Walking and Running Produce Similar Reductions in Cause-Specific Disease Mortality in Hypertensives

Paul T. Williams

Abstract—To test prospectively in hypertensives whether moderate and vigorous exercise produces equivalent reductions in mortality, Cox-proportional hazard analyses were applied to energy expenditure (metabolic equivalents hours/d [METh/d]) in 6973 walkers and 3907 runners who used hypertensive medications at baseline. A total of 1121 died during 10.2-year follow-up: 695 cardiovascular disease (International Classification of Diseases, Tenth Revision [ICD10] I00–99; 465 underlying cause and 230 contributing cause), 124 cerebrovascular disease, 353 ischemic heart disease (ICD10 I20–25; 257 underlying and 96 contributing), 122 heart failure (ICD10 I50; 24 underlying and 98 contributing), and 260 dysrhythmias (ICD10 I46–49; 24 underlying and 236 contributing). Relative to <1.07 METh/d, running or walking 1.8 to 3.6 METh/d produced significantly lower all-cause (29% reduction; 95% confidence interval [CI], 17%–39%; P = 0.0001), cardiovascular disease (34% reduction; 95% CI, 20%–46%; P = 0.0001), cerebrovascular disease (55% reduction; 95% CI, 27%–73%; P = 0.001), dysrhythmia (47% reduction; 95% CI, 27%–62%; P = 0.0001), and heart failure mortality (51% reduction; 95% CI, 21%–70%; P = 0.003), as did ≥3.6 METh/d with all-cause (22% reduction; 95% CI, 6%–35%; P = 0.005), cardiovascular disease (36% reduction; 95% CI, 19%–50%; P = 0.0002), cerebrovascular disease (47% reduction; 95% CI, 6%–71%; P = 0.03), and dysrhythmia mortality (43% reduction; 95% CI, 16%–62%; P = 0.004). Diabetes mellitus and chronic kidney disease mortality also decreased significantly with METh/d. All results remained significant when body mass index adjusted. Merely meeting guideline levels (1.07–1.8 METh/d) did not significantly reduced mortality. The dose-response was significantly nonlinear for all end points except diabetes mellitus, and cerebrovascular and chronic kidney disease. Results did not differ between running and walking. Thus, walking and running produce similar reductions in mortality in hypertensives. (Hypertension. 2013;62:00-00.) • Online Data Supplement

Key Words: cardiovascular diseases • diabetes mellitus, type 2 • exercise • hypertension • renal insufficiency, chronic

Hypertension increases the risk for stroke, ischemic heart disease (IHD), and all-cause mortality.1 Physical activity reduces the risk for these conditions, which may be, in part, because of reductions in blood pressure.2 A recent systematic review3 of 6 prospective cohort studies of hypertensives4–9 concluded that physical activity significantly decreases both all-cause and cardiovascular disease (CVD) mortality. In fact, several of these studies suggested that the risk reductions could be even greater for hypertensives than normotensives.3,5

Although hypertensives clearly benefit from physical activity, the particulars of the benefit are poorly understood, including the dose-response, the effect of intensity, and the specific diseases affected. The 6 hypertensive cohorts previously reported on were all general purpose4–9 (ie, designed to relate a variety of variables to disease). As such, their most physically active groups were often not really very active nor were their activities well quantified (eg, ≥30 minutes of moderate to vigorous exercise more than once a week,6,8 regular vigorous exercise8 or sports,9 or vigorous exercise >3×/wk7), and, therefore, the cohorts provide little insight into the optimal exercise dose. None of these studies compared the benefits of moderate versus vigorous exercise. Their end points included all-CVD,4,5,7–9 IHD,8,9 myocardial infarction,6 and cerebrovascular disease,6,9 while ignoring heart failure, cardiac dysrhythmia, and hypertensive heart disease. Hypertensives are also at increased risk for diabetes mellitus and renal failure,1 and the effects of exercise dose and intensity on these conditions also warrant investigation.

