Lifelong Exercise Patterns and Cardiovascular Health

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Abstract

Objective: To determine the relationship between lifelong exercise dose and the prevalence of cardiovascular morbidity.

Patients and Methods: From June 1, 2011, through December 31, 2014, 21,266 individuals completed an online questionnaire regarding their lifelong exercise patterns and cardiovascular health status. Cardiovascular disease (CVD) was defined as a diagnosis of myocardial infarction, stroke, or heart failure, and cardiovascular risk factors (CVRFs) were defined as hypertension, hypercholesterolemia, or type 2 diabetes. Lifelong exercise patterns were measured over a median of 32 years for 405 patients with CVD, 1379 patients with CVRFs, and 10,656 controls. Participants were categorized into nonexercisers and quintiles (Q1−Q5) of exercise dose (metabolic equivalent task [MET] minutes per week).

Results: The CVD/CVRF prevalence was lower for each exercise quintile compared with nonexercisers (CVD: nonexercisers, 9.6% vs Q1: 4.4%, Q2: 2.8%, Q3: 2.4%, Q4: 3.6%, Q5: 3.9%; $P<.001$; CVRF: nonexercisers, 24.6% vs Q1: 13.8%, Q2: 10.2%, Q3: 9.0%, Q4: 9.4%, Q5: 12.0%; $P<.001$). The lowest exercise dose (Q1) significantly reduced CVD and CVRF prevalence, but the largest reductions were found at 764 to 1091 MET-min/wk for CVD (adjusted odds ratio=0.31; 95% CI, 0.20-0.48) and CVRFs (adjusted odds ratio=0.36; 95% CI, 0.28-0.47). The CVD/CVRF prevalence did not further decrease in higher exercise dose groups. Exercise intensity did not influence the relationship between exercise patterns and CVD or CVRFs.

Conclusion: These findings demonstrate a curvilinear relationship between lifelong exercise patterns and cardiovascular morbidity. Low exercise doses can effectively reduce CVD/CVRF prevalence, but engagement in exercise for 764 to 1091 MET-min/wk is associated with the lowest CVD/CVRF prevalence. Higher exercise doses do not yield additional benefits.

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Physical inactivity is considered a major modifiable risk factor for all-cause mortality,[1,2] whereas habitual physical exercise reduces the risk of cardiovascular morbidity and mortality.[3,4] Regular exercise is also associated with increased survival in the general and athletic populations.[5-7] Therefore, the World Health Organization and the Centers for Disease Control and Prevention recommend that adults engage in at least 150 minutes of moderate-intensity exercise or 75 minutes of vigorous-intensity exercise per week for optimal cardiovascular and global health.[8-10] These guidelines also state that there is even more benefit from 300 min/wk of moderate- and 150 min/week of vigorous-intensity exercise.

Such recommendations suggest increasing benefit with increasing exercise dose, but recent studies suggest a potential U-shaped association, indicating that high doses of exercise may abolish the beneficial health effects.[11,12] Results of the Copenhagen Heart Study indicate that vigorous joggers have similar mortality rates as sedentary nonjoggers (hazard ratio, 1.97; 95% CI, 0.48-8.14; and hazard ratio, 0.66; 95% CI, 0.32-1.38, respectively).[11] The Million Women Study indicates that daily strenuous activities increase the risk of stroke and venous thromboembolism compared with strenuous activities performed for 2 to 3 sessions per week.[12] The notion that exercise might increase the risk of cardiovascular morbidity is striking, but strong evidence is currently lacking.

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To confirm or reject the U-shaped association between exercise and cardiovascular morbidity, this study aimed to determine the relationship between lifelong exercise dose and the prevalence of cardiovascular morbidity in a physically active population. We collected data from 21,266 participants in the Nijmegen Exercise Study and hypothesized that high lifelong exercise doses relate to a decrease in the prevalence of cardiovascular morbidity.

METHODS

Study Design and Study Population

The Nijmegen Exercise Study is a population-based study of participants in Dutch sporting events (International Nijmegen Four Days Marches and Seven Hills Run) and their family members and friends. The study is designed to examine the impact of a physically active lifestyle on health, quality of life, and the development and progression of cardiovascular disease (CVD). From June 1, 2011, through December 31, 2014, inactive and active participants were recruited via newsletters and Internet advertisements. Participants completed an online questionnaire about demographic characteristics, anthropometric measures, lifestyle factors, lifelong exercise patterns, cardiovascular health status, and family history of CVD. To assess the impact of lifelong physical exercise patterns on cardiac morbidity, participants aged 35 years or older were included in the present study. The study adhered to the Declaration of Helsinki. The Local Committee on Research Involving Human Subjects, region Arnhem-Nijmegen, the Netherlands, approved the study, and all the participants gave their written informed consent.

