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Title: Cross-country skiing and running's association with cardiovascular events and all-cause mortality : A review of the evidence

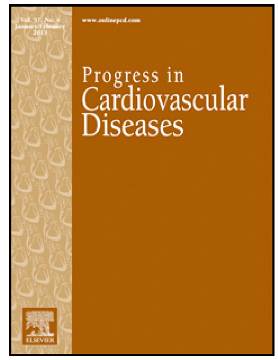
Year: 2020

Version: Accepted version (Final draft)

Please cite the original version:

Laukkanen, J. A., Kunutsor, S. K., Ozemek, C., Mäkikallio, T., Lee, D.-C., Wisloff, U., & Lavie, C. J. (2020). Cross-country skiing and running's association with cardiovascular events and all-cause mortality : A review of the evidence. Progress in Cardiovascular Diseases, 62(6), 505-514. https://doi.org/10.1016/j.pcad.2019.09.001

Journal Pre-proof



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PII: S0033-0620(19)30110-0

DOI: https://doi.org/10.1016/j.pcad.2019.09.001

Reference: YPCAD 997

To appear in: *Progress in Cardiovascular Diseases*

Please cite this article as: J.A. Laukkanen, S.K. Kunutsor, C. Ozemek, et al., Cross-country skiing and Running's association with cardiovascular events and all-cause mortality: A review of the evidence, *Progress in Cardiovascular Diseases*(2019), https://doi.org/10.1016/j.pcad.2019.09.001

Cross-Country Skiing and Running's Association with Cardiovascular Events and All-Cause Mortality: A Review of the Evidence

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Disclosures/COI: None

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A

A large body of evidence demonstrates positive, graded effects of PA on cardiovascular disease (CVD) morbidity and mortality with increasing intensity compared with lower PA intensity. Running is often designated as a high-intensity PA with substantial evidence supporting its health benefits. Cross-country skiing is among the most demanding aerobic endurance exercises and requires engaging the upper- and lower-body. Cross-country skiing is often regarded as high-intensity PA, which has been associated with significant health benefits. However, a robust body of evidence identifying the dose-response relation between cross-country skiing volume and health outcomes is sparse. Therefore, this review aims to summarize the available evidence linking cross-country skiing with CVD morbidity and all-cause mortality; postulated pathways that may elucidate the relation between these associations; outline areas of ongoing uncertainty; and the implications for primary and secondary CVD prevention. To put the findings into perspective, we also summarized the evidence linking running with CVD morbidity and all-cause mortality. Though a head-to-head comparison is not available, the evidence indicates that performing PA as cross-country skiing associates with lower mortality risk when compared with that observed in those undertaking their PA as running. Potential adverse effects of extreme high weekly doses of cross-country skiing over decades may be cardiac arrhythmias, such as atrial fibrillation. Evidence suggests that cross-country skiing may reduce the risk of CVD events and all-cause mortality via anti-inflammatory pathways, improvements in endothelial function and reduced levels of CVD risk factors, such as lipids, glucose, and blood pressure; and enhancement of cardiorespiratory fitness.

Key Words: physical activity, high-intensity physical activity, exercise, skiing, running, cardiovascular disease

Abbreviations:

ACLS-Aerobics Center Longitudinal Study

AF-Atrial fibrillation

CRF-Cardiorespiratory fitness

CV-Cardiovascular

CVD-Cardiovascular disease

HIPA-High intensity physical activity

MI-Myocardial infarction

MIPA-Moderate intensity physical activity

PA-Physical activity

RCT-Randomized controlled trial

The positive association between physical activity (PA) and/or exercise training with disease prevention is well established. [1, 2] Numerous epidemiologic and randomized controlled trials have contributed to identifying the volume of PA necessary to accumulate substantial health benefits across populations. Over the course of this work, many iterations of PA guidelines have led to the most recent recommendations of accumulating 150-300 min/week of moderate-intensity or 75-150 min/week of vigorous-intensity aerobic PA/exercise for adults, or a combination of the two in addition to completing at least two days of strength training.[1] The most common moderate- and vigorous-intensity aerobic PAs are listed in **Table 1**. These PA guidelines are purposefully broad in order to apply to most all individuals, however, there currently exists much interest in identifying ways to optimize health related outcomes that extend beyond what is generally experienced by performing the current recommendations. Many studies have presented compelling evidence suggesting vigorous or high-intensity PA (HIPA) is associated with significantly greater improvements in cardiorespiratory fitness (CRF) (well established for its beneficial effects on cardiovascular (CV) disease (CVD) outcomes and mortality[3, 4]), oxidative capacity of the skeletal muscle, vascular function, larger reductions in risk of chronic diseases, including hypertension, diabetes, CVD, as well as all-cause mortality, compared with lower or moderate intensity PA (MIPA). [5-11]

Several studies have examined the associations of participating in leisure- time moderate and high-intensity activities with CVD risk factors, risk of major chronic disease outcomes as well as all-cause mortality.[5-9, 12, 13,14] In a recent study consisting of 80,306 British adults, individuals taking part in sport or exercise activities were found to have significant reductions in all-cause mortality compared to those that did not.[15] All-cause mortality was significantly reduced in cyclists (hazard ratio (HR) 0.85, 95% confidence interval (CI) 0.76 to 0.95), swimmers (HR 0.72, 95% CI 0.65 to 0.80), racquet sports (HR 0.53, 95% CI 0.40 to 0.69) and aerobics (HR 0.73, 95% CI 0.63 to 0.83). However, only those that took part in swimming, racquet sports and aerobics experienced significant reduction in CVD mortality. The authors concluded that participation in above mentioned sport activities, which often studies should aim at strengthening the epidemiological evidence based on sports and health.

Cross-country skiing, in particular, is categorized as a HIPA that is undertaken as a leisure time PA or long-term endurance sport and is enjoyed by the general public as well as by athletes in competitive settings. While there are studies that have identified health benefits experienced with cross-country skiing, data on the association of cross-country skiing with CVD and all-cause mortality outcomes are relatively sparse compared to investigations on the effects of walking and running. The main purpose of this review is to 1) summarize the available epidemiological and interventional evidence linking cross-country skiing with CVD outcomes and all-cause mortality, 2) explore mechanisms underlying possible associations, 3) outline areas that require further investigation and 4) the implications for primary and secondary prevention. To accomplish this, we sought observational (prospective cohort, nested case-control, or case-control, retrospective cohort) studies, randomized controlled trials (RCTs), and non-RCTs from MEDLINE and EMBASE from their inception until December 2018. The computer-based searches combined free and Medical Subject Headings search terms and combination of key words related to the intervention ("skiing", "skiers") and outcomes ("cardiovascular disease", "death", "mortality"). Studies were limited to those conducted in humans, adults and written in English. Several reports have addressed the potential benefits of running, a very popular HIPA;[16-20] however, to put the findings into perspective, we also briefly summarized the existing evidence on running and its impact on CVD, as well as CVD- and all-cause mortality.