The National Runners’ and Walkers’ Health Studies10–18 are the only large prospective cohorts designed specifically to assess the health benefits of exercise. Their advantages over cohorts of a more general purpose include (1) greater statistical power because of the large sample size and broad activity range, (2) knowledgeable subjects committed to regular exercise regimens, (3) focus on specific exercises that are largely identical except for intensity, and (4) use of distance to calculate exercise energy expenditure, which has been shown to be superior to time-based calculations.13–15 More than 10000

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hypertensive medication users from these cohorts were used to test whether the dose-response relationship between exercise and mortality (1) is nonlinear; (2) differs significantly between running and walking; and (3) affects specific CVD diagnoses, diabetes mellitus, and chronic kidney disease (CKD).

Materials and Methods
Detailed descriptions of the Methods and Materials are presented in the online-only Data Supplement. The National Death Index provided mortality surveillance through 2008 for the National Runners’ and Walkers’ Health Studies.10–18 The runners reported the usual miles run per week, and the walkers reported usual miles walked per week and usual pace (minutes per mile). These values were used to estimate energy expenditure in metabolic equivalents (MET),13–15 where 1 MET is the energy expended while sitting at rest (3.5 mL O$_2$ kg$^{-1}$·min$^{-1}$).19 The study protocol was reviewed and approved by the Human Subjects Committee at Lawrence Berkeley National Laboratory for the protection of human subjects, and all subjects provided a signed statement of informed consent.

Statistics
Cox-proportional hazard analyses (STATA version 11.1, StataCorp, College Station, TX) were used to test whether all-cause mortality, mortality from major CVD (International Classification of Disease version 9 codes 390–459; version 10 code 100–99),20 IHD (International Classification of Diseases, Ninth Revision [ICD9] 410–414, ICD10 I20–25), heart failure (ICD9 428, ICD10 I50), dysrhythmia (ICD9 427, ICD10 I46–49), cerebrovascular disease (ICD9 430–438, ICD10 I60–69), hypertensive heart disease (ICD9 401–404, ICD10 I10–13), diabetes mellitus (ICD9 250, ICD10 E10–14), and CKD (ICD9 585, ICD10 N18) were different between hypertensive medication users and nonusers, and within the users whether they were significantly related to METs/d run or walked when adjusted. Underlying and contributing (nonunderlying entity axis diagnosis) causes of death were obtained from the National Death Index mortality surveillance. Results are presented as hazard ratios, their fold increases in risk, and their percentage reductions in the risk (calculated as $100\times$[hazard ratio−1]) for 7 categories of walking or running energy expenditure: falling short of the current physical activity recommendations for health (<450 MET minutes/wk=1.07 MET/d), meeting the recommendations (450–750 MET minutes/wk=1.07–1.18 MET/d), exceeding the recommendations by 1- to 2-fold (1.8–3.6 MET/d), 2- to 3-fold (3.6–5.4 MET/d), 3- to 4-fold (5.4–7.2 MET/d), 4- to 5-fold (7.2–9.0 MET/d), and ≥5-fold (9.0+ MET/d).

Results
Of the original 40670 walkers and 111 080 runners surveyed at baseline with complete body mass index (BMI) and other data, there were 6973 walkers (17.15%) and 3907 runners (3.52%) who reported taking blood pressure medications on their baseline questionnaires (10880 total subjects). As a group, the blood pressure medication users tended to be older (mean±SD, 58.5±12.04 versus 43.6±12.11 years), include more blacks (5.33% versus 1.75%), and were more likely to walk than run (64.1% versus 23.93%) than nonusers. Table S1 in the online-only Data Supplement presents the characteristics of the sample.