Lifestyle Factors

Participants were asked about their smoking status (never, former, or current) and the highest level of education they completed. Level of education was categorized as low (elementary school or basic vocational education), intermediate (secondary vocational education), or high/academic (higher professional education or academic education).

History of CVD

Participants were asked whether (yes/no) and when (age) their physician diagnosed CVD (myocardial infarction, stroke, or heart failure) or the presence of cardiovascular risk factors (CVRFs) (hypertension, hypercholesterolemia, or diabetes [type 2]). All the participants were also queried about their (cardiovascular) medication use. To validate the CVD/CVRF diagnosis, we performed a cross-check with medication use. Participants with CVD or CVRFs, who did not report cardiac medication use were excluded from the study. Participants were allocated to the control group if they had no cardiac medical history and did not use cardiac medication. When both CVD and CVRFs were diagnosed, the participant was allocated to the CVD group. Participants with congenital heart disease, defined as a diagnosis of CVD before age 35 years, were excluded from further analysis (Figure 1). Participants were also asked whether CVD was present in their immediate biological family (defined as the participant's parents, brothers, and sisters).

Lifelong Exercise Patterns

The lifelong exercise patterns before CVD/CVRF diagnosis (patients) or before study participation (controls) were evaluated via an exercise history questionnaire, distinguishing 4 age periods: (1) 18 to 29 years, (2) 30 to 49 years, (3) 50 to 64 years, and (4) 65 years and older. In these categories, participants were asked per period whether (yes/no) they performed exercise and the corresponding (1) exercise time (hours) per week and (2) self-perceived intensity (light/moderate/vigorous). Participants who did not complete the exercise questionnaire were excluded from the final analysis. Based on Ainsworth's Compendium of Physical Activities,[13] we assigned a metabolic equivalent of task (MET) value of 2.5 for light-, 4.5 for moderate-, and 8.5 for vigorous-intensity exercise. The MET minutes were calculated by multiplying the exercise time in minutes with the accompanying MET score of the self-perceived intensity.[13] The average weekly amount of lifelong exercise (MET minutes per week) was calculated between age 18 years and age at CVD/CVRF diagnosis for the patients. Calculations were made for control participants between age 18 years and

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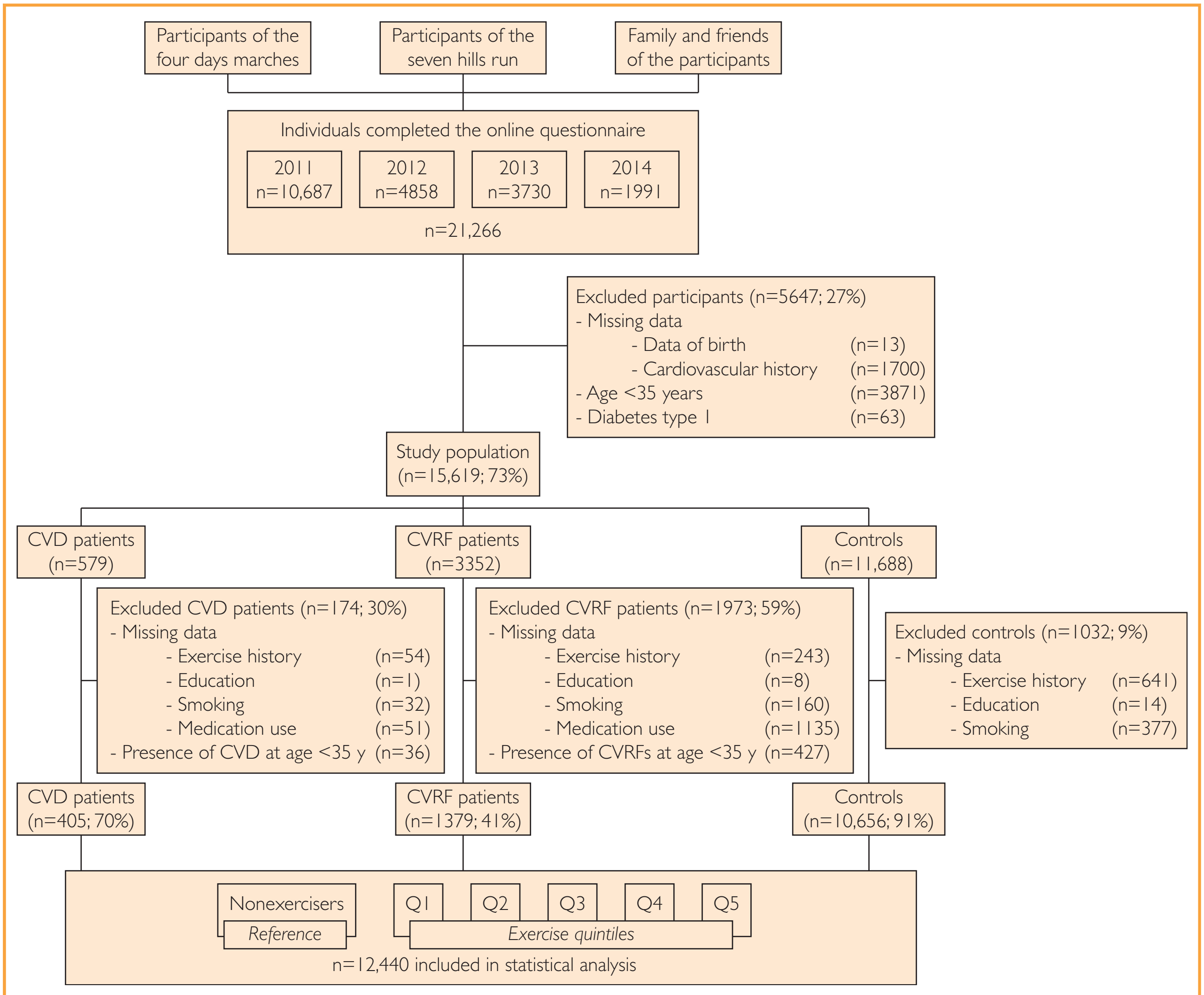