Existing Evidence on Cross-Country Skiing, CVD Morbidity and Mortality

Although interest in the relation between various sporting activities and adverse outcomes dates back several decades, the relation between cross-country skiing and mortality was first published in 1974 by Karvonen et al. In their study, 396 elite cross-country skiers were identified from records of annual national championship races and other highly competitive races. Participants were born between 1845 and 1910 and were followed up until 1967 and were found to live 4 years longer than the national the relation of cross-country skiing with CVD and mortality outcomes (**Table 2**). In 1993, Sarna and colleagues published an assessment of the life expectancy and mortality of 2613 Finnish male world class athletes who competed in cross-country skiing, track and field athletics, soccer, ice hockey, basketball, boxing, wrestling, weight lifting, or shooting.[22] This group was compared to a cohort of healthy men selected from the Finnish Defense Forces. When stratified by sport, those in the endurance category (cross-country skiing and long distance running) had the lowest mortality odds ratio [0.49, 95% CI 0.26 to 0.93] and the highest life expectancy odds ratio (75.6, 95% CI 73.6 to 77.5 years) compared to athletes in team or power sports and the healthy controls. Furthermore, the authors concluded that these observations were mainly due to decreased CVD mortality in those that participated in endurance sports. Grimsmo and colleagues compared CVD morbidity and mortality outcomes among long-term endurance cross-country skiers with that of the general population.[23] This cohort of cross-country skiers were followed for 30 years and the findings showed that these male athletes lived longer than males in the general population, where CVD was the major cause of deaths. In addition to prolonging life, prior participation in cross-country skiing has been demonstrated to reduce risk of recurrent CVD events and recovery time. The largest cohort study of 708,614 participants (Vasaloppet skiing study) matched cross-country skiers with a history of a stroke to non-skiers with a comparable history of stroke. Skiers were found to have a 30% relative risk reduction of all-cause death [adjusted HR, 0.70 (95% CI 0.56 to 0.87)], with no significant risk difference for recurrent stroke events compared with non-skiers [adjusted HR, 1.02 (95% CI 0.84 to 1.24)].[24] Furthermore, it appeared as though regularly participating in cross-country skiing attenuated post stroke functional declines as skiers maintained greater performance of activities of daily living, were less dependent, rated their health higher, were less depressed and used fewer medications compared with their non-skier counterparts who had a previous history of stroke. Hallmarker and colleagues again using the Vasaloppet study matched a cohort of cross-country skiers with a history of myocardial infarction (MI) with non-skiers and observed that skiers had a 20% lower subsequent risk of recurrent MI or death [adjusted HR, 0.80 (95% CI 0.67 to 0.97)].[25] Though these studies clearly demonstrated t a characterizing the volume of skiing performed by individuals. Therefore, our group recently quantified the volume of leisure time cross-country skiing performed by 2087 middle-aged men,[26] and examined its association with all-cause mortality over a median observation period of 26 years using the well-established Kuopio Ischemic Heart Disease (KIHD) prospective cohort study. Compared to men who did not participate in cross-country skiing, any volume of cross-country skiing was associated with significant reductions in all-cause mortality (1-200 MET hours per year, HR 0.84 95% CI, 0.73 to 0.97; >200 MET hours per year, HR 0.80, 95% CI 0.67 to 0.96). These findings were similar when separating participation by hours of skiing performed per week (1-60 min/wk, HR 0.84, 95% CI 0.72 to 0.97; >60 min/wk, HR 0.82, 95% CI 0.69 to 0.97) and independent of several potential confounders including total PA.[25] Cumulative hazard curves demonstrated a greater risk of all-cause mortality among participants who did not do any cross-country skiing (n=821) compared to the other groups (n=1266) (**Figure 1**).[26] A dose-response analysis suggested a continuous association between total volume of leisure-time cross-country skiing and the risk of all-cause mortality, consistent with a curvilinear or linear shape with no apparent threshold effect (**Figure 2**). Based on the KIHD cohort, we have recently shown that compared to men who did not participate in cross-country skiing, a volume of > 200 MET hours per year of cross-country skiing was associated with significant reduction in acute MI, multivariable adjusted HR 0.81, 95% CI 0.66 to 0.98).[27] In an investigation of all-cause mortality outcomes and health-related behavior among former Finnish male elite athletes who participated in various sports including cross-country skiing (n=900) and their age-matched brothers (n=900), the former athletes were observed to live 2-3 years longer than their brothers [age-adjusted hazard ratio for endurance sports, 0.61 (95% CI 0.45 to 0.82)].[28]In line with our demonstration of a dose-response relation, Hallmarker et al. studied 399,630 Swedish individuals in which half the sample were long-distance ski racers and the other half non-skiers. When compared to non-skiers, long distance skiers had reduced risk for all-cause mortality [adjusted HR, 0.52 (95% CI 0.49 to 0.54)], MI [adjusted HR, 0.56 (95% CI 0.52 to 0.60)], and stroke [adjusted HR, 0.63 (95% CI 0.58 to 0.67)] and for all the three outcomes combined [adjusted HR, 0.56 (95% CI 0.54 to 0.58)] compared with the general p[illegible]ers with slower racing times [age-adjusted HR per doubling of race time, 1.19 (95% CI 1.07 to 1.32)]. We have recently shown that total volume and duration of leisure time cross-country skiing are each inversely and independently associated with future risk of hypertension,[30] a leading risk factor for CVD.

Implicated Pathways Underlying Associations Between Cross-Country Skiing and Outcomes

A defining characteristic of cross-country skiing is the simultaneous use of the upper and lower body, while simultaneously working both the “pulling” and “pushing” muscles of a lower and upper body. The engagement of a larger muscle mass compared to common activities such as walking, running and cycling, increases exercise intensity and places a greater demand on the CV and metabolic systems. As a result, highly trained elite cross-country skiers have been shown to have similar relative mitochondrial volume as well as the number of capillaries per fiber area are the same in the arms and legs.[31]

There are multiple pathways by which cross-country skiing may decrease the risk of chronic diseases, such as CVD and mortality. Given the graded association between higher levels of PA with health benefits, cross-country skiing may reduce the risk of CVD and other outcomes as it is considered a HIPA. This likely occurs through physiological and metabolic adaptations, such as (i) improvements in endothelial function, decreased body weight, blood pressure, natriuretic peptides, lipid profiles, improvements in glucose tolerance, hemostatic factors, and cardiac troponin T;[12, 32-34] (ii) anti-inflammatory effects;[35, 36] and (iii) enhancement of cardiac function.[37, 38] Furthermore, cross-country skiing may increase neuromuscular function, left ventricular function and blood volume; stimulate angiogenesis; and increase vasodilation and hormonal effects, that may positively modulate oxygen uptake and CRF.[29] Also, cross-country skiing via its effect on obesity, may also reduce mortality through decreasing cancer risk.[39]

Compared to non-skiers, cross-country skiers have a better cardiometabolic risk profile. In the study of Vasaloppet skiers,[29] smoking, diabetes and hypertension, which are important risk factors for atherosclerotic CVD events, were significantly less frequent among the cross-country skiers when compared to non-skiers. In comparing CVD morbidity and mortality outcomes among long-term endurance cross-country skiers with that of the general population, Grimsmo and colleagues also observed that cross-country skiers had a favorable CVD risk profile (low blood pressure, favorable lipid levels, low prevalence of diabetes and obesity) compared with the general population.[23] In a case-control study that compared the lipid profile of healthy male sedentary controls with professional endurance athletes who included professional male cross-country skiers, adverse lipid abnormalities were mostly absent in the skiers compared to the control group.[40]

Since cross-country skiing is usually only possible during the winter months, its beneficial effects on adverse health outcomes and mortality is suggested to reflect individuals' seasonal PA habits and the ability to perform HIPA.[28, 29] Individuals who participate in long-distance ski racing have a high level of PA during the winter months, but are also likely to maintain regular PA throughout the year by walking, cycling and running. Though there is a possibility that the beneficial effects of cross-country skiing may reflect total endurance PA, our recent study on leisure-time cross-country skiing and all-cause mortality suggested otherwise.[26] Our findings showed that the association was independent of total PA, thus suggesting that the amount of skiing may have direct effects on adverse outcomes. However, some earlier studies[23,26] did not take into account the effects of other types of PA on the associations between cross-country skiing and mortality. Therefore, more evidence is still needed to examine the independent health benefits of cross-country skiing accounting for other types of PA.