There were 1121 deaths during the hypertensives’ 10.2-year average follow-up, including 695 CVD-related (465 underlying cause and 230 contributing cause), 124 cerebrovascular disease–related (57 underlying and 67 contributing), 353 IHD-related (257 underlying and 96 contributing), 122 heart failure–related (24 underlying and 98 contributing), 260 dysrhythmia-related (24 underlying and 236 contributing), 99 diabetes mellitus–related (28 underlying and 71 contributing), and 28 CKD–related deaths (6 underlying and 22 contributing). Compared with the 140870 nonusers of hypertensive medications in the total original cohort of runner and walkers, hypertensives were at significantly higher risk for mortality from all-causes (30.5% higher; 95% confidence interval [CI], 21.0%–40.8%; $P=10^{-10}$), and mortality related to CVD (47.5% higher; 95% CI, 33.5%–62.8%; $P=10^{-10}$), IHD (62.6% higher; 95% CI, 40.9%–87.6%; $P=0.009$), cerebrovascular disease (48.3% higher; 95% CI, 18.2%–86.1%; $P=0.0008$), cardiac dysrhythmia (44.6% higher; 95% CI, 23.4%–69.3%; $P=10^{-3}$), heart failure (48.2% higher; 95% CI, 17.0%–87.7%; $P=0.0006$), hypertensive heart disease (188.4% higher; 95% CI, 131.9%–258.5%; $P=10^{-15}$), and diabetes mellitus (34.2% higher; 95% CI, 0.5%–79.2%; $P=0.05$) when adjusted for age, sex, education, race, diet, aspirin use, prior heart attack, diabetes mellitus, and cholesterol medication, smoking, and exercise.

All-Cause Mortality
Total mortality significantly increased in association with smoking ($P=0.02$), prior heart attack ($P=10^{-7}$), greater alcohol intake ($P=0.05$), and diabetes mellitus medication use ($P<10^{-4}$). Figure 1 shows a leveling off of the risk reduction $>1.8$ to 3.6 METs/d (average 2.7 METs/d for the interval). Although the risk reductions were not significant for $7.2$ to $9.0$ METs/d and for $>9.0$ METs/d, these intervals each included <3% of the total sample. The shape of the graph, and the fact that for all CVD-related mortality there was no significant difference in risk among higher energy expenditures, led us to pool energy expenditure ≥3.6 METs for subsequent analyses. Table 1 shows that all-cause mortality decreased a nonsignificant 9%
by meeting the current exercise guidelines (1.07–1.8 METh/d) compared with falling short of them (<1.07 METh/d), and decreased 29% by exceeding the guidelines by 1- to-2 fold (1.8–3.6 METh/d). Energy expenditure ≥3.6 METh/d did not seem to further reduce all-cause mortality vis-à-vis 1.8 to 3.6 METh/d.

**CVD-Related Mortality**

Table 1 shows that the results were similar for CVD as an underlying cause, and total CVD-related deaths. In addition to age and sex, the risk factors for all CVD-related deaths were smoking (P<10⁻⁴), a prior heart attack (P<10⁻⁶), and diabetes mellitus medication use (P<10⁻⁷). There was a 34% decrease in total CVD-related mortality by exercising between 1.8 and 3.6 METh/d, which persisted for greater energy expenditures. Adjustment for BMI did not affect the results.

Table 2 presents more detailed analyses of CVD end points. Cerebrovascular disease–related mortality declined 19% for 1.07 to 1.8 METh/d, 55% for 1.8 to 3.6 METh/d,
and remained relatively constant thereafter. Heart failure–related and dysrhythmia-related mortality both showed ≈50% reductions in risk for 1.8 to 3.6 and ≥3.6 MET/h/d. The reduction in IHD-related mortality per MET/h/d was not as great as for these other CVD end points. Hypertensive heart disease–related mortality was unrelated to exercise energy expenditure. Adjustment for BMI had little effect on the hazard ratios of Table 2. Figure 2 shows there was a 50% decrease in the risks by 1.8 MET/h/d for all cerebrovascular disease, heart failure, and dysrhythmia-related mortality, which continued through >3.6 MET/h/d. CVD-related deaths, exclusive of these end points, showed no significant relationship to MET/h/d. Nearly identical results were obtained when the analyses were restricted to the 115 deaths that listed cerebrovascular disease, heart failure, and dysrhythmia as their underlying cause.

**Diabetes Mellitus**

On average, each MET/h/d increment in energy expenditure was associated with a 19.1% reduction in the risk for diabetes mellitus–related mortality (95% CI, 6.7%–30.5%; *P* = 0.003), which persisted when adjusted for BMI (16.4% reduction per MET/h/d; 95% CI, 3.6%–28.6%; *P* = 0.01).

