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Lower prevalence of hypertension, hypercholesterolemia, and diabetes in marathoners

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Abstract

Purpose—To test whether the prevalence of hypertension, hypercholesterolemia, and diabetes decline with marathon participation independent of annual running mileage.

Methods—Cross-sectional associations of self-reported medication use in 62,284 male and 45,040 female participants of the National Runners' Health Study adjusted for age, diet, alcohol, and annual distance run.

Results—31.7% of men and 29.1% of women reported 0.2 and 0.8 marathons/year, 8.6% of men and 4.4% of women between 1.0 and 1.8 marathons/year, and 3.8% of men and 1.5% of women reported averaging ≥ 2 marathons/year. The men's odds ratio per marathons/year run was 0.85 for anti-hypertensive ($P < 0.0001$), 0.87 for LDL-cholesterol lowering ($P = 0.002$), and 0.52 for anti-diabetic medication use ($P < 0.0001$). Compared to nonmarathoners, men who averaged 0.2–0.8 marathons/year had 13% lower odds for anti-hypertensive, 22% lower odds for LDL-cholesterol lowering, and 67% lower odds for anti-diabetic medication use. Marathon participation was also associated with lower LDL-cholesterol lowering and anti-diabetic medication use in women, but not when adjusted for annual distance run. Each additional hour required to complete their marathon had odds ratio of 1.31 and 1.22 for men's anti-hypertensive and LDL-cholesterol lowering medication use, and 2.01 for women's anti-diabetic medication use (all $P < 0.0001$). Among all runners (marathoners and nonmarathoners combined), prevalence in the use of all three medications decreased in association with the length of the longest usual run, independent of total annual mileage.

Conclusion—Prevalence of hypertension, hypercholesterolemia, and diabetes decrease with the frequency of marathon participation independent of annual running distance. This may be due to the inclusion of longer training runs in preparation for marathons or to genetic or other innate differences between marathon and nonmarathon runners.

Keywords

Exercise; running; body mass index; metabolic syndrome; prevention

Introduction

There were 403,000 marathon finishers in 2007 [28]. This 36% increase since 2000 occurred despite the fact that running marathons incurs a small risk for sudden cardiac death [18–21], and is specifically proscribed for those at high cardiovascular disease risk [20,21]. On average, eight sudden cardiac deaths occur per 1,000,000 participants, or approximately two deaths per million hours of vigorous exercise [20,21]. The most common location for these sudden deaths is within 1.6 km of the finish [20,21]. Autopsies show coronary atherosclerosis is the primary underlying cause [20,21]. Marathon participation is negatively impacted by the media attention given to these deaths, resulting in less public support for the event. Little is written about the health benefits of marathoning to counter the somewhat exaggerated portrayal of its risk.

Whether the health benefits of marathoning outweighs its risks will depend in part on whether there are additional benefits to marathon training and participation beyond those that could be obtained by accumulating the same annual mileage throughout the year.

This report compares the prevalence of hypertension, hypercholesterolemia, and diabetes by marathon participation rates in over 100,000 men and women who completed baseline surveys for the National Runners' Health Study between 1991 and 2000. We have previously shown that annual running distance is inversely associated to the prevalence of these conditions cross-sectionally [37], and to the incidence of these conditions prospectively during 7.8-year follow-up [34]. Marathon training necessarily requires long training distances, which may simply translate into greater annual mileage with increased participation. Therefore, the hypothesis to be tested is whether the prevalence of these conditions decreases with marathon participation when adjusted for total annual mileage. We also test whether faster finish times are related to lower prevalence of these conditions, and whether this differs from their expected prevalence given the runners' cardiorespiratory fitness as estimated from their 10km performance times [37]. Finally, we consider more generally the importance of longer training runs in the prevention of hypertension, hypercholesterolemia, and diabetes when adjusted for total mileage. This was done because long training runs are characteristic of marathon preparation, which could account for decreased hypertension, hypercholesterolemia, and diabetes with marathon participation.

Methods

The design and baseline characteristics of the National Runners' Health Study have been reported previously [29–39]. Briefly, a two-page questionnaire, distributed nationally at races and to subscribers of the nation's largest running magazine (Runner's World, Emmaus, PA), solicited information on demographics, running history, weight history, diet (vegetarianism and the current weekly intakes of alcohol, red meat, fish, fruit, vitamin C, vitamin E, and aspirin), cigarette use, and medications for blood pressure, thyroid conditions, cholesterol levels, or diabetes. Runners were excluded if they smoked or followed strict vegetarian diets. All participants signed a statement of informed consent in accordance with the study protocol approved by the Committee for the Protection of Human Subjects University of California, Berkeley review board.