The majority of cross-country skiers undergo intense training (HIPA) for at least four hours per week, which is on average much more than the general population. Regarding CRF levels in cross-country skiers, the maximum oxygen uptake (VO_{2max}) is between 45 and 85 $mL \cdot kg^{-1} \cdot min^{-1}$, [41-45] compared with performance. Female cross-country skiers have reported average VO_{2max} values of up to 70 mL·kg^{-1}·min^{-1},[42-45] whereas males have reported average values of up to 85 mL·kg^{-1}·min^{-1}.[43-45] In fact, elite cross-country skiers have the highest recorded VO_{2max} levels of any group of athletes; ~80 mL·kg^{-1}·min^{-1} in female and ~90 mL·kg^{-1}·min^{-1} in male cross-count skiers can be described as upper human limits in aerobic power.[45-47] Cross-country skiing involves the use of the large muscle groups of both the upper and lower body; therefore, during this HIPA, there is a large demand for oxygen to be supplied to these muscles. There is evidence to suggest that genetic differences may explain the differences in mortality risk between cross-country skiers and their non-skiing counterparts.[28] There is a possibility that genetic factors may explain different responses to regular exercise e.g. oxygen uptake or influence on risk factors.[48] An interesting question that remains to be answered is if high-level endurance athletes may have different physiologic responses to exercise and therefore lower risk for CVD.[44,49]

Potential Adverse Effects of Cross-Country Skiing

There have been previous suggestions that the HIPA might be harmful, particularly for athletes who engage in marathons and cycling races. The intensities and volumes of these HIPA regimens far exceed those proposed by guideline recommendations.[1] Indeed, biochemical as well as echocardiographic evidence of minor cardiac injury have been observed in high level endurance runners and athletes after long distance competitions.[50-52] Similar to these previous findings, there have been reports of an increased risk of acute CVD events, such as cardiac arrests and sudden cardiac deaths during long-distance skiing races.[53, 54] Available data also suggests that atrial fibrillation (AF), which is one of the most common cardiac arrhythmias, can also occur in high endurance athletes like cross-country skiers; though the evidence has been inconsistent. Among male participants of a long distance Swedish cross-country skiing event, a faster finishing time and a high number of completed races were associated with higher risk of arrhythmias, including AF.[53] In the largest study conducted among cross-country skiers and non-skiers with previous history of stroke, though cross-country skiers that compared cross-country male skiers with males from the general population, years of regular endurance exercise was found to be associated with increased risk of AF and atrial flutter.[55] Accordingly, long-term endurance cross-country skiers have a greater prevalence of AF compared to the general population.[56, 57] The majority of cross-country skiers still engage in PA or exercise after the onset of AF, as there is a potential for exercise to reduce symptoms of AF and death among veteran endurance athletes with AF.[56] Physically active people will only spend a small amount of their life time in these competitive races, hence the short-term excess risk of adverse events during these periods is by far outweighed by the long-term protective effects of cross-country skiing on mortality.[54] The high level of PA in a cohort of cross-country skiers with a history of MI protected them substantially against recurrent MI or death compared to their counterparts who were non-skiers.[25] Some other studies have however not demonstrated differences in the risk of AF between cross-country skiers and non-skiers.[29] Although there might be some adverse effects such as AF associated with high doses of cross-country skiing, there is limited data elucidating the volume of cross-country skiing beyond which does not provide additional overall health benefits (**Figure 2**).[26] Although the Vasaloppet cross-country skiers or those individuals who exercise for 20-30 hours per week have increased risk for AF, these same individuals have increased longevity. More importantly, the increased incidence of AF is not caused by too much PA in the general population, but rather too little PA in combination with an unhealthy lifestyle. Nevertheless, additional studies on the dose-response relationships between cross-country skiing and various health outcomes are warranted.

There may be an increased short-term risk of sudden coronary events during HIPA, especially in cold temperatures – a typical scenario for cross-country skiing. When emphasizing the importance of high CRF and increased PA, it is important to emphasize that exercise-related risks should also be considered as there may be more fatal adverse events among previously sedentary middle-aged and older individuals who start HIPA (without any appropriate health screening tests) than among those who have been active for long periods. Some of these acute CVD events may be due to atherosclerotic p[illegible] g

to sudden death during or after demanding HIPA/ exercise. Muscular skeletal injury rates are also very low in cross-country skiing compared to slalom or downhill skiing and are mostly chronic in nature.[58] Chronic anterior compartment syndrome is a potential cause of chronic pain in cross-country skiers.[59] and develops in cross-country athletes who practice daily at high intensity as a result of overuse injury of the muscles or muscle imbalance. Other very rare adverse effects reported are back pain, injuries and deaths associated with trauma and accidents.[60, 61]

Running and CVD and Mortality

The major emphasis of this review is cross-country skiing, as opposed to running, since many of the papers have addressed the potential benefits of running.[16-20] However, running is a very important HIPA that is available to many across the world and is possible in most seasons and climates. Running is associated with marked benefits in CVD and all-cause mortality.

Certainly, all types of PA are associated with benefits, but as reviewed above, HIPA is probably associated with more marked benefits, such as with many leisure time sporting activities and, especially, running.[16-20, 62-68] Several years ago, we reviewed the effects of running on chronic diseases and CVD and all-cause mortality,[16] and updated this more recently.[17]

Although, there are numerous studies on running and CVD in the literature, we especially reviewed the data from the National Runner's and Walker's Health Study, the Running Aging Study, the Copenhagen City Heart Study,[18, 66] and especially the Aerobics Center Longitudinal Study (ACLS),[19, 67] which are all reviewed in detail elsewhere.[16, 17] However, in this report, we will mostly emphasize the data from the ACLS, which is perhaps the largest and most robust from a CVD - and all-cause mortality standpoint, including emphasis on dose-response relationship of running and mortality.[16, 17, 19, 67, 68]

Running - ACLS Data

In the ACLS, 55,000 individuals (13,000 runners) were followed for nearly 15 years to assess the impact on CVD - and all-cause mortality compared with nonrunners. In this large study, the runners had reductions in CVD - and all-cause mortality of 30% and 45% (**Figure 3**), respectively, accounting for an estimated increase in average survival of 3.0 and 4.1 years for all-cause and CVD - related survival, respectively, after adjusting for lifestyle factors and medical conditions.[67] Persistent runners appear to receive the full benefit from running for mortality reductions, whereas those who were nonrunners but who started running during the study and those who started running but later stopped appeared to receive nearly half of the benefit received from CVD - and all-cause mortality reductions. Although, these results are impressive, many would not find this to be particularly surprising, since running may be expected to produce improvements in health, and those who were able to run may represent selection bias in favor of the runners.