**CKD and Other Mortality**

The risk for all CKD-related mortality decreased 25.4% per MET/h/d (95% CI, 4.8%–44.2%; *P* = 0.02 for a reduced model that included only significant covariates, *P* = 0.06 for the full model). The significance of MET/h/d in the reduced model remained significant when adjusted for BMI (24.2% reduction per MET/h/d; 95% CI, 3.0%–43.6%; *P* = 0.03). Table 1 shows that the 409 deaths that did not include CVD, diabetes mellitus, or CKD as an underlying or contributing causes were not significantly related to exercise energy expenditure.

**Nonlinear Dose-Response**

A significant coefficient *β* in the regression model α(MET/h/d)*β*(MET/h/d)*2* provided proof that dose-response relationship between mortality and exercise was nonlinear for total (α = 0.005), CVD- (α = 0.002), IHD- (α = 0.02), dysrhythmia- (α = 0.03), and heart failure–related mortality (α = 0.05), but not for cerebrovascular disease (α = 0.36), diabetes mellitus (α = 0.59), or CKD (α = 0.36). This represents nonlinearity in excess of that already implied by the proportional hazard model.

**Running Versus Walking**

Being a runner or a walker did not significantly affect the risk reduction for 1.8 to 3.6 MET/h/d, or ≥3.6 MET/h/d, for all CVD-related deaths (*P* = 0.24 and *P* = 0.37, respectively). CVD as the underlying cause (*P* = 0.42 and *P* = 0.24, respectively), all IHD-related deaths (*P* = 0.48 and *P* = 0.46, respectively), IHD as underlying cause (*P* = 0.09 and *P* = 0.07, respectively), and all deaths related to cerebrovascular disease (*P* = 0.93 and *P* = 0.58, respectively), heart failure (*P* = 0.23 and *P* = 0.51, respectively), and dysrhythmias (*P* = 0.95 and *P* = 0.62, respectively). Exercise mode also did not significantly affect the per MET/h/d declines in diabetes mellitus–related (*P* = 0.94) or CDK-related deaths (*P* = 0.46).

**Discussion**

Those in our study who took blood pressure medication remained at 48% greater risk for CVD compared with cohort members not taking medications. We did not find that the current exercise guidelines were adequate to significantly reduce their CVD mortality. Most of the reduction in mortality was achieved by exercising slightly more, between 1.8 and 3.6 MET/h/d. At that level, the hypertensives’ CVD risks were reduced to those of the sedentary nonusers of hypertensive medication in our cohort. We also found that the risk for 2 other fatal conditions that hypertensives are prone to developing, diabetes mellitus and CKD, declined with exercise. Running 1 km/d expends ≈1 MET/h/d, so 3.6 MET/h/d corresponds to running 15.1 miles/wk. Walking and running seemed to produce comparable risk reductions provided the energy expenditure was the same; however, one must go ≈50% further and take about twice as long to expend the same amount of energy by walking briskly as by running a 12-minute mile.

Our analyses suggest that exercise reduces the hypertensive’s risks for cerebrovascular disease, heart failure, and cardiac dysrhythmias. There were too few deaths for analyzing these conditions separately as underlying causes of death. Only 20% of the 122 heart failures, and 9% of the 260 cardiac arrhythmias, listed these conditions as the underlying cause. However, it does not seem from our analyses that the underlying cause of death provides greater specificity in defining the health benefits of exercise than all related mortality. Specifically, our results did not suggest any differences between using the 465 deaths that specifically identified CVD as the underlying cause and all 695 CVD-related causes of death. Moreover, Figure 2 shows that the risk reductions for the 115 underlying cerebrovascular disease, heart failure, and cardiac dysrhythmias deaths were entirely consistent with
those of the 428 total deaths listing these conditions are contributing or underlying causes.

