality at 1 to 2 times the minimum exercise dose; 30% to 33% less than inactive group.
	(1-2× recommendations)		
Results adjusted for age, sex smoking, alcohol use, education, marital status, cancer, heart disease history, BMI.	Vigorous: >22.5 MET hr/wk		• Mortality reduced by 38% to 41% at 3 to 5 times the minimum exercise dose than inactive group
	(3-5× recommendations)	0.61 (0.59-0.62)	• No excess risk observed at 10 or more times the minimum exercise recommendations

(continued)

Table 3. (continued)

Study characteristics	Exercise dose	Mortality	Key findings
Lee et al[33]	Nonrunners (reference)	*All-Cause Mortality and Cardiovascular Mortality*	*J-shaped* dose-response trend
Aerobic Center Longitudinal Study		HR = 1	• Significant long-term mortality benefits from slow running speed and low dose (<51 min/wk) on average mortality decreased between 15% and 42%.
American adults	Light: <51 min/wk running	0.70 (0.58-0.85)	
• *n* = 55,137			
• Follow-up: 15 years	Moderate: 81-119 min/wk running (1-1.25× recommendations)	0.67 (0.55-0.82)	• Lower mortality between 18% and 45% at 1 to 1.25 times than minimum exercise dose than inactive group
Results adjusted for			
Model 2: age, sex and examination year; smoking, alcohol consumption, other activity, genetic CVD	Vigorous: ≥176 min/wk running (above 2.25× recommendations)	0.77 (0.63-0.92)	• Significant long-term mortality benefits on average between 8% and 37% at 2.25 times than minimum exercise dose compared with the inactive group
Williams and Thompson[31]	CVD-related mortality and METs	CVD-related mortality	*J-shaped* dose-response trend
National Run/Walk Studies; US	Cardiovascular mortality (vs. inactive subjects)		
Survivors of an Myocardial Infarction			• Exercise at recommended levels did not significantly decrease CVD risk-related mortality compared with inactive group.
n = 2377 (942M/631F)	Light: 1.07 and 1.8 MET hr/d	0.75 (0.55, 1.00)	
• Follow-up: 10.4 years	Moderate:1.8-3.6 MET hr/d (1-2 fold)	0.73 (0.56-0.94)	• The risk for CVD-related mortality decreased 6% to 44%
• Cardiovascular mortality	Vigorous: >7.2 MET hr/d More than 4-fold	0.82 (0.42-1.48)	• Risk from excessive exercise was not significant compared with nonrunners
Adjusted for age and sex, education, aspirin, smoking and diet			
Wen et al[30]	Sedentary reference	*All-Cause Mortality* HR = 1	*Curvilinear* dose-response trend
MJ Health Management Institute Study, Taiwanese adults (>20)	Exercise volume and intensity Light: 15 min/d/METs Moderate: 3.0	0.86 (0.82-0.92)	• Significant long-term mortality benefits (15 min/d) on average decreased between 8% and 18%.
Cohort study	Medium: 30 min/d/METs	0.82 (0.77-0.87)	
• *n* = 416,175	Moderate: 3.0		
• Follow-up: average follow-up of 8.05 years	Vigorous: 6.0		• Decreased mortality risk from 13% to 23% (30 min/d) compared with sedentary group
Adjusted for age, sex, cardiovascular risk	Very high: 90 min/d/METs Vigorous: 6.2	0.60 (0.53-0.68)	• Vigorous-intensity exercise (90 min/d) yields greater all-cause mortality reduction than sedentary group

Note. HR = hazard ratio; MVPA = moderate-vigorous physical activity; METs = metabolic equivalents; BMI = body mass index; CVD = cardiovascular disease; PA = physical activity.
*Values >2 HR are not displayed in the Forest plot.