However, when assessing the relative doses of running, somewhat surprising results emerged. Runners generally had considerably higher levels of CRF than did nonrunners, and the levels of CRF in the runners generally progressively increased with increasing running doses (**Figure 4**).[67] Most evidence indicates better survival with estimated metabolic equivalents greater than 10, although some studies suggest progressively better survival as CRF progressively increases.[16, 17, 20, 62, 64, 69] However, when the 13,000 runners were divided into quintiles (Q) of running doses, such as miles per week, times per week, minutes per week, etc., no statistically significant differences were noted for CVD – and all-cause mortality between the five running groups (**Figure 5**), although the trend appeared to be more favorable in those with faster running times.[67] In fact, those who were in Q1 for the various dosages categories (e.g. < 6 miles per week, running only 1-2 times per week, < 51 minutes per week, and > 6 mph running pace) received the full benefit from running with respect to reductions in CVD - and all-cause mortality (**Figure 4**).[67] These results suggested that maximal benefits of this HIPA occur at quite modest running/ jogging doses and that runners in Q1 have almost similar benefit as did those Q2-4

In contrast to the results of the Copenhagen City Heart Study,[18, 66] which would suggest the loss of benefit or even potentially harm of moderate-doses of running, our results from a larger sample with much better statistical power indicated that runners with Q5 still had significantly better CVD - and all-cause survival compared with nonrunners.[16, 17, 67, 68] However, the higher doses of running were not necessary to achieve maximal CVD - and all-cause mortality reductions. Also, when we later divided the Q5 runners further into tertiles (T1-3), we found that the highest tertile (Q5,T3), or the top 7% of running doses, actually appear to lose the benefit, compared to the nonrunners, although there was no increase in mortality risk, suggesting "more was still not bad" (**Figure 6**).[19] However, when compared to the low dose of running (Q1) in MET-min/week (not compared to the nonrunners), which generally provides the most favorable mortality benefits, the relative risk of CVD mortality (HR 1.66, 95% CI 0.87 to 3.16) and all-cause mortality (HR 1.27, 95% CI 0.89 to 1.81) were higher in the highest running group (T3) although still not significant, which raised concerns that "more could be worse."

Additional Benefits of Running

Although improving CRF and CVD - and all-cause mortality are perhaps the greatest attributes to running, improvements in weight and reductions in obesity indices, hypertension, dyslipidemia, type 2 diabetes, osteoarthritis, need for hip replacement, benign prostatic hypertrophy, disability, respiratory diseases, cancers, and stroke have also been reported with running, and are reviewed in detail elsewhere.[16, 17]

Potential Adverse Effects of Very High Running Doses

Besides the potential toxicity discussed elsewhere, and which was discussed with high doses of skiing, running extreme distances can also have potential toxicity (**Figure 7**),[70] including cardiac dilation and dysfunction and the release of troponin, brain natriuretic peptides and cardiac arrhythmias, especially AF.[20, 70, 71] At present, we agree with Levine regarding the overall safety of high intensity and high endurance exercises to avoid these activities.[20, 72] Nevertheless, from a public health standpoint, it is best to emphasize that the maximal benefit of HIPA, such as running, occur at low to modest levels. Higher doses of running, however, may be required for competition (eg. to improve running times) or for those who enjoy these higher doses.[16-20, 62, 64-68, 71, 72]

Conclusions

Overall, the evidence on the potential beneficial effects of cross-country skiing on CVD morbidity and mortality are based on observational study designs, which are limited by potential biases such as reverse causation, residual confounding, and/or regression dilution bias. The majority of studies did not adjust for other types of PA. Therefore, further studies are warranted to examine the independent health benefits of cross-country skiing accounting for other types of activities. Though head-to-head comparisons are not available, the evidence based on reported risk estimates suggest that cross-country skiing may be associated with substantial mortality benefits compared with running. Although some studies suggested that there may be potential adverse effects such as AF associated with high doses of cross-country skiing,[24, 53] there is still limited data on a potential upper limit of cross-country skiing beyond which more cross-country skiing does not provide further benefits or is possibly harmful. Nevertheless, evidence on the cardiovascular and mortality benefits seems to far outweigh the risks. So far evidence from our study suggests a continuous dose-response relationship between total volume of cross-country skiing and all-cause mortality;[26] a finding which may be consistent with that of PA and outcomes, such as CVD and mortality.[11] However, more comprehensive studies on the dose-response relationships between cross-country skiing and various health outcomes are warranted.

It is reported that during winter, PA can decrease by up to 40%.[71] This subsequently results in adverse cardiometabolic risk profiles, such as increase in blood pressure, weight, and harmful cholesterol, which are precursors for coronary and other CVD mortality. There is substantial evidence that the level, including HIPA, can be tracked to promote improvements in CRF which is a key element in CVD risk reduction.[4, 74-76] Therefore, PA/exercise or sports that are attractive to and feasible for the wider population, such as running, need to be identified to promote PA/exercise and health during the winter. Cross-country skiing, as well as running and hiking, is a potential PA that can be taken up by individuals to overcome deficits in PA during winter.

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Table 1. Examples of moderate- and vigorous-intensity aerobic physical activities

Moderate-intensity physical activity	Vigorous-intensity physical activity
Brisk walking	Jogging (> 10 minutes/mile)
Bicycling (< 10 miles/hour)	Running (≤ 10 minutes/mile)
General gardening	Bicycling (≥10 miles/hour)
Ballroom dancing	Swimming laps
Water aerobics	Tennis (singles)
Tennis (doubles)	Squash or racquetball
	Rowing
	Cross-country skiing

T
cardiovascular disease and mortality outcomes

Author, year of publication [reference]	Type of cross-country skiing exposure	No. of participants	No. of cases	Exposure (Risk comparison)	Endpoints	Reported risk estimates/findings
Karvonen, 1974	Long-term endurance	396	NR	Skiers vs general population	Life expectancy	Life expectancy of general male population was 2.8 years less than the skiers
Sarna, 1993	Cross-country skiing athletes	2,613		Elite skiers vs men from Finnish Defense Forces	Life expectancy; CVD mortality	Increased life expectancies and decreased CVD mortality in skiers
Grimsmo, 2011	Long-term endurance	122	CVD (21) Mortality (37)	Skiers vs general male population	CVD morbidity; mortality	Reduced CVD morbidity and mortality compared with general population
Hallmarker, 2015	Long-term endurance	708,604	2,047	Skiers with first-time stroke (n=1083) vs non-skiers with first-time stroke (n=4881)	Recurrent stroke; mortality	HR (95% CI) for recurrent stroke 0.96 (0.79-1.17) and mortality 0.70 (0.56-0.87)
Hallmarker, 2016	Long-term endurance	703,581	1,515	Skiers with first-time MI (n=1039) vs non-skiers with first-time MI (n=6053)	Recurrent MI and mortality	HR (95% CI) for recurrent MI mortality 0.80 (0.67-0.97)
Laukkanen, 2018	Leisure-time	2,087	1,028	Volume and duration of skiing for skiers vs non-skiers	All-cause mortality	HR (95% CI) for > 200 MET hrs per year 0.80 (0.67-0.96) and > 60 mins per week 0.82 (0.69-0.97)
Kontro, 2017	Cross-country skiing athletes	1,800	1,296	Cross-country skiers with age-matched brothers	All-cause mortality	HR (95% CI) for all-cause mortality in all athletes 0.75 (0.65-0.88) and for the endurance group 0.61 (0.45-0.82)
Hallmarker, 2018	Long-term endurance	399,630	Skiers (n=4784); non-skiers (n=9399)	Skiers vs non-skiers	Mortality, MI, or stroke	HR (95% CI) for mortality 0.52 (0.49-0.54), MI 0.56 (0.52-0.60), stroke 0.63 (0.58-0.67), and all outcomes 0.56 (0.54-0.58)
Laukkanen, 2019	Leisure-time	2,589	808	Volume and duration of skiing for skiers vs non-skiers	Acute MI	HR (95% CI) for > 200 MET hrs per year 0.81 (0.66-0.98) and > 60 mins per week 0.84 (0.69-1.02)

CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; MI, myocardial infarction; NR, not reported

Figure 1. Cumulative Kaplan-Meier curves for all-cause mortality during follow-up according to total volume and duration of cross-country skiing. Reproduced with permission from Scand J Med Sci Sports. 2018 Laukkanen et al[25]