FIGURE 1. Flowchart for enrollment of the study population. A total of 21,266 participants completed the online questionnaire. Initially, 5647 participants were excluded from the study due to missing data (n=1713), age younger than 35 years (n=3871), or diabetes type 1 (n=63). The remaining 15,619 participants were divided into three groups: patients with cardiovascular disease (CVD), patients with cardiovascular risk factors (CVRFs), and controls. We excluded participants with missing data for exercise history (n=938), educational level (n=23), smoking status (n=569), cardiac medication use (n=1186), and diagnosis of CVD or CVRFs before 35 years of age (n=463). The final study consisted of 405 patients with CVD, 1379 patients with CVRFs, and 10,656 controls.

age at study participation. Participants were classified into 6 groups: nonexercisers and quintiles of weekly exercise dose (MET minutes per week).

Data Analysis

The characteristics of nonexercisers and exercisers are summarized using mean ± SD or counts and proportions. The prevalences of CVD and CVRFs were determined for each exercise dose quintile. Logistic regression was used to calculate the odds ratios (ORs) of CVD, with nonexercisers as the reference category. In the logistic regression analysis, we adjusted for the following potential confounders: age at CVD/CVRF diagnosis (patients) or age at study participation (controls), sex, smoking status, level of education, and CVD family history. To determine the impact of intensity on CVD and CVRF prevalence across exercise dose quintiles, the proportion of light, moderate, and vigorous intensity were

TABLE 1. Characteristics of Patients With CVD and Control Participants in Nonexercisers and Exerciser Quintiles of Lifelong Exercise Dose[a]

Characteristic	Nonexercisers (n=417)	Q1 (n=2130)	Q2 (n=2128)	Q3 (n=2127)	Q4 (n=2129)	Q5 (n=2130)
Male sex (No. [%])	243 (58)	1047 (49)	1048 (49)	1177 (55)	1348 (63)	1502 (71)
Age at study participation (y), mean ± SD	53±10	52±10	50±9	49±9	50±9	51±9
Positive family history (No. [%])	203 (49)	939 (44)	879 (41)	878 (41)	926 (43)	879 (41)
Lifelong exercise dose (MET-min/wk), mean ± SD	0±0	297±122	623±80	924±101	1388±181	2909±1336
Cardiovascular medical history						
Age at CVD diagnosis (y), mean ± SD[b]	53±10	51±10	49±9	49±9	50±9	50±9
Total patients with CVD (No. [%])	40 (10)	93 (4)	60 (3)	52 (2)	77 (4)	83 (4)
Myocardial infarction (No. [%])	27 (6)	43 (2)	31 (1)	22 (1)	41 (2)	43 (2)
Stroke (No. [%])	5 (1)	19 (1)	11 (1)	10 (0)	15 (1)	16 (1)
Heart failure (No. [%])	8 (2)	31 (1)	18 (1)	20 (1)	21 (1)	24 (1)
Level of education (No. [%])						
Low	88 (21)	225 (11)	126 (6)	133 (6)	165 (8)	146 (7)
Intermediate	200 (48)	856 (40)	799 (38)	804 (38)	840 (39)	831 (39)
High/academic	129 (31)	1049 (49)	1203 (57)	1190 (56)	1124 (53)	1153 (54)
Smoking status (No. [%])						
Nonsmokers	186 (45)	1054 (49)	1137 (53)	1174 (55)	1235 (58)	1307 (61)
Ex-smokers	180 (43)	950 (45)	886 (42)	846 (40)	789 (37)	713 (33)
Smokers	51 (12)	126 (6)	105 (5)	107 (5)	105 (5)	110 (5)

[a]CVD = cardiovascular disease; MET = metabolic equivalent of task; Q = quintile.
[b]Patients with CVD only.

calculated per exercise dose quintile. The analysis was performed via a 2-way analysis of variance, with factors of CVD/CVRF (yes/no) and exercise dose quintiles. All the statistical analyses were performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp). Statistical significance was assumed at $P<.05$ (2-sided).