The exercise-induced risk reductions we observed could be, in part, because of additional improvement in blood pressure control over medication alone. We have previously shown progressive, incremental reductions in both systolic and diastolic blood pressure with greater weekly running distance. There is a doubling in both IHD and cerebrovascular disease risk for every 20 mmHg increment in systolic blood pressure >115 mmHg or for every 10 mmHg increment in diastolic blood pressure >75 mmHg. Physical activity also decreases other CVD risk factors that would otherwise compound the risk from hypertension. For many end points reported here, the risk reductions were greater than generally reported by others. For example, meta-analyses of other population studies suggest that physical activity reduces stroke risk by ≈50%, which is less than the ≈50% risk reduction we observed. The risk reduction may be greater for hypertensives, or the difference could reflect the technical advantages of using runners, walkers, and a distance-based metric for energy estimation.

Heart Failure

Our data showed that exercise significantly reduced the risk of heart failure, consistent with reports from the Physician’s Health Study, Finnish men and women, and National Health and Nutrition Examination Survey (NHANES) I. The condition occurs when the heart is unable to provide adequate blood flow for tissue perfusion and metabolism. Heart failure is preceded by hypertension in ≈90% of patients and often develops from antecedent coronary heart disease. Therefore, in these hypertensives, exercise seemed to prevent or delay the cardiac remodeling that leads to heart failure.

Dysrhythmias

We also demonstrated a substantial decline in cardiac dysrhythmia with exercise that seemed to be equivalent for walkers and runners. This agrees with our recent report showing significant declines in incident physician-diagnosed cardiac arrhythmias by running and walking, whereas disagreeing with some others. The Physicians Health Study reported a 53% greater risk in men who jogged 5 to 7 days/wk vis-à-vis nonjoggers. In contrast, the Cardiovascular Health Study reported a 48% lower risk in men and women who walked ≥60 blocks/wk at >3 mph as compared with those who walked ≤4 blocks/wk at ≤2 mph.

Diabetes Mellitus

Hypertensives are 2.5-fold more likely to develop diabetes mellitus within 5 years than normotensives. Hypertension may arise in part from insulin resistance; indeed, treating insulin resistance often lowers blood pressure. Insulin resistance is associated with endothelium-dependent vasoconstriction, hyperglycemia-induced glycation of endogenous protein, increased inflammatory responses leading to vasculature damage, endothelial dysfunction, reduced peripheral capillary density, and increased blood pressure. The significant reduction in diabetes mellitus–related mortality we observed is consistent with our previous finding of equivalent risk reductions in incident nonfatal type 2 diabetes mellitus in runners and walkers.

Chronic Kidney Disease

Hypertension is both a risk factor and a consequence of chronic renal disease. Systemic elevated blood pressure leads to increased glomerular pressure, causing endothelial damage and fibrosis. Chronic renal disease activates the renin-angiotensin system, which raises blood pressure. Our analyses showed a 24.2% per MET/h/d reduction in chronic renal failure in hypertensives, independent of both diabetes mellitus and BMI.

Ischemic Heart Disease

As expected, IHD risk also declined with increasing exercise, although the effect seemed somewhat weaker than for other end points. Hypertension may increase IHD risk because coronary artery disease impedes myocardial oxygen supply. Exercise may compensate for the lack of oxygen via collateralization of coronary arteries. In addition, exercise may attenuate plaque progression in coronary arteries and prevent infarction via myocardial preconditioning. We found no association between MET/h/d run or walked and hypertensive heart disease, a condition that links arterial hypertension with left ventricular hypertrophy, myocardial fibrosis, and atherosclerotic coronary artery disease, and reduced exercise capacity.