Figure 2. Restricted cubic splines of the hazard ratios of all-cause mortality with total volume (METs per year) of cross-country skiing. Models were adjusted for age, body mass index, systolic blood pressure, high-density lipoprotein cholesterol, smoking status, alcohol consumption, prevalent coronary heart disease, history of diabetes mellitus, resting heart rate, and physical activity. Data adapted from Scand J Med Sci Sports. 2018 Laukkanen et al[25]

Figure 3. The reference group for all analyses includes nonrunners. All hazard ratios (HRs) were adjusted for baseline age (years), sex (not in sex-stratified analyses), examination year, smoking status (never, former, or current [not in smoking-stratified analyses]), alcohol consumption (heavy drinker or not [not in alcohol drinking-stratified analyses]), other physical activities except running (0, 1 to 499, or ≥500 MET-min/week), and parental cardiovascular disease (yes or no). Unhealthy was defined as the presence of 1 or more of the following health conditions: abnormal electrocardiogram (ECG), hypertension, diabetes, or hypercholesterolemia. Heavy alcohol drinking was defined as >14 and >7 drinks per week for men and women, respectively. BMI = body mass index. Reproduced from J Am Coll Cardiol 2014 Lee DC, et al.[67]

Figure 4. Cardiorespiratory fitness was estimated from the final treadmill speed and grade during the maximal exercise test in a subsample of 50,995 participants. All p values for linear trend across weekly running time were <0.001 after adjustment for age and sex (not in sex-stratified analyses). J Am Coll Cardiol 2014 Lee DC, et al.[67]

(weekly running time, distance, frequency, total amount, and speed). Participants were classified into 6 groups: nonrunners (reference group) and 5 quintiles of each running characteristic. All HRs were adjusted for baseline age (years), sex, examination year, smoking status (never, former, or current), alcohol consumption (heavy drinker or not), other physical activities except running (0, 1 to 499, or ≥500 MET-minutes/week), and parental history of cardiovascular disease (yes or no). All p values for HRs across running characteristics were <0.05 for all-cause and cardiovascular mortality except for running frequency of ≥6 times/week (p = 0.11) and speed of <6.0 miles/h (p = 0.10) for cardiovascular mortality. J Am Coll Cardiol 2014 Lee DC, et al.[67]

Figure 6. Hazard ratios of all-cause and cardiovascular disease (CVD) mortality by weekly running time, distance, frequency, and total amount. Participants were classified into 8 groups: nonrunners and 5 quintiles of each running dose (Q1 to Q5) with the last quintile (Q5) additionally categorized into 3 tertiles (Q5-T1, Q5-T2, and Q5-T3) using larger markers (7 groups for running frequency because of limited numbers in ≥ 7 times/wk). All hazard ratios were adjusted for baseline age (years), sex, examination year, smoking status (never, former, or current), alcohol consumption (heavy drinker or not), other physical activities except running (0, 1-499, or ≥500 metabolic equivalent task minutes per week [MET-min/wk]), and parental CVD (yes or no). The number of participants (number of all-cause deaths) were 42,121 (2857), 2710 (110), 2584 (116), 2505 (103), 2647 (112), 850 (33), 822 (30), and 898 (52) in the corresponding 8 running time groups from nonrunners to Q5-T3; 42,121 (2857), 2626 (105), 2473 (120), 2961 (123), 2218 (92), 885 (36), 1027 (40), and 826 (40) in running distance; 42,121 (2857), 2757 (62), 3076 (105), 2817 (131), 2500 (143), 1215 (66), and 651 (49) in running frequency; and 42,121 (2857), 2609 (109), 2598 (122), 2558 (116), 2626 (105), 863 (31), 886 (30), and 876 (43) in total running amount. The number of participants (number of CVD deaths) were 40,319 (1055), 2628 (28), 2501 (33), 2435 (33), 2567 (32), 827 (10), 801 (9), and 863 (17) in the corresponding 8 running time groups from nonrunners to Q5-T3; 40,319 (1055), 2550 (29), 2386 (33), 2874 (36), 2156 (30), 858 (9), 1001 (14), and 797 (11) in running distance; 40,319 (1055), 2714 (19),

2531 (31), 2508 (32), 2477 (35), 2553 (32), 842 (10), 864 (8), and 847 (14) in total running amount. The bars indicate 95% CIs, and hazard ratios appear next to the bars. Reproduced with permission from Mayo Clin Proc 2016 Lee DC et al.[19]

Figure 7. Proposed pathogenesis of cardiomyopathy in endurance athletes. BNP = B-type natriuretic peptide; CK-MB = creatine kinase MB; LV = left ventricle; RA = right atrium; RV = right ventricle; SCD = sudden cardiac death. Reproduced with permission from Mayo Clin Proc 2012. Reproduced with permission from Mayo Clin Proc O'Keefe JH et al.[70]

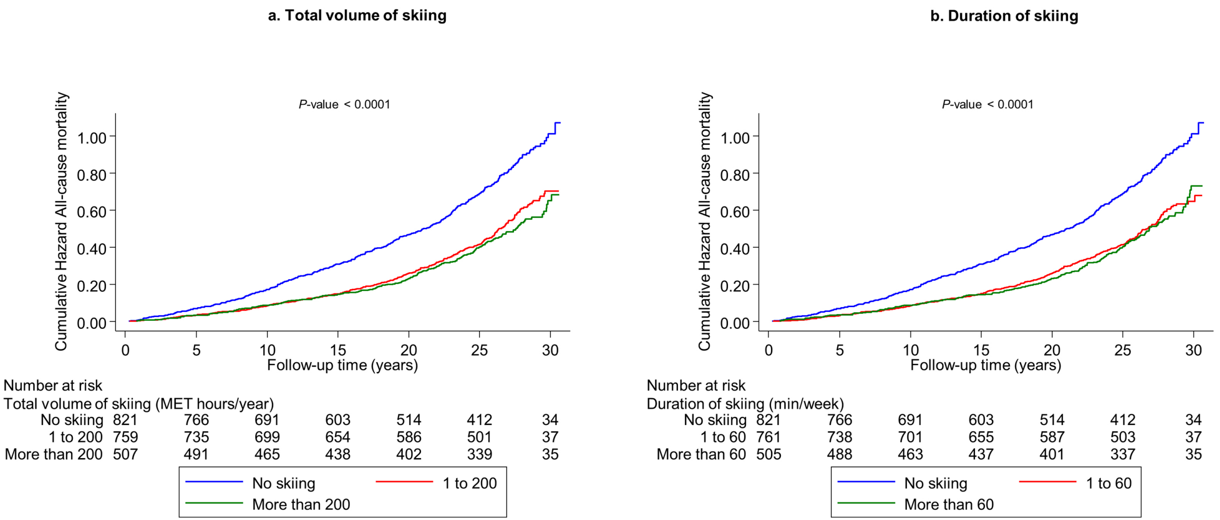

a. Total volume of skiing
P-value < 0.0001
Cumulative Hazard All-cause mortality
1.00
0.80
0.60
0.40
0.20
0.00
0 5 10 15 20 25 30
Follow-up time (years)
Number at risk
Total volume of skiing (MET hours/year)
No skiing 821 766 691 603 514 412 34
1 to 200 759 735 699 654 586 501 37
More than 200 507 491 465 438 402 339 35
No skiing
1 to 200
More than 200
b. Duration of skiing
P-value < 0.0001
Cumulative Hazard All-cause mortality
1.00
0.80
0.60
0.40
0.20
0.00
0 5 10 15 20 25 30
Follow-up time (years)
Number at risk
Duration of skiing (min/week)
No skiing 821 766 691 603 514 412 34
1 to 60 761 738 701 655 587 503 37
More than 60 505 488 463 437 401 337 35
No skiing
1 to 60
More than 60