RESULTS

Study Population

A total of 21,266 participants completed the online questionnaire. After the exclusion of participants with missing data, aged less than 35 years, or with type I diabetes, 12,440 participants were available for analysis (Figure 1). We calculated the average weekly lifelong exercise dose over a median of 32 years (interquartile range Q_{25}—Q_{75}, 26-39 years) for 405 patients with CVD, 1379 patients with CVRF, and 10,656 controls. The CVD sample most frequently had a myocardial infarction (n=207, 51%), followed by heart failure (n=122, 30%) and stroke (n=76, 19%) (Table 1). The CVRF sample most frequently had hypertension (n=992, 72%), followed by hypercholesterolemia (n=330, 24%) and diabetes (n=57, 4%) (Table 2). In general, exercisers had a 58% lower risk of CVD (adjusted OR=0.42; 95% CI, 0.29-0.60) and a 56% lower risk of CVRFs (adjusted OR=0.44; 95% CI, 0.35-0.55) compared with nonexercisers. These associations were consistent regardless of sex, age, smoking status, family history, and level of education (Figure 2).

Exercise Dose

Compared with nonexercisers, CVD prevalence was lower in all the exercise dose quintiles (nonexercisers: 9.6% vs Q1: 4.4%, Q2: 2.8%, Q3: 2.4%, Q4: 3.6%, and Q5: 3.9%; $P<.001$). After adjustment for age, sex, smoking status, level of education, and CVD family history, the adjusted ORs of CVD prevalence to lifelong exercise dose were 0.55 (95% CI, 0.36-0.82) for Q1, 0.38 (95% CI, 0.25-0.59) for Q2, 0.31 (95% CI, 0.20-0.48) for Q3, 0.41 (95% CI, 0.27-0.62) for Q4, and 0.43 (95% CI, 0.28-0.65) for Q5 (Figure 3, A). Participants who exercised at a dose of 773 to 1091 MET-min/wk (Q3) reported the lowest CVD prevalence, with a risk reduction of 69% compared with nonexercisers. An exercise dose of 773 to 1091 MET-min is equal to a weekly run of 13 to 18 km at a speed of approximately 8.0 km/h or a weekly walk of 17 to 24 km at a speed of approximately 5.6 km/h.

The CVRF prevalence was also lower in all exercise dose quintiles (nonexercisers: 24.6%

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TABLE 2. Characteristics of Patients With CVRF and Control Participants in the Nonexercisers and Exercisers Quintiles of Lifelong Exercise Dose[a]

Characteristic	Nonexercisers (n=500)	Q1 (n=2306)	Q2 (n=2307)	Q3 (n=2308)	Q4 (n=2307)	Q5 (n=2307)
Male sex (No. [%])	301 (60)	1136 (49)	1141 (49)	1282 (56)	1462 (63)	1637 (71)
Age at study participation (y), mean ± SD	55±10	52±10	50±9	49±9	51±9	51±9
Positive family history (No. [%])	242 (48)	1047 (45)	995 (43)	969 (42)	1019 (44)	983 (43)
Lifelong exercise dose (MET-min/wk), mean ± SD	0±0	290±120	616±80	919±101	1386±184	2918±1331
Cardiovascular medical history						
Age at CVRF diagnosis (y), mean ± SD[b]	52±9	51±10	49±9	49±9	50±9	50±9
Total patients with CVRF (No. [%])	123 (25)	318 (14)	236 (10)	208 (9)	218 (9)	276 (12)
Hypertension (No. [%])	92 (18)	236 (10)	169 (7)	143 (6)	154 (7)	198 (9)
Hypercholesterolemia (No. [%])	24 (5)	69 (3)	57 (2)	56 (2)	56 (2)	68 (3)
Diabetes type 2 (No. [%])	7 (1)	13 (<1)	10 (<1)	9 (<1)	8 (<1)	10 (<1)
Level of education (No. [%])						
Low	116 (23)	274 (12)	142 (6)	155 (7)	175 (8)	175 (8)
Intermediate	225 (45)	937 (41)	881 (38)	872 (38)	918 (40)	912 (40)
High/academic	159 (32)	1095 (47)	1284 (56)	1281 (56)	1214 (53)	1220 (53)
Smoking status (No. [%])						
Nonsmokers	221 (44)	1111 (48)	1222 (53)	1262 (55)	1323 (57)	1402 (61)
Ex-smokers	224 (45)	1053 (46)	974 (42)	930 (40)	878 (38)	791 (34)
Smokers	55 (11)	142 (6)	111 (5)	116 (5)	106 (5)	114 (5)

