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Association between modifiable lifestyle factors and residual lifetime risk of diabetes

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Abstract

Background and aims—While clinical trials have reported beneficial effects of diet, exercise, and weight loss on incident diabetes in subjects with obesity or impaired glucose tolerance, little is known about the incremental benefit of not smoking and moderate drinking on diabetes risk. We sought to examine the association between modifiable lifestyle factors and residual lifetime risk of diabetes.

Methods and Results—Prospective cohorts involving 20,915 men (1982–2008) and 36,594 women (1992–2008). Modifiable lifestyle factors and adiposity were ascertained at baseline in each cohort and incident diabetes was ascertained during follow up. The mean age at baseline was 53.5 y in men and 54.6 y in women. During an average follow up of 22.6 y in men and 13.0 y in women, 2,096 men and 2,390 women developed diabetes. At age 45 y, the residual lifetime risk of diabetes (95% CI) for men with 0, 1, 2, 3, and 4+ healthy lifestyle factors was 30.5 (27.3–33.7); 21.5 (19.9–23.0); 15.1 (13.9–16.3); 10.3 (9.1–11.5); and 7.3 (5.7–8.9) percent, respectively. Corresponding values for women were 31.4 (28.3–34.5); 24.1 (21.8–26.5); 14.2 (12.7–15.7); 11.6 (9.7–13.5); and 6.4 (4.2–8.6) percent, respectively.

Conclusions—These data show an inverse and graded relation between desirable lifestyle factors and residual lifetime risk of diabetes in men and women. Not smoking and moderate drinking may have additional benefits when added to exercise, weight control, and diet.

Keywords

Smoking; exercise; weight loss; diabetes; diet; risk factors; epidemiology; obesity; Physicians' Health Study; Women's Health Study

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Introduction

With the rising obesity epidemic in the US, it is anticipated that the overall burden of diabetes on healthcare expenditure will remain high in the near future[1]. While several observational studies and randomized trials have examined the association between individual lifestyle factors (including adiposity[2], physical activity[3], diet[4], alcohol intake[5], smoking[6], etc) on the general risk of diabetes, data on the joint association of all these modifiable factors on the risk of diabetes are limited[7]. While several long-term randomized trials[8–10] of exercise, weight loss, and diet have demonstrated beneficial effects of lifestyle factors on diabetes risk, most of those trials were focused on obese subjects or people with impaired glucose tolerance and it is unclear whether other lifestyle factors such as not smoking or moderate alcohol consumption have added benefits. It is also important to know if beneficial effects of lifestyle factors extend to normal weight subjects and people with normal glucose tolerance test. Lifetime risk provides an estimate of a cumulative risk of a given disease over a fixed time period while accounting for competing causes of death. In other words, a lifetime risk statistic summarizes the risk of ever developing a disease before dying of some other cause. It thus conveys the absolute risk of diabetes over one's remaining lifetime, beginning at a given age. As it is readily understandable by the lay public, lifetime risk estimates are increasingly being used in both patient education and public health planning.

Thus, to address these gaps in the literature, we used data from 22,071 men from the Physicians' Health Study I and 39,876 women from the Women's Health Study to examine the relation between modifiable lifestyle factors, considered singly and jointly, and residual lifetime risk of diabetes.

Methods

Study participants

Participants were members of the Physicians' Health Study I (PHS I) and the Women's Health Study (WHS), two completed randomized trials designed to study low-dose aspirin, and beta-carotene for men and vitamin E for women, on the primary prevention of cardiovascular disease and cancer. Detailed descriptions of the PHS I and WHS have been published[11;12]. Of the total 22,071 PHS I participants, we excluded 1156 men with prevalent diabetes or missing data lifestyle factors of interest. Of the 39,876 female health professionals, we excluded 3282 women with prevalent diabetes or missing data on lifestyle factors. Each participant signed an informed consent and the Institutional Review Board at Brigham and Women's Hospital approved the study protocol.