Figure 1

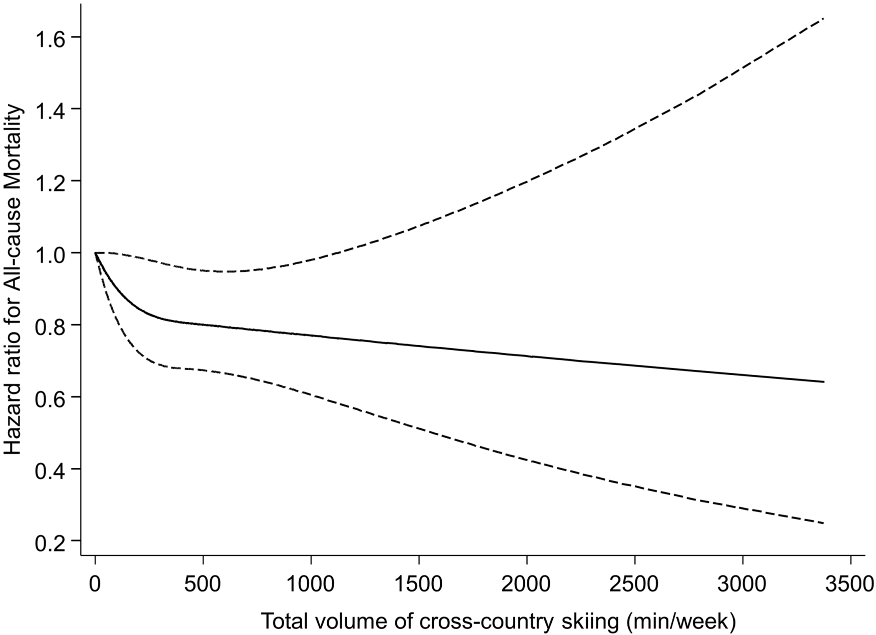

Hazard ratio for All-cause Mortality
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
500
1000
1500
2000
2500
3000
3500
Total volume of cross-country skiing (min/week)

Figure 2

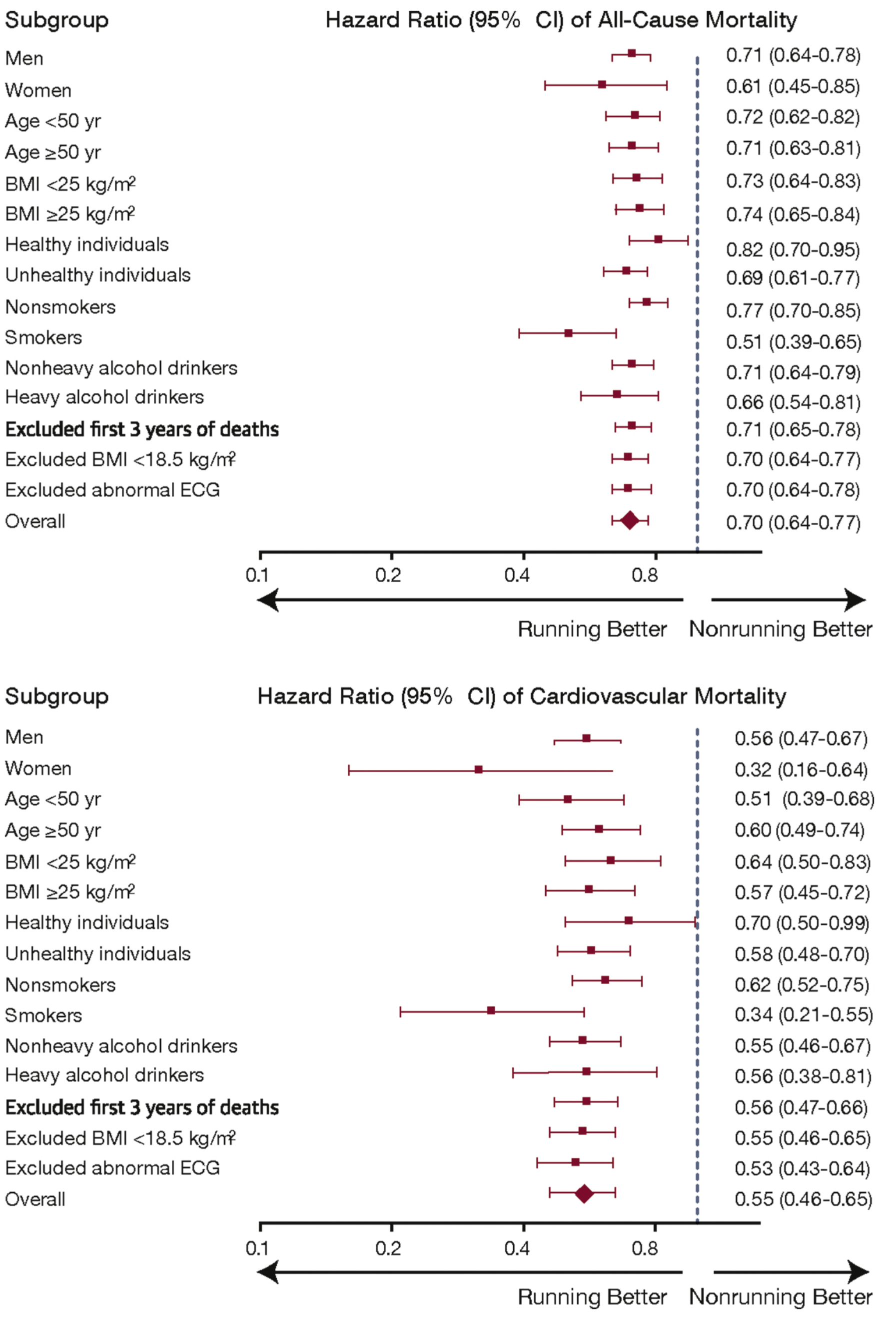
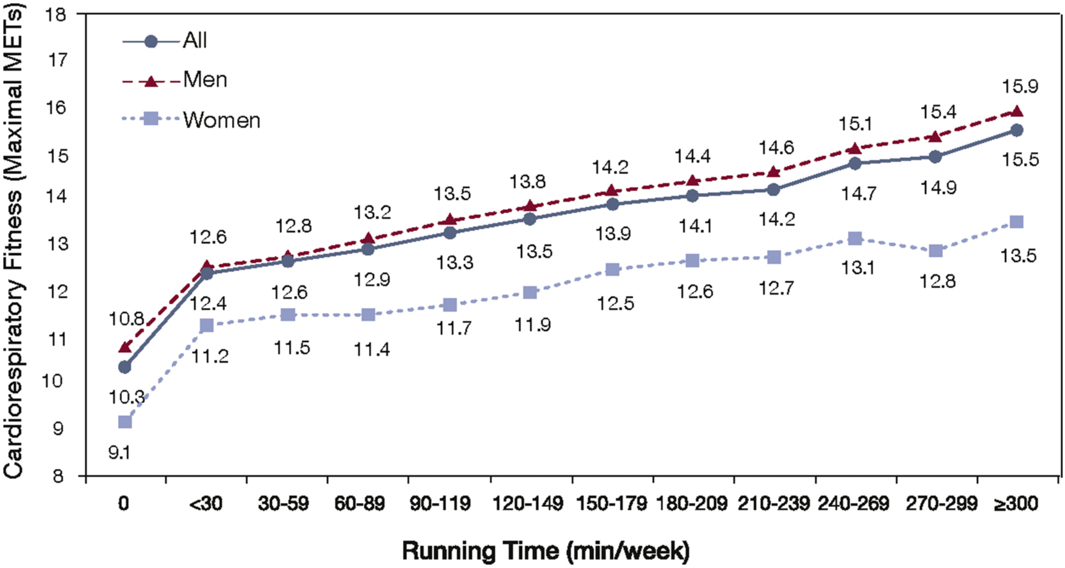