Caveats

In these analyses, hypertensives were defined as self-identified users of hypertensive medications rather than being ascertained through the direct measurement of blood pressure, hence, some hypertensives not on medications will be incorrectly assigned to the nonhypertensive group. Although the design is prospective, and deaths occurring during the first year were excluded, we cannot rule out the possibility of reverse causality (ie, that the extent of subclinical disease could affect MET/h/d run or walked). Compared with age-matched normotensive controls, hypertensive patients are reported to have ≤30% lower exercise capacity because of lower stroke volume, lower peak heart rate during exercise, and lower maximum heart rate. However, we would expect this to have a greater effect on running than walking, which was not observed. We also note the risk of confounding by indication with respect to use of antihypertensive therapy. Our use of mortality end points precludes our being able to distinguish the effects of CVD prevention from improved survival. In particular, exercise might ameliorate the hypertensives’ greater risk for death after a myocardial infarction. We also caution that physician assignment of causes of death may be problematic; however, it is unclear how this could be influenced by MET/h/d of exercise. In addition, we note that, despite their use of hypertensive medication, the cohort is likely to be more educated, and somewhat healthier as indicated by the low smoking rates, than the usual clinic population. In particular, only 3.5% of the running population reported using hypertensive medication compared with 17% of the walkers, which may be only partly because of the older age of the walkers. There may be a genetic predisposition to running, that is, untrained rats selected over multiple generations for...
high-capacity running are able to run an 8.4-fold greater distance than rats selected for low-capacity running and have substantially better CVD risk factor levels, including 13% lower 24-hour blood pressure.43 However, it is not expected that the physiological effects of running and walking on CVD, diabetes mellitus, and CKD would differ between the current sample and the general population. Consistent with this notion, the per MET/h reductions in disease risk were the same in runners and walkers, despite their difference in the prevalence of hypertension. Finally, we do not wish to imply that only those that run or walk ≥1.8 MET/h derive benefit from exercise. Others have shown that even as little as 1 hour/wk of light-to-moderate intensity activity per day is associated with lower coronary heart disease risk in women over no regular exercise.44

Conclusions
Our results provide strong justification for encouraging hypertensives to exercise. Asymptomatic hypertensive patients are known to have significantly greater carotid intima media thickness, an indicator of atherosclerosis associated with future cardiovascular events, than age-matched normotensives.45 Although exercise is clearly beneficial in normotensive patients (theoretically at least) the same benefits might not apply to exercise in hypertensives. During exercise, hypertensive patients show a greater rise in blood pressure and a blunted decline in systemic vascular resistance than normotensives.46,47 Elevated systolic blood pressure during exercise is predictive of left ventricular hypertrophy, ≥1 vessel disease during coronary angiography, positive ischemic electrocardiographic findings, and CVD mortality.48 In our study, however, regular exercise significantly lowered the risk for a broad spectrum of diseases that hypertensives are at particular risk, including stroke, IHD, heart failure, diabetes, and CKD.

Perspectives
A total of 10,880 hypertensive medication users from the National Runners’ and Walkers’ Health Studies were used to test whether the dose-response relationship between exercise and mortality (1) is nonlinear; (2) differs significantly between running and walking; and (3) affects specific CVD diagnoses, diabetes mellitus, and CKD. Those in our study who took blood pressure medications remained at 60% greater risk for CVD compared with those not taking medications. We did not find that the current exercise guidelines were adequate to significantly reduce their CVD mortality. Most of the reduction in mortality was achieved by exercising slightly more, between 1.8 and 3.6 MET/h/d. At that level, the hypertensives’ CVD risks were reduced to those of sedentary normotensives. Specifically, the risks of cerebrovascular disease, heart failure, and dysrhythmias were each reduced between 40% and 50%. IHD risk also declined with increasing exercise, although the effect seemed somewhat weaker than for these other end points. We also found that the risk for 2 other fatal conditions that hypertensives are prone to developing, diabetes mellitus and CKD, declined with exercise. Walking and running seemed to produce comparable risk reductions, provided the energy expenditure was the same; however, one must go ≥50% further and take about twice as long to expend the same amount of energy by walking briskly as by running a 12-minute mile. For many end points reported here, the risk reductions were greater than generally reported by others, which may reflect the technical advantages of using runners, walkers, and a distance-based metric for energy estimation.

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Disclosures
None.

References
47. Novelties and Significance

**What Is New?**

- In hypertensives, running or walking an average of 2.7 metabolic equivalent hours/week (equivalent to running 18.5 km or 11.5 miles/wk) was associated with significantly lower all-causes (29% lower), cardiovascular disease (39%), stroke (55%), ischemic heart disease (29%), heart failure (51%), and dysrhythmia mortality (47%).
- Each kilometer run or walked per day was associated with a 19% reduction in diabetes mellitus and 25% reduction in chronic kidney disease mortality.
- The benefits of walking and running in hypertensives were the same, provided that the total energy expended was the same; however, the patient would need to go ~50% further and take twice as long to expend the same amount of energy by walking briskly as by running a 12-minute mile.