Marathon participation was determined by the survey questions "How many marathons did you run during the previous five years (write zero if none)?" and "What was your best marathon time during the previous five years (minutes, leave blank if none)". Running distances, reported in miles run per week, has been shown to have a strong correlation between repeated questionnaires ($r=0.89$) [31]. Running was the predominant physical activity of the study population. Although other leisure-time physical activities were not recorded for many in this cohort, data from runners recruited after 1998 (when the question was introduced in the survey) show that running represents (mean $\pm$ SD) 91.5 $\pm$ 19.1% and 85.2 $\pm$ 24.0% of all vigorously intense activity in men and women, respectively, and 73.5 $\pm$ 23.7% and 69.4 $\pm$ 25.7% of total leisure-time physical activity. Use of anti-diabetic, anti-hypertensive, or LDL-C lowering medications was reported by the participants as part of their baseline survey.

Statistical analyses

Table 1 presents means $\pm$ SD for all variables assessed; all other statistics are expressed as mean $\pm$ SE or coefficients $\pm$ SE. The logistic regression models (JMP version 5.1, SAS Institute, Cary SC) were computed with the log odds of medication users as linear functions of annual distances and marathon participation rates.

Results

There were 62,284 male and 45,040 female nonsmoking runners who provided complete information on usual running distance and BMI. By self report, 31.7% of men and 29.1% of women ran 0.2 and 0.8 marathons/year, 8.6% of men and 4.4% of women ran between 1.0 and 1.8 marathons/year, and 3.8% of men and 1.5% of women ran an average of ≥ 2 marathons/year. Table 1 shows that the more avid marathoners tended to be older, somewhat more educated, consume less meat and more fruit, and were generally leaner than nonmarathoners. As expected, total annual running distance increased with participation, and those who ran more marathons were fitter as measured by their 10km performance times.

Annual marathon participation

Table 2 shows that men who ran more marathons per year had significantly lower odds for using medications, which remained significant when adjusted for annual running distance. Adjustment for BMI had little effect on their odds ratios. Marathon participation was also associated with lower use of LDL-cholesterol lowering and anti-diabetic medication in women, but not when adjusted for annual distance. Although women and men had similar adjusted odds ratio for the cholesterol lowering medications, the women's odds ratio probably failed to achieve statistical significance due to insufficient statistical power. Adjustment for 10-km performance time in addition to annual mileage did not eliminate the significance of the odds ratios for marathons/year versus anti-diabetic ($P=0.005$), LDL-cholesterol lowering ($P=0.02$), or anti-diabetic medications ($P=0.002$) in the 49,755 men who provided these data (analyses not displayed).

Figure 1 (left) shows that compared to nonmarathoners, men who averaged 0.2–0.8 marathons/year had 13% lower odds for anti-hypertensive, 22% lower odds for LDL-cholesterol lowering, and 32% lower odds for anti-diabetic medication use when adjusted for annual mileage (km/year). There were significant incremental reductions in anti-hypertensive medication use in men who ran ≥ 1.0 vis-à-vis 0.2 to 0.8 marathons/year ($P<0.0001$), and ≥ 2 vis-à-vis 1 to 1.8 marathons/year ($P=0.03$). A significant dose-response relationship is also shown through 1.0–1.8 marathons/year for men's use of anti-diabetic and LDL-cholesterol lowering medications. Men who averaged ≥ 2 marathons/year had 41% lower odds for anti-hypertensive, 32% lower odds for LDL-cholesterol lowering, and 87% lower odds for anti-diabetic medication use than nonmarathoners.

Marathon finish time

The analyses of Table 3 is restricted to the 88% subset men and 80% subset of women with 10-km performance times in addition to their marathon finish times. The slower men were at significantly greater odds for using medications for hypertension and hypercholesterolemia independent of their BMI and annual running distance, which remained statistically significant when adjusted for the number of marathons run per year. Their significance was lost when adjusted for 10 km performance times. The slower women runners were more likely to use anti-diabetic medications, which was not accounted for by annual mileage, marathon participation, or even 10 km performance times.