Subgroup
Hazard Ratio (95% CI) of All-Cause Mortality
Men 0.71 (0.64-0.78)
Women 0.61 (0.45-0.85)
Age <50 yr 0.72 (0.62-0.82)
Age ≥50 yr 0.71 (0.63-0.81)
BMI <25 kg/m2 0.73 (0.64-0.83)
BMI ≥25 kg/m2 0.74 (0.65-0.84)
Healthy individuals 0.82 (0.70-0.95)
Unhealthy individuals 0.69 (0.61-0.77)
Nonsmokers 0.77 (0.70-0.85)
Smokers 0.51 (0.39-0.65)
Nonheavy alcohol drinkers 0.71 (0.64-0.79)
Heavy alcohol drinkers 0.66 (0.54-0.81)
Excluded first 3 years of deaths 0.71 (0.65-0.78)
Excluded BMI <18.5 kg/m2 0.70 (0.64-0.77)
Excluded abnormal ECG 0.70 (0.64-0.78)
Overall 0.70 (0.64-0.77)
0.1
0.2
0.4
0.8
Running Better
Nonrunning Better
Subgroup
Hazard Ratio (95% CI) of Cardiovascular Mortality
Men 0.56 (0.47-0.67)
Women 0.32 (0.16-0.64)
Age <50 yr 0.51 (0.39-0.68)
Age ≥50 yr 0.60 (0.49-0.74)
BMI <25 kg/m2 0.64 (0.50-0.83)
BMI ≥25 kg/m2 0.57 (0.45-0.72)
Healthy individuals 0.70 (0.50-0.99)
Unhealthy individuals 0.58 (0.48-0.70)
Nonsmokers 0.62 (0.52-0.75)
Smokers 0.34 (0.21-0.55)
Nonheavy alcohol drinkers 0.55 (0.46-0.67)
Heavy alcohol drinkers 0.56 (0.38-0.81)
Excluded first 3 years of deaths 0.56 (0.47-0.66)
Excluded BMI <18.5 kg/m2 0.55 (0.46-0.65)
Excluded abnormal ECG 0.53 (0.43-0.64)
Overall 0.55 (0.46-0.65)
0.1
0.2
0.4
0.8
Running Better
Nonrunning Better

Figure 3


Cardiorespiratory Fitness (Maximal METs)
Running Time (min/week)
All
Men
Women
18
17
16
15
14
13
12
11
10
9
8
0
<30
30-59
60-89
90-119
120-149
150-179
180-209
210-239
240-269
270-299
≥300
10.8
12.6
12.8
13.2
13.5
13.8
14.2
14.4
14.6
15.1
15.4
15.9
10.3
12.4
12.6
12.9
13.3
13.5
13.9
14.1
14.2
14.7
14.9
15.5
9.1
11.2
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12.5
12.6
12.7
13.1
12.8
13.5

Figure 4

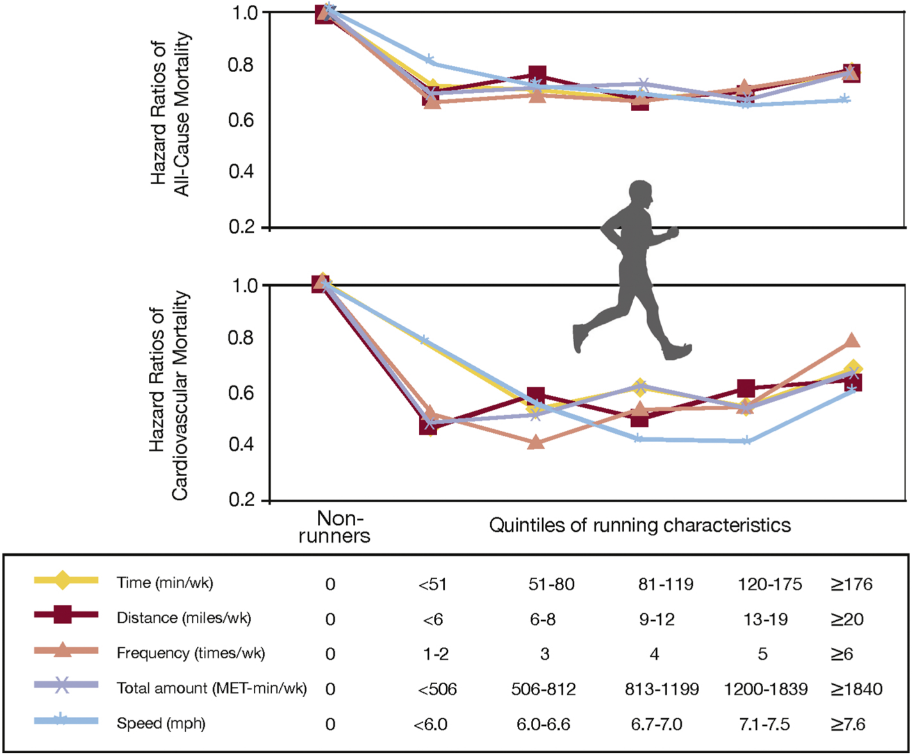
Hazard Ratios of All-Cause Mortality
1.0
0.8
0.6
0.4
0.2
Hazard Ratios of Cardiovascular Mortality
1.0
0.8
0.6
0.4
0.2
Non-runners
Quintiles of running characteristics
Time (min/wk) 0 <51 51-80 81-119 120-175 ≥176
Distance (miles/wk) 0 <6 6-8 9-12 13-19 ≥20
Frequency (times/wk) 0 1-2 3 4 5 ≥6
Total amount (MET-min/wk) 0 <506 506-812 813-1199 1200-1839 ≥1840
Speed (mph) 0 <6.0 6.0-6.6 6.7-7.0 7.1-7.5 ≥7.6