**What Is Relevant?**

- Getting hypertensive patients to exercise may be one of the single most important things they can do for their health.

**Summary**

Running and walking substantially reduce mortality risk in hypertensives.
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Walking and running produce similar reductions in cause-specific disease mortality in hypertensives

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Short title: Walking vs. running in hypertensives

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Expanded Materials and Methods

The National Death Index provided mortality surveillance through 2008 for three cohorts: the first and second National Runners’ Health Study cohorts (NRHS-I and NRHS-II) and the National Walkers’ Health Study (NWHS). NRHS-I was recruited between 1991 and 1994 (primarily 1993), while NRHS-II and NWHS were recruited primarily between 1998 and 2001 [1-9]. The three cohorts may be more accurately characterized as a single cohort that targeted runners and walkers, since all three used the same questionnaire (modified slightly for the different activities), the same sampling domain (subscription lists to running and walking publications, running and walking events), the same survey staff, and were funded by the same grants. The National Death Index uses probabilistic matching based on available information on phonetic name, sex, social security number, birth date, and race to match cause of death to state-supplied date and causes of death from death certificates [10]. It has shown to identify over 90% of decedents and to show discrepancy from nosologist assigned causes of death in 4% of cases [11].

Participants completed baseline questionnaires on exercise, height, body weight, body circumferences, diet, cigarette use, and history of disease. The runners reported the usual miles run per week, and the walkers reported usual miles walked per week and usual pace (minutes per mile). These values were used to estimate energy expenditure in metabolic equivalents (MET), where one MET is the energy expended while sitting at rest (3.5 ml O₂•kg⁻¹•min⁻¹) [12]. In walkers, MET/h walked was calculated by converting reported distances into durations (i.e., distance/mph), which were then multiplied by the MET value for the reported pace [4,6]. In runners, MET/h run was calculated as km run*1.02 MET/h km [5,6].
Statistics Two sample t-tests were used to compare the characteristics of the hypertensive medication users and non-users. Cox proportional hazard analyses (STATA version 11.1, StataCorp, College Station, TX) were used to test whether all cause mortality, and mortality from major cardiovascular disease (International Classification of Disease version 9 codes 390 to 459, version 10 code I00-99 [13]), ischemic heart disease (ICD9 410 –414, ICD10 I20-25), heart failure (ICD9 428, ICD10 I50), dysrhythmia (ICD9 427, ICD10 I46-49), cerebrovascular disease (ICD9 430 –438, ICD10 I60-69), hypertensive heart disease (ICD9 401-404, ICD10 I10-13), diabetes (ICD9 250, ICD10 E10-14), and chronic kidney disease (CKD, ICD9 585, ICD10 N18) were different between hypertensive medication users and non-users, and among users whether they were significantly related to METH/d run or walked when adjusted. Covariates included sex, baseline age (age and age^{2}), education, African-American ethnicity, smoking, prior heart attack, diabetes and cholesterol medication use, aspirin (tablets/day), intakes of red meat, fruit, and alcohol, and cohort effects (NRHS-I, NRHS-II, NWHS). The covariates were chosen for their observed or accepted associations with disease outcomes, and to control for any differences between cohorts. Underlying and contributing (entity axis) causes of death were obtained from the National Death Index mortality surveillance [10]. Results are presented as hazard ratios (HR), their fold increases in risk, and their percent reductions in the risk (calculated as 100*(HR-1)) for seven categories of walking or running energy expenditure: falling short of the current physical activity recommendations for health (<450 MET minutes per week =1.07 METH/d), meeting the recommendations (450 to 750 MET minutes per week =1.07 to 1.8 METH/d), exceeding the recommendations by 1- to 2-fold (1.8 to 3.6 METH/d), 2- to 3-fold (3.6-5.4 METH/d), 3 to 4-fold (5.4-7.2 METH/d), 4 to 5-fold (7.2-9.0 METH/d), and exceeding the recommendations by greater than or equal to 5-fold [12]. A quadratic
equation of METh/d run or walked was used to test for significant nonlinearity of each mortality-exercise relationship. Specifically, the significance of the coefficient “β” in the regression model “α(METh/d) + β(METh/d)^2 in Cox proportional hazard analyses was used to formally prove that the dose-response relationship between mortality and exercise was nonlinear. Deaths occurring within one year of the baseline survey were excluded.
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Table S1. Baseline characteristics (percent or mean±SD) of blood pressure medication users

