Lifestyle Risk Factors and New-Onset Diabetes Mellitus in Older Adults:

The Cardiovascular Health Study

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Abstract

Background—The combined impact of lifestyle factors on incidence of diabetes mellitus later in life is not well established. The objective of this study was to determine how lifestyle factors, assessed in combination, relate to new-onset diabetes in a broad and relatively unselected population of older adults.

Methods—We prospectively examined associations of lifestyle factors, measured using repeated assessments later in life, with incident diabetes mellitus during a 10-year period (1989–1998) among 4883 men and women 65 years or older (mean [SD] age at baseline, 73[6] years) enrolled in the Cardiovascular Health Study. Low-risk lifestyle groups were defined by physical activity level (leisure-time activity and walking pace) above the median; dietary score (higher fiber intake and polyunsaturated to saturated fat ratio, lower *trans*-fat intake and lower mean glycemic index) in the top 2 quintiles; never smoked or former smoker more than 20 years ago or for fewer than 5 pack-years; alcohol use (predominantly light or moderate); body mass index less than 25 (calculated as weight in kilograms divided by height in meters squared); and waist circumference of 88 cm for women or 92 cm for men. The main outcome measure was incident diabetes defined annually by new use of insulin or oral hypoglycemic medications. We also evaluated fasting and 2-hour postchallenge glucose levels.

Results—During 34 539 person-years, 337 new cases of drug-treated diabetes mellitus occurred (9.8 per 1000 person-years). After adjustment for age, sex, race, educational level, and annual income, each lifestyle factor was independently associated with incident diabetes. Overall, the rate of incident

diabetes was 35% lower (relative risk, 0.65; 95% confidence interval, 0.59–0.71) for each 1 additional lifestyle factor in the low-risk group. Participants whose physical activity level and dietary, smoking, and alcohol habits were all in the low-risk group had an 82% lower incidence of diabetes (relative risk, 0.18; 95% confidence interval, 0.06–0.56) compared with all other participants. When absence of adiposity (either body mass index <25 or waist circumference ≤88/92 cm for women/men) was added to the other 4 low-risk lifestyle factors, incidence of diabetes was 89% lower (relative risk, 0.11; 95% confidence interval, 0.01–0.76). Overall, 9 of 10 new cases of diabetes appeared to be attributable to these 5 lifestyle factors. Associations were slightly attenuated, but still highly significant, for incident diabetes defined by medication use or glucose level.

Conclusion—Even later in life, combined lifestyle factors are associated with a markedly lower incidence of new-onset diabetes mellitus.

Given medical challenges, health care costs, long-term complications, and growing incidence and prevalence of type 2 diabetes mellitus, preventing the onset of clinical diabetes is of paramount importance. Long-term treatment with drugs such as metformin may prevent or delay onset of diabetes among specific high-risk subgroups.[1] Modest changes in diet and exercise also prevent onset of diabetes in these high-risk subgroups, to a greater extent than metformin[1,2]; improve a broad range of other metabolic risk factors that are largely unaffected by met-formin[3]; and may be more applicable to a broader population than long-term drug treatment. Lifestyle factors linked to incidence of diabetes or diabetes-related risk factors include physical activity level, dietary habits, adiposity, alcohol use, and smoking habits.[4–15] In secondary analyses from the Diabetes Prevention Program trial, structured advice on diet and activity was most effective at reducing diabetes risk among the oldest participants (60–85 years),[16] which suggests that lifestyle habits might be particularly important, rather than less effective, for preventing diabetes later in life. However, this was a post hoc analysis of a trial with high-risk participants (overweight or obese individuals having both elevated fasting glucose and elevated 2-hour postchallenge glucose levels) who were also participating in a highly structured intervention; therefore, applicability of these results to a broader population of older adults is unclear. In addition, effects on diabetes risk from smoking habits and alcohol use were not evaluated in this trial.

Considering evidence from observational and clinical studies that certain lifestyle behaviors can lower diabetes risk, the reasonable corollary is that absence of these low-risk lifestyle behaviors increases risk. Most previous studies have considered each lifestyle factor individually, but low-risk lifestyle habits are often intercorrelated and may be most effective when present in combination. In a cohort of predominantly middle-aged women of higher socioeconomic status, suboptimal lifestyle risk factors, evaluated in combination, appeared to account for the great majority of cases of incident diabetes.[7] However, the combined impact of several lifestyle risk factors on the incidence of diabetes in a general population of older adults is largely unknown. To address this question, we prospectively investigated the relationships of lifestyle risk factors, evaluated in combination, with incidence of diabetes during a 10-year period among 4883 men and women 65 years and older enrolled in the Cardiovascular Health Study, a prospective cohort study of determinants of cardiovascular risk in older adults sponsored by the National Heart, Lung, and Blood Institute. We hypothesized that older adults with a set of more optimal lifestyle characteristics would experience a markedly lower incidence of diabetes compared with older adults who did not have these characteristics and that lack of adherence to these more optimal lifestyle factors would account for a large proportion of cases of new-onset diabetes later in life.

METHODS

DESIGN AND POPULATION

Design and recruitment for the Cardiovascular Health Study have been described previously. [17,18] Briefly, 5201 ambulatory, noninstitutionalized men and women 65 years and older were randomly selected and enrolled from Medicare eligibility lists in 4 US communities from 1989 through 1990; an additional 687 black participants were recruited and enrolled in 1992. Each center's institutional review committee approved the study, and all participants gave informed consent. Baseline evaluation included standardized physical examination, diagnostic testing, laboratory evaluation, and questionnaires to determine health status, medical history, and cardiovascular and lifestyle risk factors.[17–20] After excluding 501 individuals with prevalent diabetes at baseline, defined by treatment with oral hypoglycemic agents or insulin, and 504 individuals with missing information on lifestyle risk factors, 4883 participants were included in this analysis.