Longest usual weekly run

The question about longest weekly run was not included in the survey until 1998 and therefore its analyses include only 24,120 men and 27,226 women (Table 4). Longer usual run was associated with reduced use of all three medications, however the odds ratios remain significant in men but not women when adjusted for total annual mileage, and when adjusted for both BMI and annual mileage albeit less significantly so. Figure 1 (right), which displays the odds ratio for medication use versus longest usual run, shows that the odds for medication use

declined incrementally through 10-km distance runs. Compared to men whose longest run was <5 km, those running ≥ 15 km had 39% lower odds for using anti-hypertensive medications, 34% lower odds for LDL-cholesterol lowering medications, and 65% lower odds for using anti-diabetic medications when adjusted for total annual mileage (km/year). The odds reductions associated with longer usual runs remained significant when adjusted for BMI.

Discussion

Although differences between marathon runners and sedentary men, sedentary women, and those engaged in other activities are widely reported, to our knowledge this report is unique in assessing the potential health benefits of marathon participation while controlling for total annual mileage. The current findings show that being genetically predisposed to run longer distances, or endurance training itself, are associated with substantially lower medication use for these three afflictions, even when adjusted for total annual running distance. The adjustment demonstrates that higher total annual mileage per se, shown elsewhere to be associated with the lower prevalence and incidence of diabetes, hypertension, and hypercholesterolemia [34, 37], does not explain the reduced medication use of the more avid marathoners.

Marathoners are distinguished from shorter-distanced recreational runners in their ability to meet the energy requirements of two to five hours of sustained vigorous exercise using fat and carbohydrates derived from liver, adipose tissue, and muscle stores [24]. Marathon training increases the muscles uptake of plasma free fatty acids, storage and oxidation of intramuscular triacylglycerol, and reliance on fat oxidation to spare carbohydrates [9]. Dramatic fatigue occurs with muscle glycogen depletion and hypoglycemia [2,7]. Marathon training also decreases slow-twitch (MHC I) and fast-twitch (MHC IIa) myosin heavy chain muscle fiber size without loss of strength so that the force per cross-sectional area is increased [27]. The smaller size may facilitate endurance by reducing the diffusion distance for oxygen and substrates during running [27]. Marathon training also increases capillary density, mitochondrial density, oxidative enzymes, and myoglobin in muscle cells [26].

In addition to training effects, men and women who run marathons may be genetically endowed with greater exercise capacity due to better aerobic metabolism, which may in itself confer lower risks of diabetes and hypertension and improved lipoprotein metabolism. In addition to their 350% greater running capacity, rats bred over 11 generations for high intrinsic exercise capacity showed 39% lower percent visceral fat than those bred for low running capacity, in addition to 16% lower fasting glucose, 57% lower insulin, 63% lower triglycerides, and 48% lower free fatty acid concentrations in plasma [39]. The high capacity rats also had 13% lower 24-hour blood pressure in association with improved endothelial function [39].

Hyperinsulinemia of rats bred for low intrinsic exercise capacity has been attributed to reduced insulin clearance rather than impaired secretion [39]. Impaired insulin-stimulated glucose uptake in skeletal muscle may arise from the increased intracellular levels of various lipid metabolites [22] due to less lipid oxidation by mitochondria [17]. Data in humans and rats suggest that the muscular adaptations to training may contribute to lower risk for diabetes. The muscles of high exercise capacity rats have 46% lower triglyceride and 56% diacylglycerol content and 73% higher triglyceride lipase activity than low capacity rats [23]. Impairment in the muscle oxidative capacity in type 2 diabetic has been attributed to low mitochondrial numbers rather than impaired mitochondrial function [4]. Chronic training increases mitochondrial biogenesis whereas mitochondrial number is reduced by inactivity [13]. Exercise may also improve insulin sensitivity through its effects on skeletal muscle GLUT 4 content and capillary density [10].