<table>
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<tr>
<td>Female (%)</td>
<td>65.96</td>
<td>63.28</td>
<td>49.81</td>
<td>32.27</td>
</tr>
<tr>
<td>Runners (%)</td>
<td>17.63</td>
<td>13.28</td>
<td>33.90</td>
<td>69.24</td>
</tr>
<tr>
<td>African-American (%)</td>
<td>8.29</td>
<td>4.85</td>
<td>3.94</td>
<td>4.39</td>
</tr>
<tr>
<td>Cholesterol medication (%)</td>
<td>27.92</td>
<td>25.80</td>
<td>23.00</td>
<td>16.01</td>
</tr>
<tr>
<td>Diabetes medication (%)</td>
<td>13.68</td>
<td>9.77</td>
<td>6.71</td>
<td>3.44</td>
</tr>
<tr>
<td>Aspirin (tablets/day)</td>
<td>0.47±0.76</td>
<td>0.48±0.78</td>
<td>0.45±0.63</td>
<td>0.53±0.85</td>
</tr>
<tr>
<td>Prior heart attack (%)</td>
<td>11.23</td>
<td>10.34</td>
<td>8.40</td>
<td>6.64</td>
</tr>
<tr>
<td>Deaths (%)</td>
<td>14.49</td>
<td>11.94</td>
<td>8.43</td>
<td>7.58</td>
</tr>
<tr>
<td>CVD deaths-underlying (%)</td>
<td>6.30</td>
<td>4.98</td>
<td>3.19</td>
<td>3.23</td>
</tr>
<tr>
<td>CVD deaths-total related (%)</td>
<td>9.48</td>
<td>8.05</td>
<td>5.04</td>
<td>4.07</td>
</tr>
<tr>
<td>Energy expenditure (METH/d)</td>
<td>0.47±0.34</td>
<td>1.45±0.22</td>
<td>2.69±0.55</td>
<td>6.00±2.17</td>
</tr>
<tr>
<td>Follow-up (y)</td>
<td>9.31±1.83</td>
<td>9.39±1.70</td>
<td>10.27±2.57</td>
<td>11.60±3.12</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.00±12.80</td>
<td>61.03±11.67</td>
<td>58.76±11.49</td>
<td>54.57±11.03</td>
</tr>
<tr>
<td>Education (years)</td>
<td>14.95±2.73</td>
<td>15.34±2.77</td>
<td>15.54±2.72</td>
<td>15.80±2.78</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>5.49</td>
<td>2.94</td>
<td>2.63</td>
<td>1.90</td>
</tr>
<tr>
<td>Ex-smokers (%)</td>
<td>42.27</td>
<td>44.32</td>
<td>48.39</td>
<td>47.37</td>
</tr>
<tr>
<td>Alcohol (g/day)</td>
<td>6.28±13.79</td>
<td>7.98±13.53</td>
<td>9.68±15.47</td>
<td>12.62±19.19</td>
</tr>
<tr>
<td>Red meat (servings/ day)</td>
<td>0.46±0.40</td>
<td>0.42±0.38</td>
<td>0.41±0.40</td>
<td>0.36±0.36</td>
</tr>
<tr>
<td>Fruit (pieces/ day)</td>
<td>1.41±1.17</td>
<td>1.60±1.25</td>
<td>1.64±1.18</td>
<td>1.72±1.32</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>29.46±6.73</td>
<td>27.66±5.37</td>
<td>26.61±4.73</td>
<td>24.86±3.81</td>
</tr>
</tbody>
</table>