ASSESSMENT OF LIFESTYLE FACTORS

Lifestyle risk factors of interest included physical activity level, dietary habits, smoking habits, alcohol use, and adiposity. At annual study visits, participants responded to standardized questionnaires and were examined by study investigators. Usual walking habits, including average pace (gait speed) and distance walked, were assessed by self-report at baseline and again annually at each follow-up visit, and leisure-time activity (modified Minnesota Leisure-Time Activities questionnaire[21]) and exercise intensity (low, medium, or high[22]) were assessed by self-report at the baseline, third, and seventh annual visits. Usual dietary habits were assessed at baseline in the original cohort using the picture-sort National Cancer Institute food frequency questionnaire[20,23] and again at the sixth annual visit using the Willett food frequency questionnaire.[24,25] Alcohol use was assessed at baseline and again at each annual visit except the second visit, including information on usual frequency of use and types of alcohol consumed. Smoking status was assessed at baseline and again at each annual visit; baseline information on years since quitting among former smokers and lifetime pack-years of smoking was also obtained. Trained personnel used standardized methods to measure weight at baseline and again at each annual visit, as well as height and waist circumference at the baseline, third, and seventh annual visits. To assess long-term effects and minimize misclassification owing to errors in measurement and changes in lifestyle, these repeated measures were used to update lifestyle exposures over time using time-varying covariates, with simple updating for smoking habits and cumulative averaging for other lifestyle factors. For example, baseline walking pace was related to incidence of diabetes from baseline to visit 2, the mean walking pace from baseline and visit 2 was related to incidence of diabetes from visit 2 to visit 3, and so on.

CHARACTERIZATION OF LOW-RISK GROUPS

To investigate how modest differences in lifestyle factors related to diabetes risk, each lifestyle risk factor was dichotomized. Leisure-time activity score (ordinal score for quintiles) and pace of walking (ordinal score for pace <2, 2–3, and >3 mph) were combined into a physical activity score, which was dichotomized at the median level. Post hoc evaluations of specific activity cutoff points (eg, 1000 kcal/wk for leisure-time activity and 1 m/s for gait speed) did not improve discrimination of diabetes risk and were not used. Exercise intensity and distance walked were not significantly associated with diabetes risk after accounting for leisure-time activity and pace walked and were not included. For smoking, low risk was defined as never smoking. To facilitate public health recommendations, we also evaluated former smoking according to years since quitting and lifetime pack-years and added former smokers who were at similar risk as those who had never smoked. High levels of alcohol use were rare among these older adults (46.7% reported no alcohol use and an additional 47.4% consumed ≤2 drinks per day), and thus low risk was defined as any use. Low risk for body mass index (BMI)

(calculated as weight in kilograms divided by height in meters squared) was defined as not being overweight (BMI <25); low risk for waist circumference was defined as less than 88 cm in women or 92 cm in men (Adult Treatment Panel III criteria[26]). Consistent with methods used in previous studies,[7,27] dietary habits were dichotomized by the upper 2 quintiles of a dietary score; each person was assigned a score from 1 to 5 corresponding to their quintile of intake of higher dietary fiber, lower glycemic index foods, lower *trans* fats, and higher polyunsaturated to saturated fat ratio, and these values were summed to compute the dietary score. Data on coffee, tea, and total caffeine consumption and incident diabetes are being evaluated in detail in a separate analysis.

IDENTIFICATION OF INCIDENT DIABETES

Participants underwent annual study examinations for 10 years and interim 6-month telephone contact.[28] At each visit, detailed information was obtained on medications used by means of medication inventories.[29] At baseline, study interviewers visited participants in their homes and asked to see all prescription medications taken during the previous 2 weeks. At follow-up examinations, participants brought to the clinic all prescription medications taken in the previous 2 weeks. Information on drug name, dose, and frequency of use was recorded and coded according to Medi-Span files of prescription medications (Wolters Kluwer Health, Indianapolis, Indiana). The primary outcome was incident diabetes, defined by new use of insulin or oral hypoglycemic medication (ie, drug-treated diabetes) at each annual visit. We also secondarily evaluated incident diabetes based on medication use or fasting serum glucose level of 126 mg/dL or more (to convert to millimoles per liter, multiply by 0.0555) (measured at visits 3 and 7) or based on medication use, fasting glucose level, or 2-hour post-challenge glucose level of 200 mg/dL or more (measured at visit 7), excluding individuals meeting these criteria at baseline (except for postchallenge glucose level in the black participants enrolled in 1992, which was not measured at baseline).

STATISTICAL ANALYSIS

Cox proportional hazards models were used to estimate the relative risk (RR) (hazard ratio [HR]) of incident diabetes, with time at risk until first diagnosis of diabetes, the last follow-up visit with information on medication use, or administrative censoring at the last annual examination (1998), which was the latest date data were available on adjudicated medication use. Follow-up for vital status was 100% complete; 3.6% of person-time was censored early because of missing medication use information at the last visit or planned visit (if alive but did not attend). Categories of low-risk groups were evaluated; ordinal variables were entered into the model for tests for trend. Multivariable models were evaluated adjusted for age, sex, race, educational level, annual income, and, in analyses of the individual lifestyle factors, each of the other lifestyle factors. Biological parameters (eg, serum lipid levels) and medication use were not included as covariates because such factors could be mediators or directly correlated with mediators in the causal pathway for effects of lifestyle on diabetes risk. Using time-varying covariates, variables were updated over time to account for previous and current lifestyle and minimize misclassification; for interim missing values, the most recent nonmissing cumulative mean values were carried forward. Missing covariate information on educational level (0.3% missing) and annual income (6.5% missing) were imputed using data on age, sex, race, and enrollment site. Risk factors were evaluated in combination to estimate the proportion of cases in the population that might be attributable to suboptimal levels of these risk factors (population attributable risk [PAR%]). The PAR% was calculated using the formula p(RR−1)/(1 + p[RR −1]), where p is the prevalence of individuals not in the low-risk group and RR is the associated multivariable-adjusted relative risk. Upper and lower 95% confidence intervals (CIs) of the PAR% were derived using this formula and the upper and lower 95% CI estimates of the multivariable-adjusted RR. Potential effect modification was evaluated for sex, age, and (for the other lifestyle factors) BMI using stratified analyses and multiplicative interaction terms

with likelihood ratio tests. Analyses were performed using Stata statistical software, version 8.2 (Stata Corp, College Station, Texas). All *P* values were 2-tailed (α = .05).

RESULTS

At baseline, the mean (SD) participant age was 72.7 (5.5) years (range, 65–98 years), 58.6% were women, and 11.4% were nonwhite; 95.0% of nonwhite participants were black. Distributions of individual lifestyle risk factors at baseline are shown in Table 1. A plurality of participants reported a usual walking pace of 2 to 3 mph, with the remainder equally distributed between slower and faster paces. Approximately half of these older adults had never smoked, and 11.7% were current smokers. About half of the participants reported no regular alcohol use; among those consuming alcohol, most consumed alcohol moderately (≤1 drink per day, 88.6%; ≤2 drinks per day, 94.1%). Four in 10 participants were overweight, and another 2 in 10 were obese.