Figure 1 shows that even among those genetically predisposed to have run at least one marathon, men who ran one or more marathons annually had lower odds for using anti-hypertensive ($P<0.0001$), LDL-cholesterol lowering ($P=0.03$), and anti-diabetic medications ($P=0.01$) than those who ran fewer. This suggests to us that the effects may be at least partially due to training, independent of both total annual mileage and BMI. Longest mileage covered per training session is the best predictor for the successful marathon completion [40]. The more frequent marathoners will have included longer runs as a more regular component of training. Table 4 shows that for runners in general, the length of the usual longest run contributes significantly to lower odds for anti-hypertension, LDL-cholesterol lowering, and anti-diabetic medication use, and in men this effect was independent of both total annual distance and BMI. The importance of including extended activity sessions does not appear to be limited to vigorous exercise, i.e. in walkers we have shown that the length of the longest usual walk was a better discriminator of diabetes, hypertension, and hypercholesterolemia than the total cumulative mileage, particularly in men [35]. Although marathon training is unlikely to be formally included in public health guidelines, the current findings suggest that some importance should be assigned to exercise of extended duration [11]. The current analyses do not address the question of whether the same exercise dose accumulated over multiple sessions versus a single session yields the same health benefits.

Except for diabetes medication in women, faster marathon finish times were not indicative of less prevalent medication use when adjusted for 10-km race performance. Others have argued that 10-km performance times reflect VO_2max [1,6,12]. Thus the decline in medication use with finish time may reflect its reduction with greater cardiorespiratory fitness, as previously shown [34,37]. Marathon training may have less effect on increasing VO_2max than reducing oxygen consumption at submaximal running speed [14]. The declines in medication use with faster finish times were independent of both total annual mileage and BMI, which led us once again to speculate that genes related to innate differences in cardiorespiratory fitness or the ability to improve fitness with training play a role. The heritability of cross-sectional differences in VO_2max (estimated as high as 50% in sedentary individuals) and longitudinal changes in VO_2max with training are well documented [3,8,25].

In comparing low and high mileage runners, differences in BMI contribute significantly to both lower prevalence cross-sectionally [34] and lower incidence prospectively [37] of diabetes, hypertension and hypercholesterolemia. Even among ostensibly healthy-weight men and women ($\text{BMI} \leq 25 \text{ kg/m}^2$) being less fat is associated with significantly lower risk all three afflictions [38]. The lower BMI of the longer-distanced runners is not due exclusively to self-selection [33], and is due in part to the attenuation of age-related weight gain [32], particularly among those who exercise consistently [36]. Although the more avid marathoners were significantly leaner than other runners, adjustment for BMI had remarkably little effect on the odds for anti-diabetic, anti-hypertensive, and LDL-cholesterol lowering medication use beyond that already explained by annual running distance. However, BMI may be a poor indicator of reductions in total fat mass associated with marathon frequency. For example, marathoners are reported to have one-half the total fat mass and two-thirds of the percent body fat as BMI-matched sedentary controls [14], and correspondingly lower leptin concentrations [14].

The limitation of these analyses warrants acknowledgement. As with all cross-sectional associations, it is not possible to distinguish the causal direction of the relationship, that is, whether marathon training reduces the need for medications, or contrariwise, whether medications reduce marathon participation and performance. More avid marathon runners might also be less willing to take medications. Marathoners are likely to differ from other runners and from nonrunners (Table 1). There may also be a tendency for individuals with higher VO_2max to self-select for marathon running [14].

We also acknowledge the error inherent to self-reported survey data. Weekly running distances are reported with error, and marathon frequency may achieve statistical significance in part because: 1) for any given reported distance those reporting more marathons actually run further weekly, and 2) average running distance may fail to include atypical training in preparation for a marathon (more likely for the occasional marathoner than those averaging ≥ 2 marathons per year). Although self-reported hypertension and high cholesterol have been demonstrated by others as generally reliable using repeated surveys and confirmed diagnosis from medical records [5] their self-report in our study may be subject to greater error than in cohorts of physicians or nurses despite the runners' average four-year post high school education. Errors in reporting these outcomes will contribute to less statistical power to detect an association, but there is no a priori reason to assume that this would vary by marathon participation or performance. We do not believe that the declining incidence of hypertension, hypercholesterolemia, and diabetes with running is due to avoidance of opportunities for diagnosis in the more athletic men. The Health Professionals Follow-up Study reported that their more vigorously active participants had more routine medical check-ups than less active men [15] and there was no difference in routine medical check-up by activity level in the Nurses' Health Study [16].

In summary, the limitation of these cross-sectional associations notwithstanding, these results suggest that there may be additional benefits to the more strenuous training required to run marathons, or important genetic effects associated with marathon participation, in lowering metabolic disease risk.