[a]CVRF = cardiovascular risk factor; MET = metabolic equivalent of task; Q = quintile.
[b]Patients with CVRFs only.

vs Q1: 13.8%, Q2: 10.2%, Q3: 9.0%, Q4: 9.4%, and Q5: 12.0%; *P*<.001). After adjustment for age, sex, smoking status, level of education, and CVD family history, the adjusted OR of CVRF prevalence to lifelong exercise dose were 0.57 (95% CI, 0.44-0.72) for Q1, 0.43 (95% CI, 0.33-0.55) for Q2, 0.36 (95% CI, 0.28-0.47) for Q3, 0.36 (95% CI, 0.28-0.47) for Q4, and 0.47 (95% CI, 0.37-0.60) for Q5 (Figure 3, B). Participants who exercised at a dose of 764 to 1085 MET-min/wk (Q3) reported the lowest CVRF prevalence, with a risk reduction of 64% compared with nonexercisers.

Exercise Intensity

In general, CVD, CVRF, and control participants exercised mostly at moderate intensity (71%), followed by vigorous intensity (16%) and light intensity (13%). The proportion of light- and moderate-intensity exercise decreased with higher exercise dose quintiles (*P*<.001), whereas the proportion of vigorous-intensity exercise increased with higher exercise dose quintiles (*P*<.001). Participants with CVD and CVRFs performed more light-intensity exercise compared with controls across quintiles (CVD: $P_{interaction}$=.03; CVRFs: $P_{interaction}$=.001). Proportions of moderate-intensity exercise (CVD: *P*=.48; CVRFs: *P*=.17) and vigorous-intensity exercise (CVD: *P*=.20; CVRFs: *P*=.36) did not differ between CVD/CVRF and control participants across quintiles (Figure 4).

DISCUSSION

This study presents several major findings. First, exercise below the recommended dose is associated with reduced cardiovascular morbidity. Second, performing exercise at a dose of 764 to 1091 MET-min/wk is associated with the lowest reduction in CVD/CVRF prevalence, approximating 69% for CVD and 64% for CVRFs. Third, a higher exercise dose does not yield additional cardiovascular benefits; we observed that CVD and CVRF prevalence did not further decrease in the highest exercise dose groups. Fourth, these data do not support the presence of the U-shaped association between exercise and CVD prevalence but reinforce the hypothesis that regular exercise performance is a potent lifestyle intervention for reducing the cardiovascular burden.

Several studies reported the favorable health effects of exercise,[7,14-16] as evidenced