During 10 years (34 539 person-years) of follow-up, 337 new cases of diabetes occurred (9.8 per 1000 person-years). For each lifestyle factor, the low-risk group represented between one-third to one-half of the population (Table 2); that is, each low-risk lifestyle factor was achieved by a substantial proportion of these older adults. After adjustment for age, sex, race, educational level, annual income, and other lifestyle factors simultaneously, each lifestyle risk factor was independently associated with incidence of diabetes, with 26%, 31%, 23%, 34%, 45%, and 46% lower risk among older adults in the low-risk groups for physical activity level, dietary habits, smoking habits, alcohol use, BMI, and waist circumference, respectively (Table 2). In combination, a robust graded inverse association was present between the number of lifestyle factors an individual had in the low-risk group and risk of diabetes (*P* < .001) (Figure 1). Evaluated ordinally, each additional lifestyle factor an individual had in the low-risk group was associated with a 35% lower risk of diabetes (HR, 0.65; 95% CI, 0.59–0.71).

Because BMI and waist circumference may not be as readily modifiable as other lifestyle risks, we also evaluated only physical activity level and dietary, smoking, and alcohol habits as lifestyle risk factors, while simultaneously adjusting for age, sex, race, educational level, annual income, BMI, and waist circumference. Compared with individuals not in the low-risk group for any of these 4 lifestyle factors (9% of participants), individuals had lower diabetes risk if they were in the low-risk group for only 1 lifestyle factor (HR, 0.70; 95% CI, 0.51–0.96; 29% of participants), 2 lifestyle factors (HR, 0.63; 95% CI, 0.46–0.87; 36% of participants), 3 lifestyle factors (HR, 0.35; 95% CI, 0.23–0.53; 21% of participants), or 4 lifestyle factors (HR, 0.05; 95% CI, 0.01–0.33; 5% of participants) (*P*<.001). Evaluated ordinally, each 1 additional of these 4 lifestyle factors an individual had in the low-risk group was associated with a 29% lower risk of diabetes (HR, 0.71; 95% CI, 0.64–0.80).

To further stratify risk among former smokers, we used information on years since quitting and lifetime quantity of smoking in pack-years. Compared with never smokers, the adjusted RR (covariates as in Table 2) of incident diabetes among former smokers was 1.05 for those who had quit at least 20 years ago or smoked for no more than 5 pack-years (95% CI, 0.68–1.60; 9% of participants); 1.40 for those who quit 15 to 19 years ago or smoked for 6 to 20 pack-years (95% CI, 1.03–1.91; 16% of participants); 1.27 for those who quit 10 to 14 years ago or smoked for 21 to 40 pack-years (95% CI, 0.90–1.79; 12% of participants); and 1.49 for those who quit fewer than 10 years ago or smoked for more than 40 pack-years (95% CI, 1.04–2.14; 9% of participants). To consider as liberal a definition of low risk as possible, former smokers who quit at least 20 years ago or smoked for no more than 5 pack-years were added to the low-risk group (together with never smokers) in subsequent analyses.

We evaluated diabetes risk among older adults with specific combinations of low-risk lifestyle factors, compared with all others not in that group, with a focus on lifestyle behaviors that may be more readily modifiable (Table 3). Individuals in the low-risk category for only physical activity level and dietary habits (nearly 1 in 4 adults) had a 46% lower incidence of diabetes, and 2 in 5 new cases of diabetes appeared attributable to not being in the low-risk group for these 2 lifestyle factors. Twelve percent of individuals were in the low-risk category for physical activity, dietary habits, and smoking habits, with a 58% lower incidence of diabetes; about half of new cases of diabetes appeared to be attributable to not being in the low-risk group for these 3 lifestyle factors. The 13% of participants in the low-risk category for physical activity level, dietary habits, and alcohol use had a 68% lower risk of diabetes, and nearly two-thirds of new cases of diabetes appeared to be attributable to not being in the low-risk group for these 3 lifestyle factors. Combining low-risk groups for physical activity level, dietary habits, smoking habits, and alcohol use (6% of participants), an 82% lower risk of diabetes was present, and 4 in 5 new cases of diabetes appeared to be attributable to not having these low-risk lifestyle factors. Adding either not being overweight or not having large waist circumference, an 89% lower risk of diabetes was present, and 9 in 10 new cases of diabetes appeared to be attributable to not having these low-risk lifestyle factors.

We assessed potential effect modification of the association of lifestyle factors with new-onset diabetes by sex, age (65–74 vs ≥75 years), and, for the other lifestyle factors, BMI (<25 vs ≥25). Although healthy lifestyle factors were associated with a lower risk of diabetes among men and women, this relationship appeared more pronounced in women compared with men (*P* for interaction=.005). Among women, each additional lifestyle factor in the low-risk group was associated with a 41% lower risk of diabetes (HR, 0.59; 95% CI, 0.52–0.67); among men, each additional lifestyle factor in the low-risk group was associated with a 27% lower risk (HR, 0.73; 95% CI, 0.64–0.83). This difference was driven by stronger associations in women (although also present in men) of BMI and waist circumference with diabetes; associations of physical activity level, dietary habits, smoking habits, and alcohol use with diabetes were relatively similar among women and men (data not shown). There was little evidence that relationships of lifestyle factors with diabetes risk varied significantly according to age (*P* for interaction=.27) or BMI (*P* for interaction=.76).

We also evaluated incident diabetes defined by medication use or fasting glucose level (measured at years 3 and 7) (256 cases) or by medication use, fasting glucose level, or 2-hour postchallenge glucose level (measured at year 7) (296 cases), excluding individuals who met these criteria at baseline. For specific combinations of low-risk lifestyle factors (as specified and in the order listed in Table 3), the PAR%s for diabetes determined by medication use or fasting glucose level were 26%, 51%, 27%, 77%, and 87%, respectively; and the PAR%s for diabetes determined by medication use, fasting glucose level, or postchallenge glucose level were 21%, 17%, 26%, 27%, and 55%, respectively. Evaluated in combination, a robust graded inverse association was present between the number of lifestyle factors an individual had in the low- risk group and risk of diabetes by medication use or laboratory criteria (*P*<.001) (Figure 2 and Figure 3). Evaluated ordinally, each additional low-risk lifestyle factor an individual had was associated with a 27% lower risk of diabetes defined by medication use or fasting glucose level (HR, 0.73; 95% CI, 0.66–0.80) and a 22% lower risk of diabetes defined by medication use, fasting glucose level, or postchallenge glucose level (HR, 0.78; 95% CI, 0.71–0.85).