Figure 5

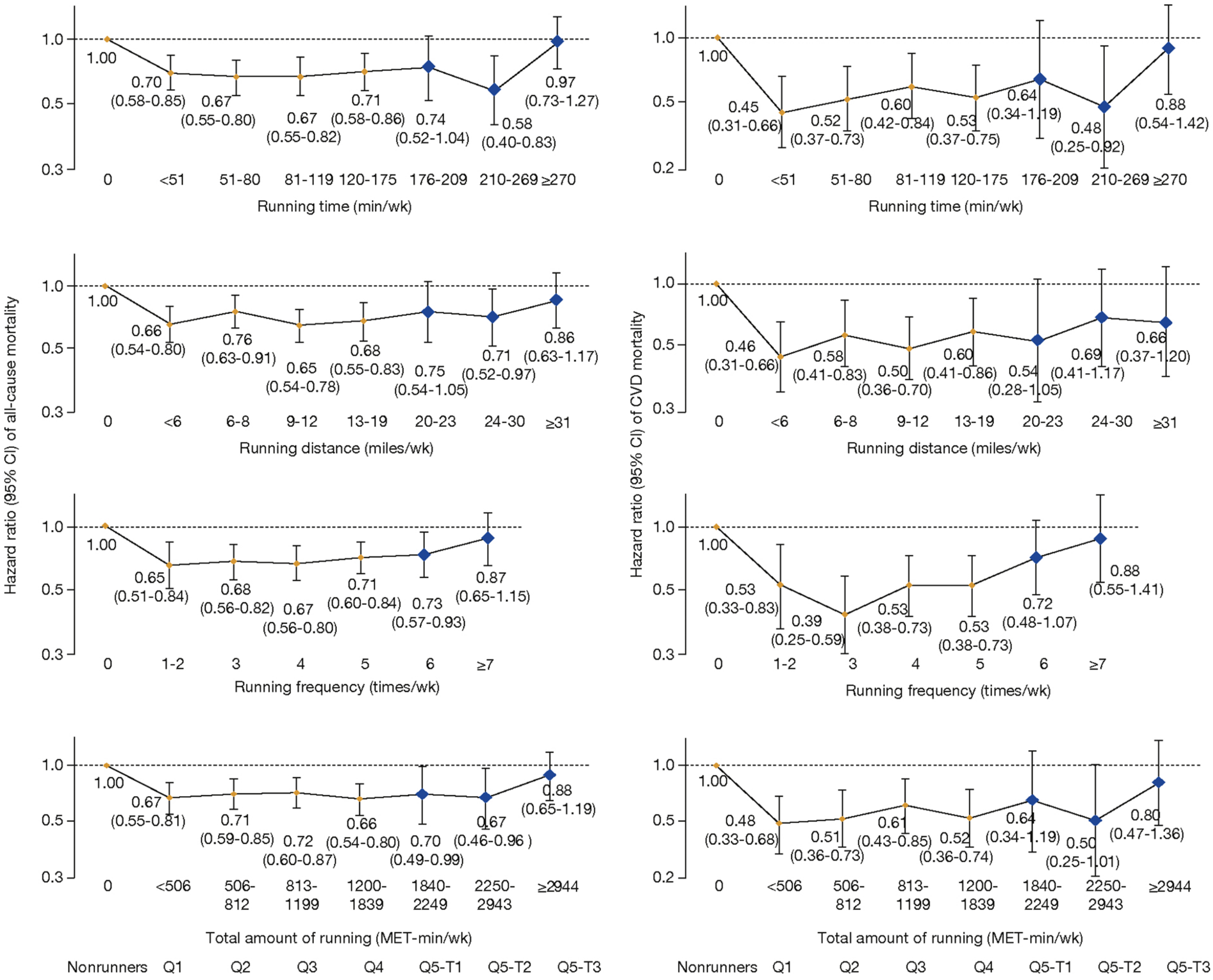
Hazard ratio (95% CI) of all-cause mortality
Hazard ratio (95% CI) of CVD mortality
1.0
0.5
0.3
0.2
1.00
0.70 (0.58-0.85)
0.67 (0.55-0.80)
0.67 (0.55-0.82)
0.71 (0.58-0.86)
0.74 (0.52-1.04)
0.58 (0.40-0.83)
0.97 (0.73-1.27)
0 <51 51-80 81-119 120-175 176-209 210-269 ≥270
Running time (min/wk)
0.45 (0.31-0.66)
0.52 (0.37-0.73)
0.60 (0.42-0.84)
0.53 (0.37-0.75)
0.64 (0.34-1.19)
0.48 (0.25-0.92)
0.88 (0.54-1.42)
0.66 (0.54-0.80)
0.76 (0.63-0.91)
0.65 (0.54-0.78)
0.68 (0.55-0.83)
0.75 (0.54-1.05)
0.71 (0.52-0.97)
0.86 (0.63-1.17)
0 <6 6-8 9-12 13-19 20-23 24-30 ≥31
Running distance (miles/wk)
0.46 (0.31-0.66)
0.58 (0.41-0.83)
0.50 (0.36-0.70)
0.60 (0.41-0.86)
0.54 (0.28-1.05)
0.69 (0.41-1.17)
0.66 (0.37-1.20)
0.65 (0.51-0.84)
0.68 (0.56-0.82)
0.67 (0.56-0.80)
0.71 (0.60-0.84)
0.73 (0.57-0.93)
0.87 (0.65-1.15)
0 1-2 3 4 5 6 ≥7
Running frequency (times/wk)
0.53 (0.33-0.83)
0.39 (0.25-0.59)
0.53 (0.38-0.73)
0.53 (0.38-0.73)
0.72 (0.48-1.07)
0.88 (0.55-1.41)
0.67 (0.55-0.81)
0.71 (0.59-0.85)
0.72 (0.60-0.87)
0.66 (0.54-0.80)
0.70 (0.49-0.99)
0.67 (0.46-0.96)
0.88 (0.65-1.19)
0 <506 506-812 813-1199 1200-1839 1840-2249 2250-2943 ≥2944
Total amount of running (MET-min/wk)
Nonrunners Q1 Q2 Q3 Q4 Q5-T1 Q5-T2 Q5-T3
0.48 (0.33-0.68)
0.51 (0.36-0.73)
0.61 (0.43-0.85)
0.52 (0.36-0.74)
0.64 (0.34-1.19)
0.50 (0.25-1.01)
0.80 (0.47-1.36)

Figure 6

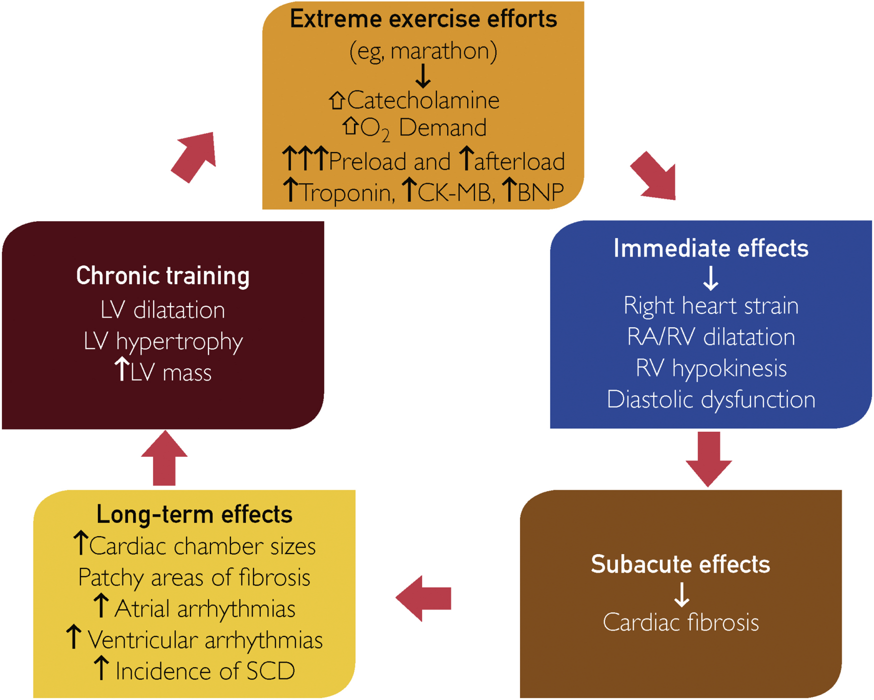
Extreme exercise efforts
(eg, marathon)
↓
⇧Catecholamine
⇧O_2 Demand
↑↑↑Preload and ↑afterload
↑Troponin, ↑CK-MB, ↑BNP
Immediate effects
↓
Right heart strain
RA/RV dilatation
RV hypokinesis
Diastolic dysfunction
Subacute effects
↓
Cardiac fibrosis
Long-term effects
↑Cardiac chamber sizes
Patchy areas of fibrosis
↑ Atrial arrhythmias
↑ Ventricular arrhythmias
↑ Incidence of SCD
Chronic training
LV dilatation
LV hypertrophy
↑LV mass

Figure 7