Ascertainment of diabetes in PHS I and WHS

We have validated the diagnosis of self-reported diabetes mellitus DM in a sample of PHS participants. Of the 186 men who suffered myocardial infarction after a self-reported diagnosis of diabetes, we randomly selected half (93 people) for chart review. Medical records were available for 60 subjects. Two physicians independently reviewed these charts. A diagnosis of DM was made if there was sufficient evidence in the chart defined as one of the following: a) diagnosis of DM on the discharge summary, b) current treatment with insulin or oral hypoglycemic agents, or c) fasting glucose above 126 mg/dl or non-fasting glucose above 200 mg/dl. Using these criteria, DM was confirmed in 59 out of 60 cases (98.3%). There was an excellent agreement between the two examiners (kappa=100%).

Among the female health professionals, self-reports of type 2 diabetes were validated using American Diabetes Association criteria, by obtaining additional information using telephone interview, supplemental questionnaire, or review of medical records from treating

physicians[13]. Among all women who reported a diagnosis of type 2 diabetes on a follow-up questionnaire, type 2 diabetes was subsequently validated in 91% of the cases[13].

Ascertainment of lifestyle factors

We focused on modifiable lifestyle factors that have been shown to influence the risk of DM. These included physical activity, smoking, alcohol consumption, adiposity, and dietary habits. At baseline, each man provided information on exercise [how often do you exercise vigorously enough to work up sweat? Possible answers included rarely/never, 1–3/month, 1/week, 2–4/week, 5–6/week, and daily]; smoking (never, former, and current smoker); and alcohol intake (servings per month, week, and day). We used an abbreviated food frequency questionnaire to obtain self-reported information on selected foods such as egg consumption, fruit and vegetables, and breakfast cereal. Among women, self-reported walking, stair climbing, and participation in eight groups of recreational activities was obtained[14]. Diet was assessed using a 128-item food frequency questionnaire whose validity has been published[15]. Self-reported baseline weight and height were used to compute body mass index (weight in kilograms divided by height in meter squared).

Definition of lifestyle groups

To investigate the association between healthy lifestyle factors and the lifetime risk of DM, each lifestyle risk factor was dichotomized as follows: never smoker vs. ever smoker; normal weight (BMI <25 kg/m²) vs. overweight/obese (BMI ≥25 kg/m²); regular exercise (2 or more times per week) vs. infrequent/no exercise (< 2 times per week) for men or being in the top 2 quintiles of energy expenditure (MET-h/week) in women. We created a dietary score using selected foods available in men that have been shown to be associated with type 2 diabetes (breakfast cereals and egg consumption) and a 128-item food frequency questionnaire data in women. Among men, a score of 1 was assigned to breakfast cereal consumption of 5 or more servings per week and 0 otherwise. For moderate drinking, a score of 1 was assigned to self-report of up to one drink per day for women and up to 2 drinks per day for men as defined by US dietary guidelines and 0 otherwise [of note is that a small proportion (3%) of the total sample reported alcohol consumption of 2+/d]. We chose the cut points above based on prior associations between individual lifestyle factors and type 2 diabetes risk in this cohort or public health recommendations. A dietary score then was computed for men as a sum of individual scores obtained for eggs and breakfast cereals based on previous publications[16;17]. A corresponding dietary score for women was derived by summing individual rank assigned to quintiles of dietary fiber, polyunsaturated-to-saturated fat ratio, trans fat, glycemic index, and dietary cholesterol (a score of 5 was considered best; i.e. highest quintile of trans fat had a score of 0). Finally, healthy diet was defined as being in the upper 2 quintiles of the sex-specific dietary score derived above. To account for possible change in lifestyle behavior over time, we used a cumulative average over repeated assessments where available. For example, a subject with three body mass index assessments was assigned the average body mass index computed from the measurements collected prior to the occurrence of diabetes. The latter average was then used to classify subject into healthy vs. undesirable body weight.

Each subject could have a minimum of 0 and a maximum of 5 healthy lifestyle factors. Since only 248 (1.2%) men and 858 (2.3%) women were in the categories with 5 healthy lifestyle factors respectively, we collapsed the upper 2 categories to obtain stable estimates (subsequently referred to as the 4+ group). Thus, study participants were categorized according to the number of desirable lifestyle factors (0, 1, 2, 3, and 4+).