COMMENT

In this large, prospective cohort study of older US adults, lifestyle factors including physical activity level, dietary habits, smoking habits, alcohol use, and adiposity measures, assessed late in life, were each independently associated with risk of new-onset diabetes. In combination,

these basic lifestyle risk factors strongly predicted diabetes incidence, with an approximately 50% lower risk with only physical activity level and dietary habits in the low-risk group and an approximately 80% lower risk with physical activity level, dietary habits, smoking habits, and alcohol use in the low-risk group. In sum, 8 in 10 cases of diabetes in this population of older adults appeared attributable to these 4 lifestyle factors, suggesting that, if these associations are causal, 8 in 10 new cases of diabetes might have been prevented if all older adults were in the low-risk group for these lifestyle factors. Adding either not being overweight or not having a high waist circumference, nearly 9 in 10 new cases of diabetes appeared attributable to not being in the low-risk group for these lifestyle factors. These findings provide an estimate of the public health burden of combined nonoptimal lifestyle risk factors for incidence of diabetes in older adults, the fastest growing segment of the US population.

We assessed incidence of diabetes defined by drug treatment alone; by drug treatment or abnormal fasting glucose level; or by drug treatment, abnormal fasting glucose level, or abnormal 2-hour postchallenge glucose level. Each of these different diagnostic classes may have different clinical implications and even potentially different underlying pathophysiological characteristics. Because fasting glucose and oral glucose tolerance testing were not available at each annual visit, our findings likely underestimate the incidence of diabetes defined by these criteria. Nevertheless, we observed similar relationships between lifestyle and incident diabetes by each of these definitions, suggesting robust effects of lifestyle factors on diabetes risk among older adults regardless of the methods for diagnosis.

Quantifying the impact of all of the different possible combinations of different lifestyle factors on diabetes incidence among older adults would be difficult or even unethical in randomized controlled trials. Our results provide evidence for a tremendous combined impact of lifestyle on diabetes risk in older adults. Notably, the magnitudes of diabetes prevention from intervening on only 2 lifestyle factors (diet and physical activity) in structured randomized trials among selected high-risk adults[1,2] are quite consistent with our observed PAR% for these same 2 lifestyle factors. In the Diabetes Prevention Program trial, which included overweight or obese adults with both elevated fasting glucose levels and elevated 2-hour post-challenge glucose levels, structured advice to adopt a healthy low-calorie diet and be moderately active (eg, walking briskly on most days of the week) reduced incidence of diabetes by 58%.[1] Similarly, in the Finnish Diabetes Prevention Study, which included overweight middle-aged adults with abnormal 2-hour postchallenge glucose levels, incidence of diabetes was reduced 58% by a structured program to increase physical activity to at least 30 min/d and to promote a healthy low-calorie diet that included whole-grain products, vegetables, fruits, low-fat milk and meat products, and soft margarines and vegetable oils.[2] The magnitude of our findings—approximately 50% lower incidence of diabetes with only moderate physical activity and better dietary habits (Table 3)—are consistent with the magnitude of effect in these trials, suggesting that the substantial benefits of moderate physical activity and diet for preventing diabetes seen in the high-risk trials extend to a much broader and much less selected general population of older adults.

In the Finnish trial, no cases of diabetes occurred among individuals in either the control or intervention group who achieved at least 4 of 5 main activity, dietary, and weight loss goals. [2] Although numbers were small (only 64 participants achieved 4 or more goals), these findings suggested that diabetes may be almost entirely preventable in this high-risk middle-aged population. Our observational findings in a large cohort of older men and women suggest, similarly, that diabetes may be largely preventable among older adults through adherence to a similar set of relatively modest lifestyle goals.

The magnitudes of our findings are further supported by the effects of diet and physical activity evaluated singly or together in controlled trials and cohort studies, often with lifestyle

assessment occurring in midlife. In controlled trials of intermediate endpoints, physical activity improves fasting and postprandial glucose-insulin homeostasis, induces and maintains weight loss, raises high-density lipoprotein cholesterol levels, lowers low-density lipoprotein cholesterol and triglyceride levels, lowers blood pressure, and probably lowers inflammation and improves endothelial function.[6,30] These benefits are achieved with moderate activity, eg, 30 minutes of brisk walking on most days.[4–7,30,31] Several dietary factors have been associated with lower incidence of diabetes, including higher consumption of dietary fiber and polyunsaturated fats and lower consumption of *trans* fats and easily digestible (higher glycemic index) carbohydrates.[8,9] In controlled trials, dietary habits affect fasting and postprandial glucose-insulin homeostasis, inflammatory pathways, and satiety; benefits may be greatest in persons most predisposed to diabetes.[32] In the Diabetes Prevention Program trial, advice to improve dietary habits and physical activity improved multiple cardio-metabolic risk factors, including lowering of systolic and diastolic blood pressure, improving heart rate variability, lowering of triglyceride levels and raising of high-density lipoprotein cholesterol levels, and reducing prevalence of hypertension and hyperlipidemia.[3,33] In comparison, metformin treatment reduced glucose levels and slightly raised high-density lipoprotein cholesterol levels, but produced none of these other additional benefits.[3,33]

We also found smoking and alcohol habits to be independently associated with diabetes incidence among older adults. In a meta-analysis of prospective cohort studies with a total of 1.2 million participants, current and former smokers had a higher incidence of diabetes compared with those who had never smoked.[15] Based on the estimates in this meta-analysis and the weighted mean of former and current smokers in our cohort, our participants who had never smoked would have been expected to have a 22% lower risk of diabetes—very similar to the observed 23% lower risk. Smoking is proinflammatory[34,35] and may also induce insulin resistance[36–38] and increase visceral adiposity,[39–41] each of which is strong risk factor for diabetes. Consistent with the time course of our results for diabetes incidence, several years of smoking cessation are required among older men and women for C-reactive protein levels to approach those of individuals who never smoked.[35] Modest alcohol consumption is also associated with lower diabetes risk: 2 meta-analyses of prospective observational studies[13,14] found an approximately 30% lower diabetes incidence with modest consumption (eg, 0.5–2.5 drinks per day[14]) compared with nonconsumers. In contrast, high consumption (≥3 drinks per day) was not associated with lower diabetes risk.[13,14] The observed lower risk (approximately 30%) in the present study of older adults (mean age, 73 years at baseline) is consistent with these previous findings in predominantly middle-aged populations. In our population, few individuals (6%) consumed more than 2 drinks per day, and thus the observed lower risk should be interpreted as that largely associated with modest intake (≤2 drinks per day). In a meta-analysis of controlled trials, alcohol improved lipid levels associated with diabetic dyslipidemia, with approximately 2 drinks per day increasing high-density lipoprotein cholesterol by 4 mg/dL and decreasing triglyceride levels by 5.7 mg/dL (to convert to millimoles per liter, multiply by 0.0113).[42] In patients with type 2 diabetes mellitus, randomization to 1 glass of wine vs nonalcoholic beer with dinner for 3 months lowered fasting glucose from 140 to 118 mg/dL (P=.02); glycosylated hemoglobin levels also decreased (from 7.4% to 7.1%; P<.05), although this decrease was not significantly different from the control group.[43] Metabolism of alcohol increases the hepatic cytosolic ratio of NADH to NAD+ (NADH dehydrogenase/nicotinamide adenine dinucleotide) and may inhibit gluconeogenesis, increase antioxidant capacity, and lower advanced glycation end products,[44] suggesting potential biological mechanisms whereby modest alcohol intake may lower diabetes risk.