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Figure 1.

Odds ratios for medication use by marathon participation rate relative to nonmarathoners in men (left) and longest usual run relative to men whose longest run ≤ 5 km (right), adjusted for age, intakes of meat, fish, fruit, and alcohol. Additional adjustment for annual running distance (km/year) and BMI where indicated. Brackets designate 95% confidence intervals.

Significance levels relative to nonmarathoners or men whose longest run was ≤ 5 km are coded * $P < 0.05$, † $P < 0.01$, ‡ $P < 0.001$, § $P < 0.0001$. Significance levels relative to all men of with greater participation (left) or longer usual run (right) are presented above the bars and to the left of the arrows (e.g., men who ran an average of one or more marathons per year were

significantly less likely to use LDL-cholesterol lowering medications than those who ran 0.2–0.8 marathons/year at $P=0.03$).

Table 1

Sample characteristics by marathon participation in 62,284 male and 45,040 female runners.

	Mean±SD by participation (marathons/year)				Significance (P)
	None	0.2–0.8	1.0–1.8	≥2.0	
Males					
N	34,827	19,755	5,367	2,335	
Anti-hypertensive medication (%)	5.49	3.68	3.41	3.04	<0.0001
LDL-cholesterol lowering medication (%)	4.01	2.44	2.46	2.48	<0.0001
Anti-diabetic medication (%)	0.74	0.41	0.30	0.09	<0.0001
Running distance (km/year)	1585.62±1007.92	2175.40±1129.94	2779.74±1237.87	3227.64±1385.44	<0.0001
10 km performance (m/s)	3.77±0.58	3.97±0.52	4.11±0.51	4.14±0.49	<0.0001
Age (years)	44.84±11.53	43.18±9.96	45.04±9.51	47.52±9.69	0.12
Education (years)	16.38±2.51	16.48±2.46	16.50±2.55	16.57±2.76	<0.0001
BMI (kg/m ²)	24.42±2.95	23.94±2.64	23.55±2.47	23.43±2.55	<0.0001
Meat intake (serving/wk)	3.07±2.87	2.80±2.64	2.65±2.65	2.54±2.91	<0.0001
Fruit intake (pieces/wk)	10.40±10.15	10.76±9.57	11.45±9.36	12.19±10.01	<0.0001
Alcohol intake (ml/wk)	79.99±112.49	78.25±109.86	81.32±110.88	83.41±123.27	0.49
Females					
N	29,257	13,121	1,989	673	
Anti-hypertensive medication (%)	2.10	1.37	1.76	2.38	<0.0001
LDL-cholesterol lowering medication (%)	0.77	0.42	0.25	1.04	<0.0001
Anti-diabetic medication (%)	0.36	0.24	0.15	0.15	0.06
Running distance (km/year)	1469.91±952.13	2135.25±1078.31	2793.81±1211.80	3209.39±1503.28	<0.0001
10 km performance (m/s)	3.31±0.56	3.47±0.51	3.67±0.47	3.71±0.50	<0.0001
Age (years)	38.23±10.58	37.60±9.03	40.57±9.08	43.12±9.29	<0.0001
Education (years)	15.93±2.66	16.30±2.33	16.24±2.40	16.13±2.42	<0.0001
BMI (kg/m ²)	21.79±2.88	21.39±2.35	21.05±2.16	21.40±2.60	<0.0001
Meat intake (serving/wk)	1.89±2.16	1.62±2.11	1.49±2.06	1.45±2.04	<0.0001
Fruit intake (pieces/wk)	10.54±8.23	10.74±9.01	11.43±8.17	11.51±8.09	<0.0001
Alcohol intake (ml/wk)	48.98±72.55	48.52±68.66	48.90±72.85	53.53±84.45	<0.0001

Table 2

Odds ratio (95% confidence intervals) for the prevalence of anti-hypertensive, LDL-cholesterol lowering, and anti-diabetic medication use per marathons/year run in male and female runners.