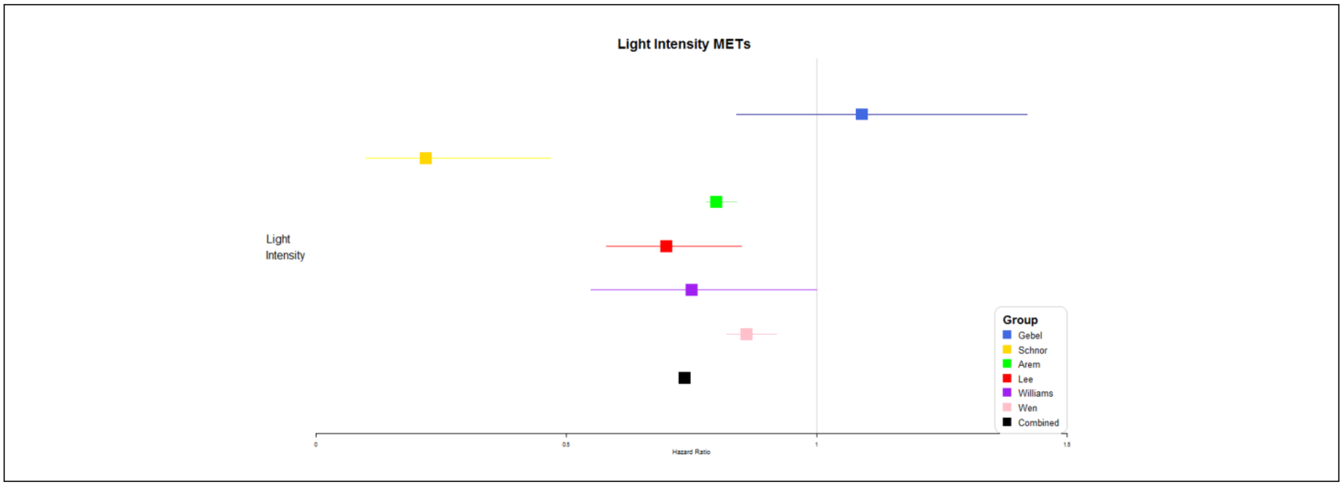

Figure 2. Light-intensity metabolic equivalents.

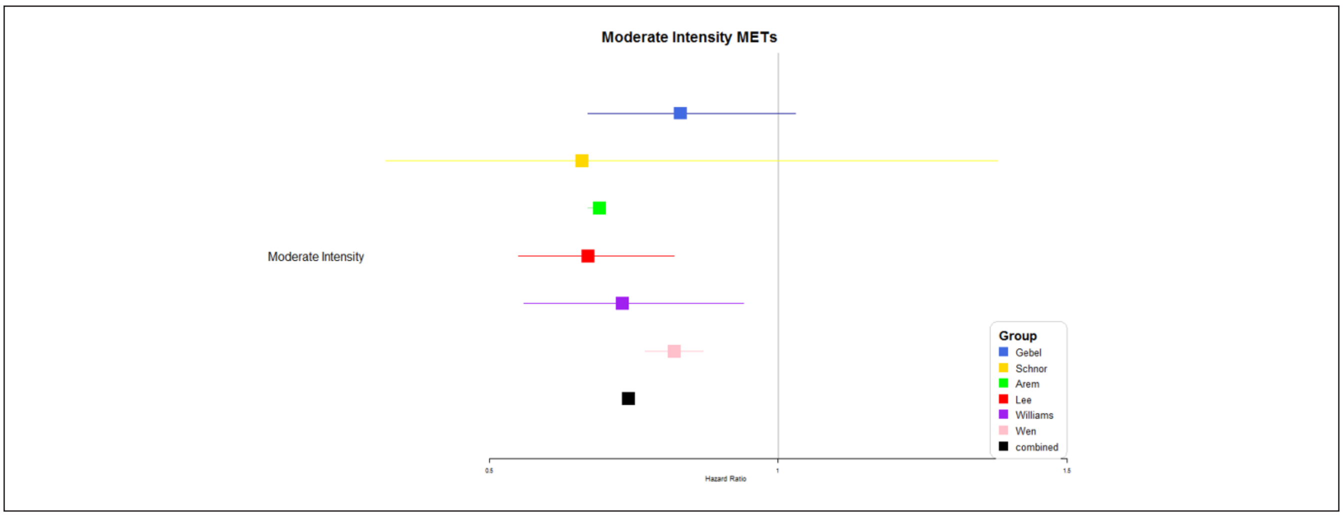

Figure 3. Moderate-intensity metabolic equivalents.