The strong associations and likely causal effects of adiposity, particularly central adiposity, for diabetes risk do not require further elaboration.[7,10] Comorbidity and frailty are common among older adults, and changes in lean body mass may reduce the precision of BMI and waist circumference for assessing central adiposity later in life.[45] Nevertheless, we found that both

adiposity measures were independently associated with diabetes risk among older adults. However, even adjusting for the adiposity measures, differences in other lifestyle factors including physical activity, diet, smoking, and alcohol use together explained much of the incidence of diabetes. This is likely because many effects of these lifestyle factors are independent of effects on adiposity. Because some other effects of these lifestyle habits are mediated through effects on adiposity, adjustment for adiposity when evaluating these lifestyle habits would also in part represent overadjustment.

Our analysis had several strengths. Information on sociodemographic factors, lifestyle risk factors, and diabetes incidence were prospectively collected in a well-established multicenter cohort study with little loss to follow-up. Repeated assessments over time allowed updating of lifestyle factors during follow-up, minimizing misclassification. Adequate numbers of events provided sufficient power to detect modest associations with risk. Participants were randomly selected and enrolled from Medicare eligibility lists in several US communities, providing a population-based sample of older adults and increasing generalizability.

Potential limitations should also be considered. Although we adjusted for major sociodemographic characteristics and lifestyle factors simultaneously, residual confounding by unknown or unmeasured factors may be present. Conversely, given the magnitude of many of the risk estimates (including several RRs <0.20) and consistency of our results with prior controlled trials of some lifestyle factors, it is improbable that all of the observed risk differences are owing to residual confounding. Data on fasting and postchallenge glucose levels were available at limited time points, and thus diabetes incidence based on these criteria might be misclassified. This could partly account for the somewhat less pronounced associations between lifestyle factors and diabetes by laboratory criteria; it is also possible that lifestyle factors have greater effect on incidence of medically treated, and presumably more severe, diabetes. The diagnosis of medically treated diabetes could also relate to lifestyle. Individuals with poor lifestyle could receive closer medical attention, causing overestimation of diabetes incidence among those with less healthy lifestyles; alternatively, individuals with healthier lifestyles might be more likely to have access to or seek medical care, causing overestimation of diabetes incidence among those with more healthy lifestyles. Some effects of dietary and physical activity habits are likely mediated through changes in adiposity, and, therefore, adiposity-adjusted analyses might underestimate the full impact of diet and physical activity. Some misclassification of lifestyle factors, particularly diet and physical activity, is probable, which would likely attenuate findings toward the null and underestimate the true magnitude of the associations. Dichotimization of different lifestyle variables (diet, activity, adiposity, etc) that have graded effects on risk would also attenuate the magnitude of association compared with other comparisons (eg, continuous or across quintiles). Therefore, our findings likely underestimate the importance of each of the individual lifestyle factors and their combined effects on disease risk; even small changes are likely to have an important effect on a population level. Finally, although the Cardiovascular Health Study represents a population-based survey from 4 US communities, the least healthy individuals are often less likely to participate in long-term studies. Thus, prevalence of healthier lifestyles may be overestimated and extremes of poor lifestyle habits underestimated, so that the RRs and PAR%s may be underestimates of the true effects.

Our findings suggest that, even later in life, the great majority of cases of diabetes are related to lifestyle factors. Our results support the need for emphasizing healthy and achievable physical activity and dietary goals among older adults, including moderate leisure-time activity and walking pace, higher intake of dietary fiber and polyunsaturated fat, and lower intake of *trans* fats and easily digestible carbohydrates. Although public health complexities and competing risks do not support recommending alcohol use to reduce diabetes incidence among older adults, our findings are consistent with recommendations that do not prohibit moderate

alcohol use among older adults having no contraindications. Given low risk among nonsmokers or former smokers who quit at least 20 years ago or smoked for no more than 5 pack-years, our findings also support the importance of reducing smoking, and preventing initiation of smoking, earlier in life. Most of these moderate lifestyle behaviors will also reduce central obesity and its adverse metabolic consequences, further contributing to reduced incidence of diabetes in older adults.