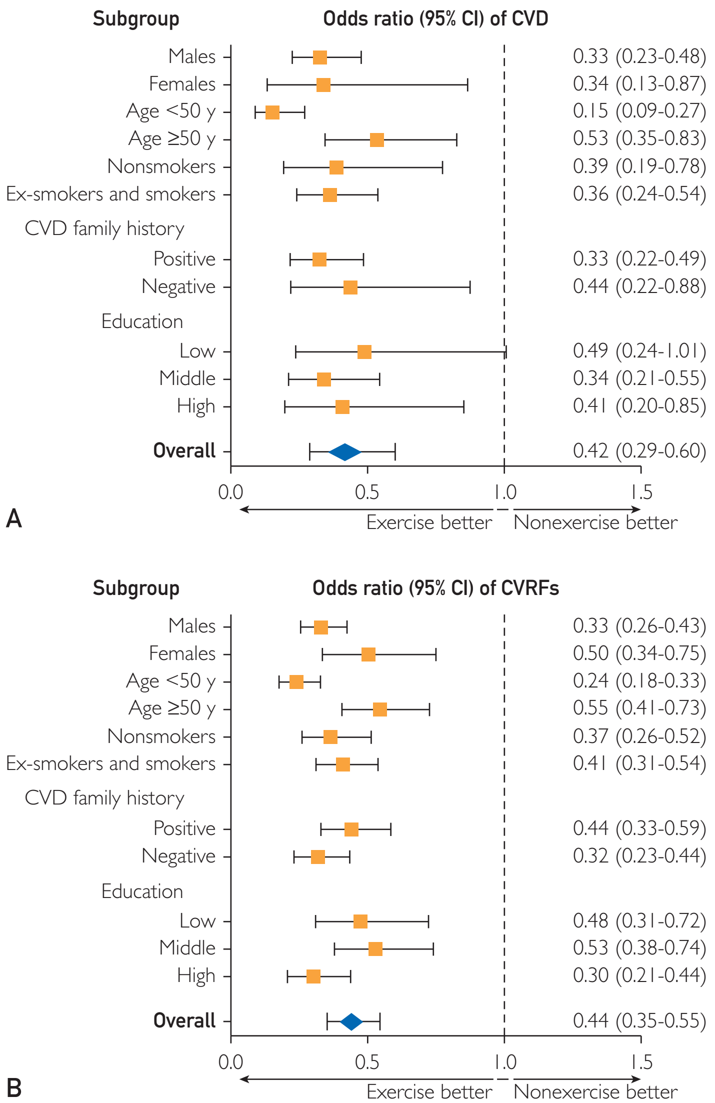

FIGURE 2. Odds ratios of cardiovascular disease (CVD) (A) and cardiovascular risk factors (CVRFs) (B) by subgroup. The reference group was nonexercisers. Exercisers had a 58% lower risk of CVD and a 56% lower risk of CVRFs compared with nonexercisers. These associations were consistent regardless of sex, age, smoking status, family history, and level of education. The overall odds ratio was adjusted for age, sex, smoking status (never, former, or current smoker), level of education (low, middle, or high education), and CVD family history (positive or negative).

by reductions in mortality risk in physically active individuals. The present study focused on cardiovascular morbidity only and found reduced CVD and CVRF prevalences across all exercise quintiles. Current exercise guidelines recommended a (minimum) weekly exercise dose of 675 MET-min (5 d/wk of moderate-intensity exercise [∼4.5 MET] for 30 min/d).[10] We found in the least active quintile significant cardiovascular benefits of 45% and 43% reduction in CVD and CVRF prevalence, respectively. The Q1 participants exercised, on average, 297 MET-min/wk, which is equal to the effort of a weekly 4.8-km run at 8 km/h (∼8.3 MET) or a 6.4-km walk at 5.6 km/h (∼4.3 MET). These findings reinforce previous observations that low doses of exercise can induce significant health effects.[14,15,17] The high "return on investment" of low exercise doses could encourage inactive and vulnerable populations to start exercise and gain subsequent cardiovascular benefits.

The quest for identification of the optimal exercise dose for cardiovascular health is challenging because it includes exercise time, intensity, or a combination of both.[18] The present study found the lowest prevalence of CVD and CVRFs at 764 to 1091 MET-min/wk, which is in agreement with the exercise recommendations of the World Health Organization.[10] This optimal exercise dose is a feasible goal for many individuals and includes 170 to 242 min/wk of moderate-intensity exercise or 90 to 128 min/wk of vigorous-intensity exercise. With a reduction of 69% for CVD prevalence and 64% for CVRF prevalence, these exercise doses importantly contribute to primary prevention and, hence, to a reduction in CVD-related health care expenses.

Interestingly, few studies revealed an upturn in mortality[11,19] or morbidity[12] risk with higher doses of exercise. The exercise dose of the highest quintile (Q5) is equal to the effort of a weekly approximately 350-minute run at approximately 8 km/h (∼8.3 MET) or a total running distance of ∼47 km/wk. Although these extreme exercisers did not report the lowest CVD or CVRF prevalence, a 57% reduction in CVD and a 53% reduction in CVRFs were found compared with nonexercisers. One might argue that the absence of a further decline in cardiovascular benefits at the higher exercise doses could relate to the amount of vigorous-intensity exercise, which these individuals (Q5) experienced. Vigorous endurance exercise is known to induce atherosclerotic plaque rupture,[20-22] transient cardiac dysfunction, and cardiac remodeling.[22-25] Indeed, Q5 participants exercised significantly more ($P<.001$) on