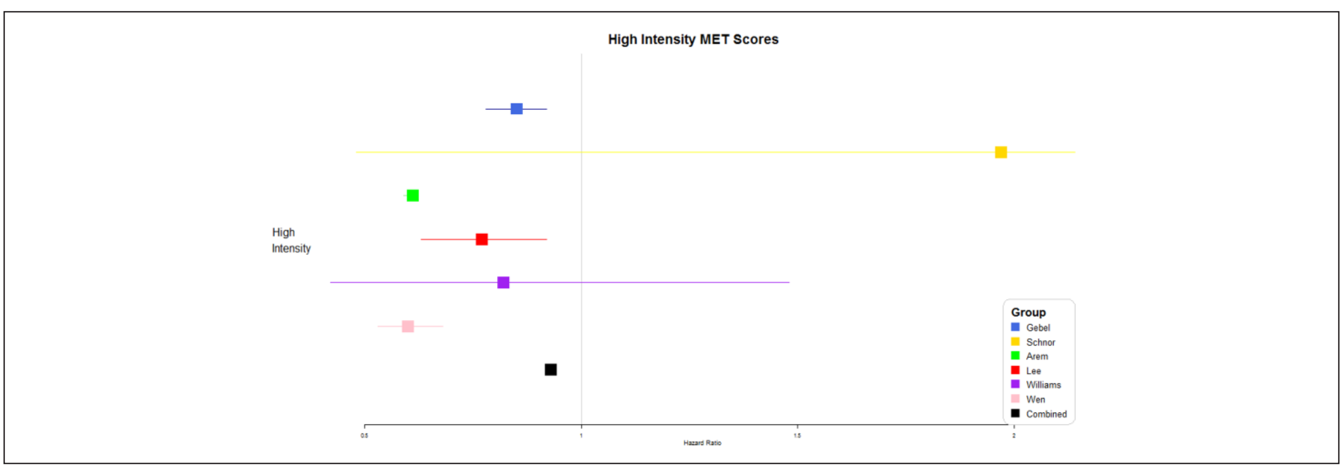

Figure 4. High-intensity metabolic equivalent scores.

(Figure 3; Table 3). Lee et al[33] observed the greatest benefit of 18% to 45% improvement in all-cause and cardiovascular mortality (observed as a combined category) in runners who ran <51 minutes per week compared with nonrunners. The precise outcomes of Arem et al[29] demonstrated a 30% to 33% reduction in all-cause mortality from walking at a moderate intensity, while Williams and Thompson[31] observed a variable 6% to 44% improvement in cardiovascular mortality. Wen et al[30] observed a 3% to 23% benefit in all-cause mortality, with a 4% improvement found from each subsequent 15-minute increase in exercise duration (Table 3, Figure 4).

Vigorous-Dose Exercise

The estimated combined average benefit from vigorous activity ranged from 7.6% to 41% (Figure 3; Table 3) in the studies, with the exception of Schnor et al,[32] who reported an extreme CI (HR = 1.97; CI = 0.48-8.14) in their findings. Arem et al[29] favored vigorous activity observing a 38% to 41% mortality benefit, followed by Wen et al (32%-47%),[30] Lee et al (8%-37%),[33] and finally, Gebel et al (8%-22%)[34] who demonstrated less conclusive findings. No additional reduction in all-cause mortality was observed when vigorous doses were compared with moderate doses. The Quade test did not detect a significant difference among the three doses for the six studies ($P = .59$).[36]

Discussion

An analysis of the outcomes of the studies reviewed in this research suggests that low-intensity exercise provided a similar benefit for all-cause and cardiovascular mortality as compared with moderate-intensity exercise. The determination of an *ideal* exercise dose, considered suitable for all individuals, was, however, difficult to ascertain.[33] We therefore consider the health concern of physical inactivity, a more urgent concern than the "too much exercise hypothesis."

Low- to Moderate-Dose Exercise

The majority of study outcomes[29,30,33] indicated a significant mortality benefit from low (8.6%-38%) to moderate (4%-42%) dose exercise when compared with sedentary behavior (Figures 2 and 3). According to a recent report, regular physical activity of at least 1 MET, that is, the oxygen required during rest, improved survival by up to 15%[5] at doses below the guidelines. Most benefits were observed in the first 15 minutes; daily brisk walking for 15 minutes at a moderate intensity improved the risk for all-cause mortality,[30] while 5 to 10 minutes of daily running improved cardiovascular mortality, and years of running was associated with reduced all-cause mortality.[33] The greatest health benefits were found from low-intensity activity at doses below the physical activity recommended guidelines.[29] Although Gebel et al[34] did not observe low-dose exercise beneficial, their methodology for classifying exercise must be considered as they categorized moderate-dose exercise as low-dose exercise based on the ACSM classifications[21] (Table 3).

In the majority of studies,[29,30,33] significant mortality benefits were from exercise performed at a moderate dose, and for those that observed different outcomes,[31,32] their methodology must be considered. According to Williams and Thompson,[31] frequency most significantly impacted mortality, a finding[31] consistent with the notable outcomes of Mons et al[37] who observed greater mortality benefits from two to four sessions per week at a low to moderate intensity rather than more frequent exercise sessions. The American Heart Association and the American College of Cardiology had similar recommendations.[17] Overall, health benefits were improved when dose of exercise was increased to an amount consistent with the physical activity guidelines.

Vigorous-Dose Exercise

Vigorous-dose exercise was considered beneficial in the outcomes of four studies, although these outcomes varied according to dose component.[29,30,33] In general, the study outcomes indicated intensity was a key component for health benefits; vigorous-intensity exercise was more beneficial than moderate intensity.[30] Mortality improved when at least 30% of exercise was performed at a higher intensity,[34] and at quantities equivalent to 2.25 times the recommended guidelines[29] (Table 3). In fact, a significant mortality reduction (38%-41%) was observed from quantities of exercise at 3 to 5 times the guidelines (450 min/week) as compared with sedentary behavior.[29] A threshold occurred when exercise quantities exceeded the lowest recommended dose for vigorous exercise, suggesting additional doses would yield diminishing returns.[33] For example, although Lee et al[33] observed a significant reduction in cardiovascular mortality from greater doses than the guidelines, no additional benefit was observed from running 51 minutes per week compared with running 51 to 176 minutes per week. Similarly, Williams and Thompson[31] observed an equivalent mortality risk from running 7.1 km/day or walking 10.7 km/day compared with sedentary behavior.