Acknowledgments

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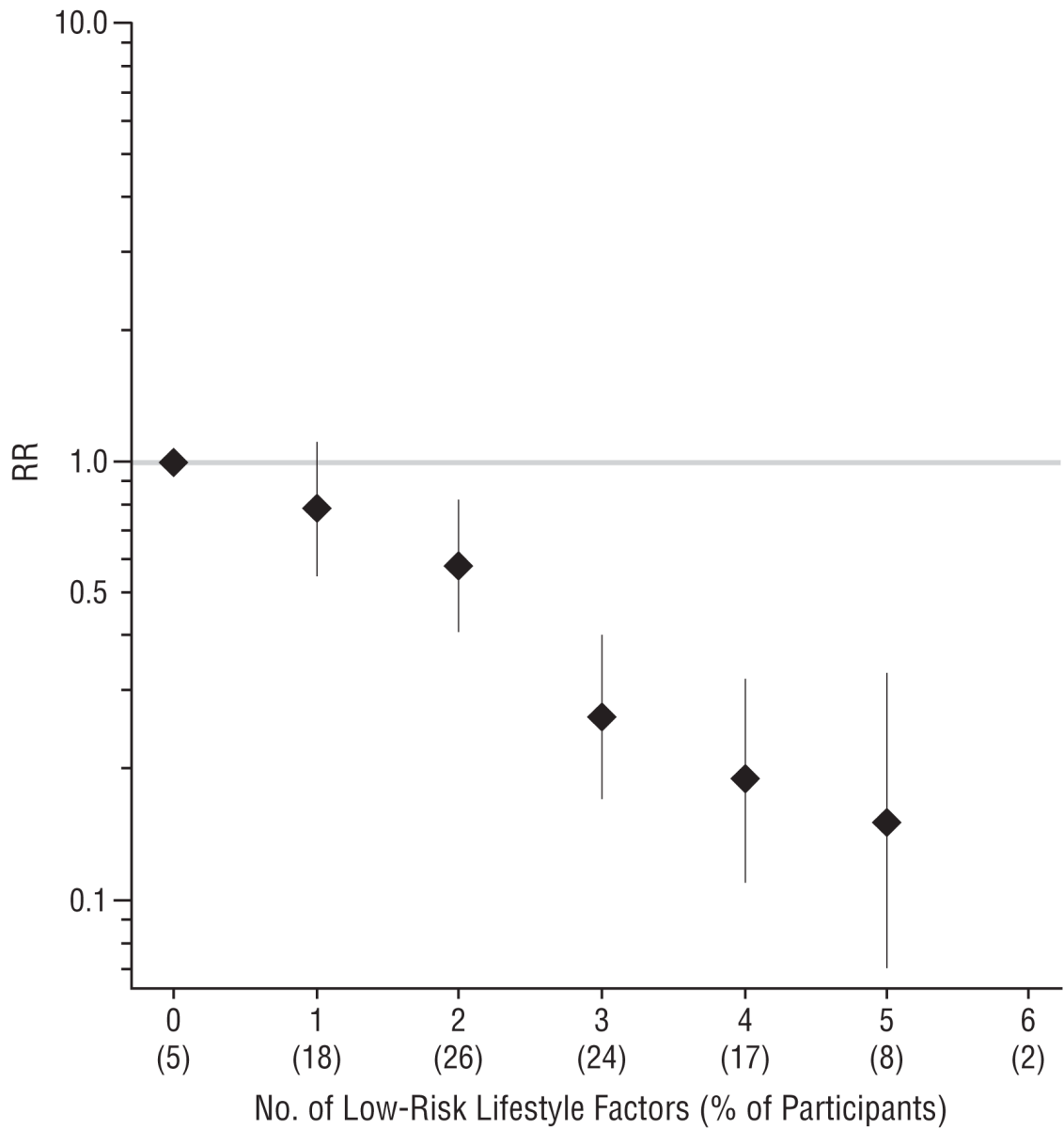
Figure 1.
Relative risk (RR) of incident diabetes mellitus according to the number of low-risk lifestyle factors among 4883 older adults from 1989 to 1998. Diabetes was defined by new use of insulin or oral hypoglycemic medication (assessed annually). Low-risk lifestyle factors included physical activity above the median level, dietary score in the upper 2 quintiles, never smoking, alcohol use, body mass index less than 25 (calculated as weight in kilograms divided by height in meters squared), and waist circumference less than 88 cm for women or 92 cm for men. Adjusted for age (years), sex (male vs female), race (white vs nonwhite), educational level (<high school, high school, and >high school), and annual income (<$25 000, $25 000–$49