	Unadjusted for km/ year and BMI	Adjusted for km/year	Adjusted for km/ year and BMI
Males			
Anti-hypertension	0.77 [§] (0.72, 0.82)	0.85 [§] (0.79, 0.91)	0.85 [§] (0.80, 0.91)
LDL-cholesterol lowering	0.77 [§] (0.71, 0.83)	0.87 [‡] (0.81, 0.94)	0.87 [‡] (0.81, 0.94)
Anti-diabetic	0.46 [§] (0.34, 0.63)	0.52 [§] (0.38, 0.71)	0.53 [§] (0.39, 0.72)
Females			
Anti-hypertension	0.94 (0.83, 1.06)	1.04 (0.93, 1.16)	1.02 (0.91, 1.14)
LDL-cholesterol lowering	0.74 [*] (0.55, 0.94)	0.88 (0.66, 1.16)	0.86 (0.65, 1.13)
Anti-diabetic	0.51 [*] (0.28, 0.94)	0.77 (0.45, 1.33)	0.77 (0.45, 1.30)

Odds ratios adjusted for age (age and age²), and intakes of meat, fish, fruit, and alcohol. Additional adjustment for annual running distance (km/year and km²/year²) and BMI (BMI and BMI²) where indicated. Significance levels are coded

* P<0.05,

[†] P<0.01,

[‡] P<0.001, and

[§] P<0.0001.

Table 3

Odds ratio (95% confidence intervals) for the prevalence of anti-hypertensive, LDL-cholesterol lowering, and anti-diabetic medication use per hour to complete a marathon in 24,296 male and 12,618 female runners.

	Unadjusted for marathons/year & 10 km performance (m/ s)	Adjusted for marathons/year	Adjusted for marathons/year & 10 km performance (m/ s)
Males			
Anti-hypertension	1.34 [§] (1.21, 1.49)	1.31 [§] (1.17, 1.46)	1.09 (0.95, 1.25)
LDL-cholesterol lowering	1.34 [§] (1.19, 1.51)	1.22 [‡] (1.07, 1.39)	1.04 (0.88, 1.24)
Anti-diabetic	1.35 (0.98, 1.85)	1.23 (0.88, 1.72)	0.97 (0.61, 1.53)
Females			
Anti-hypertension	1.09 (0.88, 1.37)	1.12 (0.90, 1.41)	1.01 (0.76, 1.33)
LDL-cholesterol lowering	0.97 (0.66, 1.43)	0.99 (0.67, 1.47)	0.98 (0.61, 1.58)
Anti-diabetic	2.03 [‡] (1.34, 3.07)	2.01 [‡] (1.31, 2.08)	1.68 [*] (0.99, 2.85)

Odds ratios adjusted for age (age and age²), BMI (BMI and BMI²), annual running distance (km/year and km²/year²), and intakes of meat, fish, fruit, and alcohol. Additional adjustment for the number of marathons run per year and 10-km performance where indicated. Significance levels are coded

* P<0.05,

[‡] P<0.01,

[‡] P<0.001, and

[§] P<0.0001.

Table 4

Odds ratio (95% confidence intervals) for the prevalence of anti-hypertensive, LDL-cholesterol lowering, and anti-diabetic medication use per km of longest usual weekly run in 24,120 male and 27,226 female runners.

	Unadjusted for annual running distance & BMI (m/s)	Adjusted for annual running distance	Adjusted for annual running distance & BMI (m/s)
Males			
Anti-hypertension	0.966 [§] (0.956, 0.976)	0.977 [‡] (0.963, 0.991)	0.984 [*] (0.970, 0.998)
LDL-cholesterol lowering	0.962 [§] (0.951, 0.973)	0.979 [‡] (0.964, 0.994)	0.983 [*] (0.968, 0.998)
Anti-diabetic	0.932 [§] (0.903, 0.962)	0.947 [‡] (0.907, 0.989)	0.957 [*] (0.918, 0.999)
Females			
Anti-hypertension	0.979 [‡] (0.963, 0.996)	1.008 (0.987, 1.030)	1.014 (0.993, 1.036)
LDL-cholesterol lowering	0.957 [‡] (0.928, 0.986)	0.978 (0.939, 1.018)	0.983 (0.946, 1.023)
Anti-diabetic	0.921 [‡] (0.875, 0.969)	0.973 (0.908, 1.041)	0.990 (0.929, 1.055)

Odds ratios adjusted for age (age and age²), and intakes of meat, fish, fruit, and alcohol. Additional adjustment for usual distance run (km/year and km²/year²) and BMI (BMI and BMI²) where indicated. Significance levels are coded

* P<0.05,

† P<0.01,

‡ P<0.001, and

§ P<0.0001.