Extreme-Dose Exercise

The health outcomes from extreme exercise have not been established; thus, a safe upper limit of exercise is not known. Few studies have examined extreme dose of exercise making comparisons among the findings difficult to ascertain. Arem et al[29] found significant benefits from exercise performed at 10 times the current guidelines with no additional risk, although the benefits observed were no greater than at doses of 3 to 5 times the recommended guidelines. Schnor et al[32] found the mortality benefits from strenuous jogging at least 240 minutes per week, or 3 to 5 sessions per week, 4 or more hours at a high intensity, consistent with that of sedentary nonjoggers. However, their[32] methodology involved arbitrary measurements such as a category of "non-joggers" who in reality exercised at least 2 hours per week, two reported deaths from nondisclosed etiologies, in addition to an extremely wide CI in their outcomes, and 36 of 1098 individuals who were classified as "strenuous joggers." All of these factors contributed to the lack of a definitive association between extreme exercise and mortality.

Implications for Home Health Care

Health care providers have a key role in educating individuals to incorporate exercise into lifestyle for improved adherence and cardiovascular health benefits. The American Heart Association recommends assessing exercise during routine examinations[5] for classification of these habits by considering medical history, personal health characteristics, and individual genotype to provide a basis for better identification of an accurate exercise prescription, especially for those who are at greatest risk.[5,38]

Low-intensity exercise is considered safe for sedentary individuals once a history and physical examination have been completed and the determination that no additional cardiac testing is necessary.[21] Ongoing monitoring to evaluate exercise response is recommended, however, to avoid injuries and prevent additional cardiovascular risk.[38] If low-intensity exercise is tolerated, gradual increases in each of the dose components with the addition of resistance training 2 times per week to quantities consistent with the current guidelines are recommended. Social support may improve compliance[39] impacting long-term health outcomes. For those with a history of cardiovascular disease, cardiac rehabilitation programs educate regarding nutrition, stress management, and prevention in a setting that provides social support and supervised exercise sessions; however, only 62% of individuals are referred to cardiac rehabilitation upon discharge.[40]

Limitations

Limitations exist in this systematic review of six studies, such as the lack of a definitive recommendation for a precise minimum or maximal quantity of exercise. Studies either measured exercise according to intensity, which varied among study methodology, or exercise was measured by overall quantity, in which individuals, for the most part, actually participated in light, moderate, or vigorous exercise doses. Second, the subjects for the various studies were not matched for age, sex, and other demographic variables. Third, each study was an observational study rather than a randomized experiment, and therefore, suggested exercise was associated with health outcomes. These limitations present the difficulty of linking outcomes of mortality and cardiovascular disease entirely to dose of physical activity or exercise.

Future Research

The scarcity of literature available to practitioners to provide clarity with respect to safe, effective exercise doses is compounded by the lack of randomized studies evaluating exercise-related outcomes. Additional research is necessary to determine individualized prescriptions and equip health care providers with the necessary parameters to accurately recommend exercise for all individuals 2018 Physical Activity Guidelines Advisory Committee. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. Washington, DC: U.S. Department of Health and Human Services, 2018, with a variety of baseline exercise habits. Evidence-based strategies are key to alter existing exercise habits and effectively increase physical activity levels, whether as an established session for individuals or aimed at several participants. Although exercise requires a substantial time commitment to achieve quantities of exercise consist with the guidelines, it is worth the effort for improved quality of life and health-related benefits.

Conclusion

The message that physical activity and exercise are essential to improve health and decrease cardiovascular risk must never be forgotten.[41] As the vast majority of individuals engage in too little physical activity rather than too much, the key concern for all individuals is to determine a safe, sustainable exercise prescription that can be incorporated into lifestyle. Engaging in the lowest dose of physical activity, or short bouts, demonstrate improvements in cardiovascular and all-cause mortality benefits so everyone has *time* to exercise. Moderate-intensity activity improves health and the greatest dose of moderate-intensity exercise provides additional health-related benefits; therefore, exercise should be increased to a quantity that is consistent with the current recommended guidelines is recommended in all individuals. Exercising beyond the lowest dose of vigorous-intensity exercise to an excess of 300 or greater minutes (5 hours) per week did not demonstrate additional health benefits and, therefore, does not appear *necessary*. More research involving consistency in methodology and measurement for the purpose of providing additional clarity for exercise-related health benefits is currently warranted.

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