999, and ≥\$50 000). No cases of incident diabetes occurred among individuals with all 6 low-risk lifestyle factors.
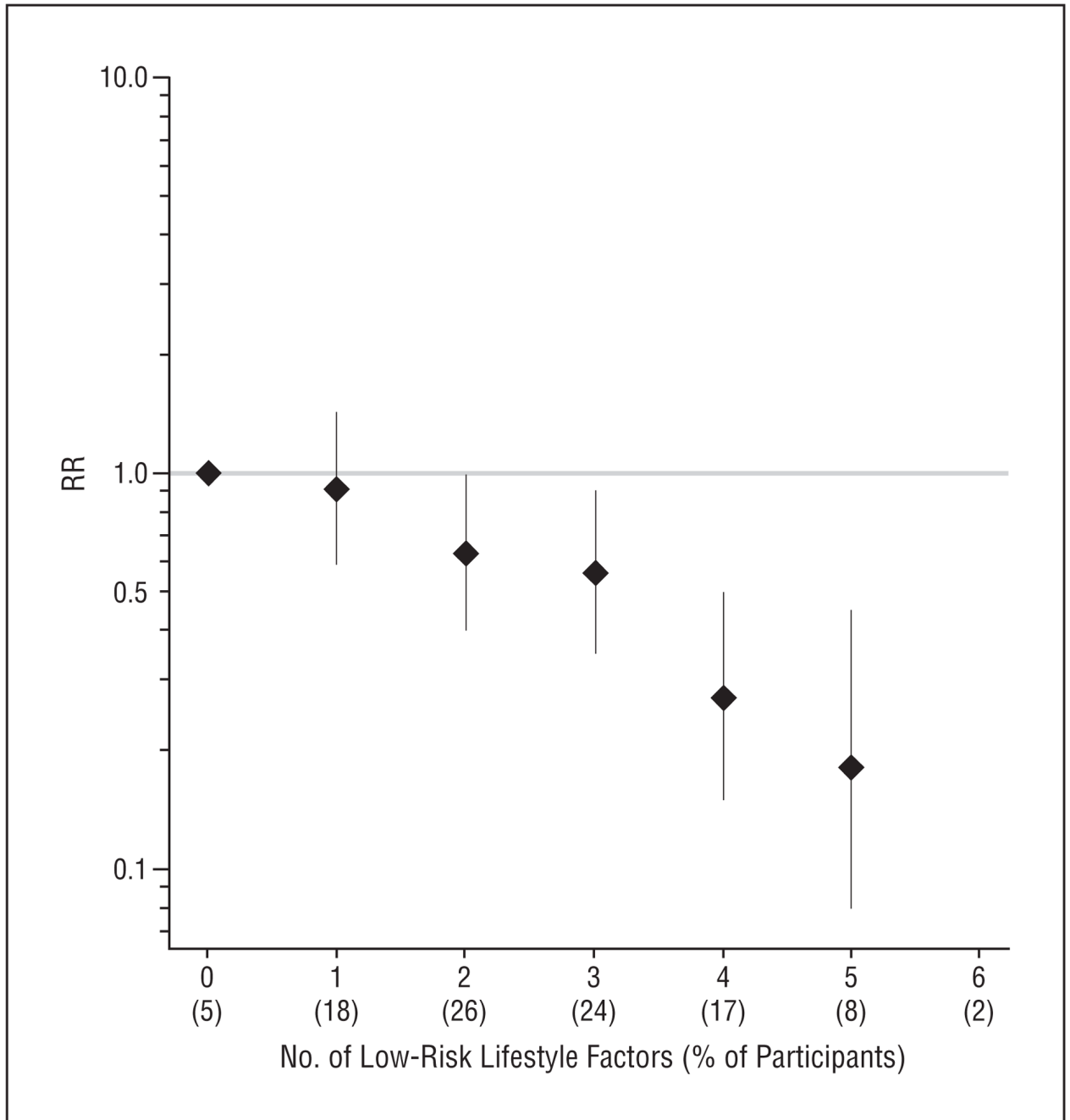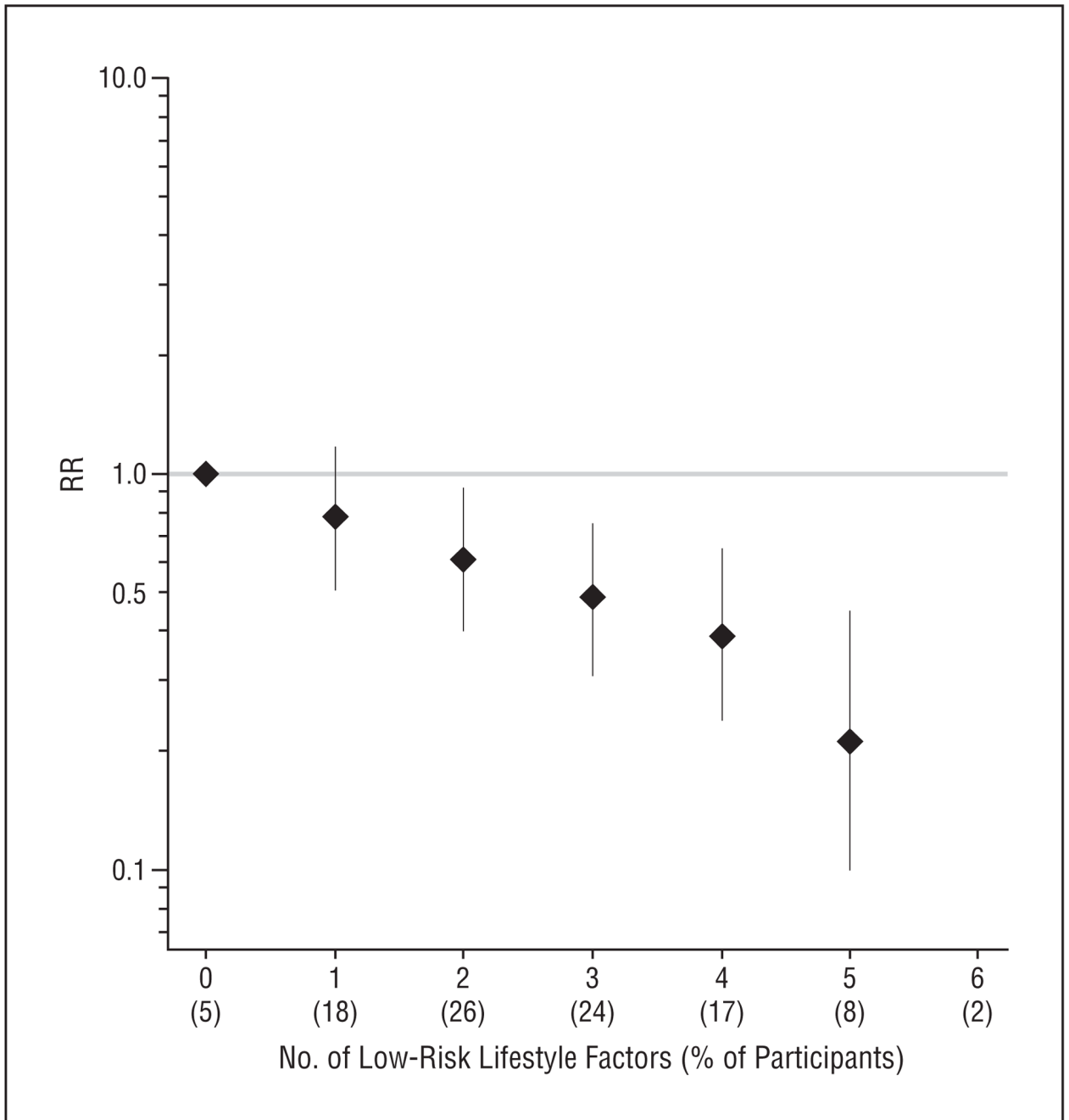
Figure 2.
Relative risk (RR) of incident diabetes mellitus determined by medication use or fasting glucose level criteria according to the number of low-risk lifestyle factors among 4526 older adults from 1989 to 1998. Diabetes was defined by new use of insulin or oral hypoglycemic medication (assessed annually) or a fasting glucose level of 126 mg/dL or higher (to convert to millimoles per liter, multiply by 0.0555) (assessed at years 3 and 7), excluding individuals who met these criteria at baseline. Low-risk lifestyle factors included physical activity above the median level, dietary score in the upper 2 quintiles, never smoking, alcohol use, body mass index less than 25 (calculated as weight in kilograms divided by height in meters squared), and waist circumference less than 88 cm for women or 92 cm for men. Adjusted for age (years),

sex (male vs female), race (white vs nonwhite), educational level (<high school, high school, and >high school), and annual income (<$25 000, $25 000–$49 999, and ≥$50 000). No cases of incident diabetes occurred among individuals with all 6 low-risk lifestyle factors.

Figure 3.
Relative risk (RR) of incident diabetes mellitus determined by medication use, fasting glucose level, or 2-hour postchallenge glucose level criteria according to the number of low-risk lifestyle factors among 4155 older adults from 1989 to 1998. Diabetes was defined by new use of insulin or oral hypoglycemic medication (assessed annually), fasting glucose level of 126 mg/dL or higher (to convert to millimoles per liter, multiply by 0.0555) (assessed at years 3 and 7), or 2-hour postchallenge glucose of 200 mg/dL or higher (assessed at year 7), excluding individuals who met these criteria at baseline. Low-risk lifestyle factors included physical activity above the median level, dietary score in the upper 2 quintiles, never smoking, alcohol use, body mass index less than 25 (calculated as weight in kilograms divided by height in

meters squared), and waist circumference less than 88 cm for women or 92 cm for men. Adjusted for age (years), sex (male vs female), race (white vs nonwhite), educational level (<high school, high school, and >high school), and annual income (<$25 000, $25 000–$49 999, and ≥$50 000). Incident diabetes among individuals with all 6 low-risk lifestyle factors (n=2) was too infrequent to estimate risk reliably.