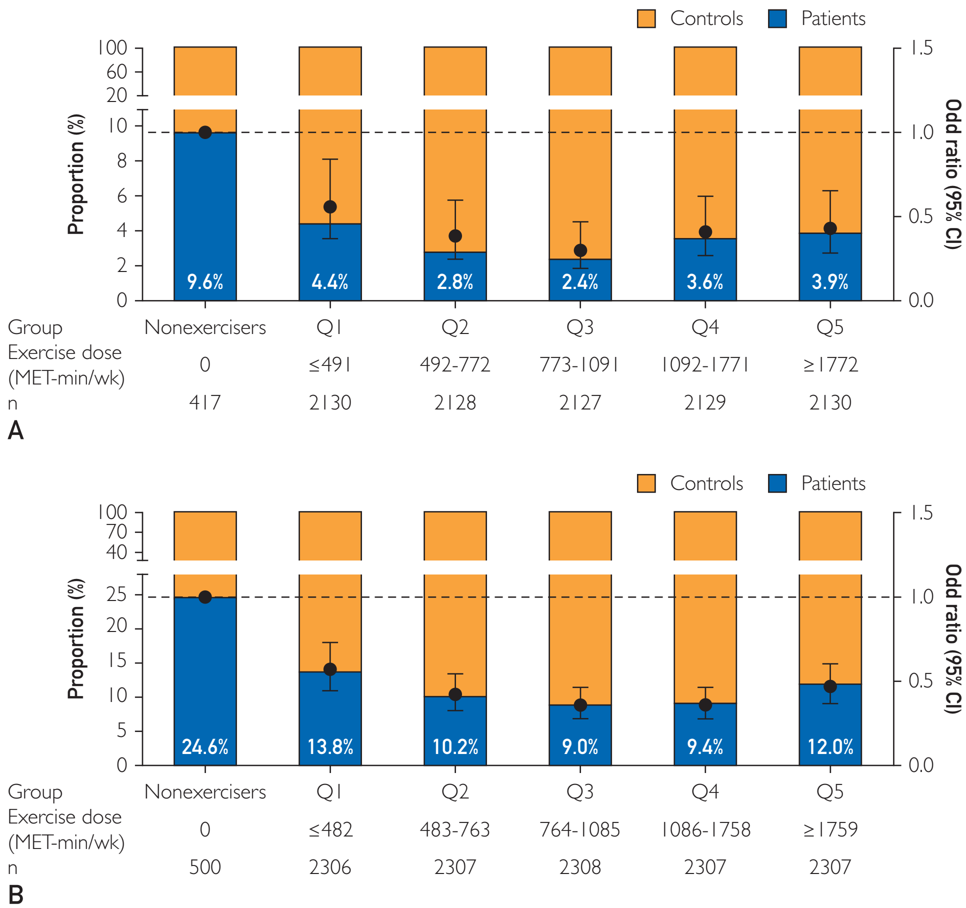

FIGURE 3. The association between the prevalence of cardiovascular morbidity and exercise dose per quintile (Q). The proportion of participants with cardiovascular disease (CVD) (A) and cardiovascular risk factors (B) per exercise dose (metabolic equivalent of task [MET] minutes per week) in quintiles is shown. Nonexercisers were set as the reference group, where the dotted line represents an odds ratio of 1. During the analysis, we adjusted for the following potential confounders: age, sex, smoking status, level of education, and CVD family history.

a vigorous-intensity level (47%) compared with all other quintiles (Q1: 3%, Q2: 6%, Q3: 6%, and Q4: 16%). However, the proportion of vigorous-intensity exercise did not differ between CVD/CVRF and control participants in Q5 (CVD: 50% vs control: 44%; P=.22; CVRFs: 46% vs control: 44%; P=.30). Other studies found increased longevity of 2.8 to 6 years in elite athletes with high-intensity exercise compared with reference cohorts.[6,26,27] Likewise, Gebel et al,[28] reported that vigorous-intensity activity was associated with a strong inverse relationship with mortality in the 45 and Up Study (n=204,542; aged 45-75 years). Larger doses of vigorous-intensity exercise yielded a larger decline in (cardiovascular) mortality compared with exercise at a moderate-intensity level alone. Although a higher exercise dose does not yield additional health benefits, it is unlikely that the amount of vigorous-intensity exercise contributes to this finding.

The present study found a curvilinear relationship between exercise and cardiovascular health. Hence, these findings contradict recent studies suggesting a potential U-shaped association.[11,12] There are several explanations for these different study outcomes. The results of the Copenhagen Heart Study[11] are difficult to interpret because of the low number of deaths (n=2) in the vigorous-intensity exercise group

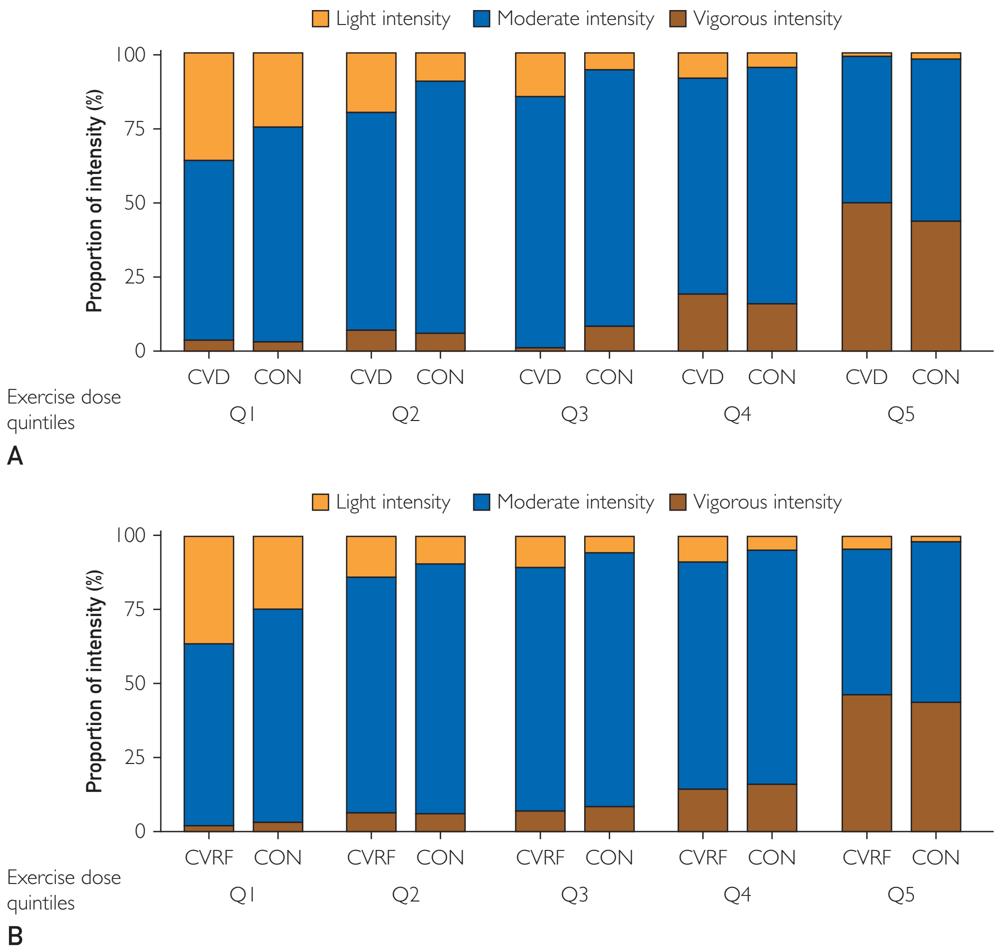

FIGURE 4. Proportion of light, moderate, and vigorous intensity per exercise dose quintile (Q). We categorized the total amount of lifelong exercise dose into light, moderate, and vigorous intensity based on the self-reported perceived intensity of the participant. The bars represent the proportion of intensity per exercise dose quintile for control participants (CON) vs patients with cardiovascular disease (CVD) (A) and patients with cardiovascular risk factors (CVRFs) (B). The proportion of light- and moderate-intensity exercise decreased with higher exercise dose quintiles ($P<.001$), whereas the proportion of vigorous-intensity exercise increased with higher exercise dose quintiles ($P<.001$). Patients with CVD or CVRFs performed more light-intensity exercise across quintiles compared with CONs, whereas moderate- and vigorous-intensity exercise did not differ between patients with CVD or CVRFs and CONs across quintiles.

(n=38).[29] Furthermore, the sedentary (reference) group was allowed to bike or walk for a maximum of 120 min/wk,[11] suggesting the possibility that they already gained cardiovascular health benefits from these low exercise doses.[15] Hence, the comparison between the sedentary and vigorous-intensity exercise group is likely to underestimate the true exercise benefits. In the Million Women Study by Armstrong et al,[12] the prevalence of current smokers was surprisingly higher in the daily strenuous exercises compared with those who did strenuous exercise 1 to 6 times per week (~26% vs ~15%). The authors acknowledge that even after adjusting for smoking, residual confounding may have occurred, which could explain the increased cardiovascular morbidity in vigorous exercisers.

The main strength of this study is the extensive period of exercise history (32 years

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[interquartile range Q_{25}—Q_{75}, 26-39 years]) over which we were able to calculate the exercise dose. Other studies comprised shorter periods or questioned the exercise characteristics over only a single time point.[11,12] The primary limitation of this study is that the exercise data were entirely dependent on self-report. This limitation is, however, applicable to nearly all epidemiologic studies because almost no studies have objectively measured lifelong exercise. Similarly, CVD data were obtained by questionnaires, but we confirmed the CVD status of each individual via cardiovascular medication use. Despite efforts to correct for all the potential confounders, it is possible that residual confounding may have occurred in the present study. Another caveat may be a recall bias regarding the exercise history of the participants. To reduce this potential error to the minimum, participants were blinded to the study hypothesis.[30]

CONCLUSION

In the present study, a regular low dose of exercise reduced cardiovascular morbidity, with further risk reduction at higher doses. Optimal health benefits were present with 170 to 242 min/wk of moderate-intensity exercise or 90 to 128 min/wk of vigorous-intensity exercise. The CVD/CVRF prevalence did not further decrease in higher exercise dose groups. Therefore, this study does not confirm the recently reported U-shaped association between exercise and morbidity in healthy individuals but suggests a curvilinear relationship between lifelong exercise patterns and cardiovascular health.

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Abbreviations and Acronyms: **CVD** = cardiovascular disease; **CVRF** = cardiovascular risk factor; **MET** = metabolic equivalent of task; **OR** = odds ratio; **Q** = quintile

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