Table 1

Sociodemographic and Lifestyle Characteristics at Baseline Among 4883 Older Adults[a]

Characteristic	Participants (N=4883)
Age, mean (SD), y	72.7 (5.5)
Sex	
Male	2024 (41.4)
Female	2859 (58.6)
Race	
White	4325 (88.6)
Nonwhite	558 (11.4)
Educational level	
<High school	1305 (26.7)
High school graduate	1388 (28.4)
>High school	2190 (44.8)
Annual income, $	
<25 000	3001 (61.5)
25 000–49 999	1230 (25.2)
≥50 000	652 (13.4)
Leisure-time activity, mean (SD), kcal/wk	1790 (2047)
Usual walking pace, mph	
<2	1358 (27.8)
2–3	2119 (43.4)
>3	1406 (28.8)
Dietary fiber, mean (SD), g/d	18 (7)
Trans fat, mean (SD), % of daily calories	1.6 (0.6)
Glycemic index, mean (SD)	50.8 (3.5)
Polyunsaturated:saturated fat ratio, mean (SD)	0.74 (0.25)
Smoking habits	
Never	2279 (46.7)
Former	2035 (41.7)
Current	569 (11.7)
Alcohol use	
None	2281 (46.7)
<1 drink per week	989 (20.3)
1–2 drinks per week	666 (13.6)
3–7 drinks per week	392 (8.0)
>1–2 drinks per day	268 (5.5)
>2 drinks per day	287 (5.9)
Body mass index[b]	
<23.0	1052 (21.5)
23.0–24.9	915 (18.7)
25.0–29.9	2044 (41.9)

Characteristic	Participants (N=4883)
≥30.0	872 (17.9)
Waist circumference, mean (SD), cm	93.6 (12.8)

[a]Data are given as the number (percentage) of participants unless otherwise indicated. Percentages may not total 100 because of rounding.

[b]Calculated as weight in kilograms divided by height in meters squared.

Table 2

Individual Lifestyle Risk Factors and Risk of Incident Diabetes Mellitus

Lifestyle Risk Factor	% of 4883 Participants	Person-Years of Follow-up	Diabetes Mellitus, No. of Cases	Hazard Ratio (95% Confidence Interval)[a]	
				Multivariable Model	Multivariable + Lifestyle Model
Physical activity score[b]					
<Median	56.9	19 643	227	1 [Reference]	1 [Reference]
≥Median	43.1	14 896	110	0.63 (0.50–0.80)	0.74 (0.58–0.93)
Dietary score[c]					
Lower 3 quintiles	54.7	18 918	232	1 [Reference]	1 [Reference]
Upper 2 quintiles	45.3	15 621	105	0.64 (0.50–0.81)	0.69 (0.54–0.87)
Smoking habits					
Never	46.7	16 139	135	0.83 (0.66–1.04)	0.77 (0.61–0.97)
Former or current	53.3	18 400	202	1 [Reference]	1 [Reference]
Alcohol use					
No	52.4	18 133	217	1 [Reference]	1 [Reference]
Yes[d]	47.6	16 406	120	0.66 (0.52–0.84)	0.66 (0.52–0.84)
Body mass index[e]					
<25	40.2	13 873	64	0.38 (0.29–0.51)	0.55 (0.40–0.77)
≥25	59.8	20 666	273	1 [Reference]	1 [Reference]
Waist circumference, cm					
<88 for women and <92 for men	35.4	12 200	51	0.36 (0.27–0.48)	0.54 (0.38–0.77)
≥88 for women and ≥92 for men	64.6	22 339	286	1 [Reference]	1 [Reference]

[a] Multivariable model adjusted for age (years), sex (male vs female), race (white vs nonwhite), educational level (<high school, high school, and >high school), and annual income (<$25 000, $25 000–$49 999, and ≥$50 000). Multivariable + lifestyle model simultaneously adjusted for each of the other lifestyle risk factors in the table.

[b] Combining leisure-time activity (quintiles) and pace of walking (3 categories).

[c] Upper 2 quintiles to be consistent with previous studies reporting a dietary score combining intake of dietary fiber, glycemic index, and *trans* fats and polyunsaturated:saturated fat ratio, each in quintiles.

[d] Most (94.1%) consumed 2 or fewer drinks per day.

[e] Calculated as weight in kilograms divided by height in meters squared.

Table 3

Risk of Incident Diabetes Mellitus and Population Attributable Risk According to Low-Risk Lifestyle Factors

No. of Low-Risk Lifestyle Factors	% of 4883 Participants	Hazard Ratio[a] (95% Confidence Interval)	Population Attributable Risk (95% Confidence Interval), %
2 Low-risk lifestyle factors Physical activity level >median[b] Dietary score upper 2 quintiles[c]	22.3	0.54 (0.38–0.76)	40 (20–56)
3 Low-risk lifestyle factors Physical activity level >median[b] Dietary score upper 2 quintiles[c] Never smoked or former smoker, ≤5 pack-years or quit ≥20 y ago	12.0	0.42 (0.25–0.71)	55 (26–73)
3 Low-risk lifestyle factors Physical activity level >median[b] Dietary score upper 2 quintiles[c] Alcohol use[d]	12.8	0.32 (0.18–0.55)	65 (42–80)
4 Low-risk lifestyle factors Physical activity level >median[b] Dietary score upper 2 quintiles[c] Never smoked or former smoker, ≤5 pack-years or quit ≥20 y ago Alcohol use[d]	6.0	0.18 (0.06–0.56)	81 (42–94)
5 Low-risk lifestyle factors Physical activity level >median[b] Dietary score upper 2 quintiles[c] Never smoked or former smoker, ≤5 pack-years or quit ≥20 y ago Alcohol use[d] Body mass index[e] <25 or waist circumference <88 cm in women or <92 cm in men	3.4	0.11 (0.01–0.76)	89 (23–99)

[a]Compared with all other participants not in this low-risk group. The population attributable risk is the percentage of new cases of diabetes in the population attributable to nonadherence to the specified set of lifestyle factors. All models adjusted for age (years), sex (male vs female), race (white vs nonwhite), educational level (<high school, high school, and >high school), annual income (<$25 000, $25 000–$49 999, and ≥$50 000), and each of the other lifestyle risk factors not already included in the low-risk group.

[b]Combining leisure-time activity (quintiles) and pace of walking (3 categories).

[c]Upper 2 quintiles to be consistent with previous studies reporting a dietary score combining intake of dietary fiber, glycemic index, and *trans* fats and polyunsaturated:saturated fat ratio, each in quintiles.

[d]Most (94.1%) consumed 2 or fewer drinks per day.

[e]Calculated as weight in kilograms divided by height in meters squared.