Statistical analyses

Because few subjects survived past age 90 lifetime risk estimates were calculated only through age 90. Each subject in the study sample was followed from baseline until either the year of a first DM event, the year of death, or attainment of age 90 years. The lifetime risk was calculated separately for the index age of 45, 50, 55, 60, 65, 70, 75, and 80 years. Risk estimates were produced using the Practical Incidence Estimators Macro which has been described in detail[18].

The calculation of lifetime risks was stratified by individual lifestyle factors and number of healthy lifestyle factors as described above. In a sensitivity analysis, we examined whether family history of DM modified the association in women (where information on family history of DM was available). All analyses were performed using SAS, version 9.1 (Cary, North Carolina) and the alpha level was set at 0.05. All p values were 2-sided.

Results

Characteristics

During an average follow-up of 22.6 years in men and 13.0 y in women, 2096 (10%) men and 2390 women (6.5%) developed DM. Their baseline characteristics according to the number of healthy lifestyle factors are presented in Tables 1 and 2.

Overall residual lifetime risk of DM

At age 45, the residual lifetime risk of DM was 15.7% (95% CI: 15.0% to 16.4%) in men and 16.3 % (95% CI: 15.3% to 17.2%) in women (Online Table 1). The residual lifetime risk declined with aging in both sexes (Online Table 1).

Lifestyle factors and residual lifetime risk of DM

Assessed individually, maintaining a normal weight had the strongest association with residual lifetime risk of DM while smoking had the weakest association in both genders (Online Table 2). Using cumulative updating to account for change in lifestyle factors over time yielded similar estimates (data not presented).

There was evidence for an inverse and graded relation between the number of healthy lifestyle factors and residual lifetime risk of DM in either gender (Figure 1) with the lowest lifetime risk of DM observed in subjects adhering to 4+ healthy lifestyle factors (7.3% [5.7% to 8.9%] for men and 6.4% [4.2% to 8.6%] for women). We observed similar relations between lifestyle factors and residual lifetime risk of DM in women with and without a family history of DM. In women without a family history of DM, residual lifetime risk of DM was 23.7 % (95% CI: 20.6% to 26.8%) for women who adhered to none of the healthy behaviors; 19.6% (95% CI: 16.6% to 22.5%) in those adhering to 1 healthy behavior; 11.3% (95% CI: 9.7% to 12.8%) for those adhering to 2 healthy behaviors; 8.8% (95% CI: 6.7% to 10.9%) for women with 3 healthy behaviors; and 3.9% (95% CI: 1.9% to 6.0%) in women with 4+ healthy lifestyle factors. For women with a positive family history of DM, corresponding values were 36.3% (95% CI: 32.2% to 40.3%), 22.5% (95% CI: 19.1% to 25.8%), 20.4% (95% CI: 16.3% to 24.5%), and 14.4% (95% CI: 8.2% to 20.6%) for women with 1, 2, 3, and 4+ healthy lifestyle factors; there were not enough events among women with no healthy lifestyle factor for a stable estimate.

Discussion

In this prospective cohort of male and female health care professionals, we estimated that at age 45, about 1 in 6 men or women will develop diabetes in their remaining lifetimes. This

risk declined with aging to reach 1 in 10 at age 65 and about 1 in 17 at age 75. Examined individually, smoking was least associated with the residual lifetime risk of diabetes whereas adiposity had the most influence. There was an inverse and graded relation between the number of healthy lifestyle factors and residual lifetime risk of diabetes in both genders. The residual lifetime risk was about 1 in 3 in the absence of any of the five healthy lifestyle factors examined and was lowest in the presence of 4+ healthy lifestyle factors (about 1 in 13 in men and 1 in 15 for women).

Our data are consistent with a previous report from the general US population in which the lifetime risk of DM at age 40 was 25.3 % (95% CI: 23.0% to 28.1%) for white men, 27.7% (95% CI: 25.4% to 30.4%) for white women, and above 40% for minority populations[19]. Since most of our participants were Caucasians, we were unable to estimate the lifetime risk of DM in non-white subjects in our cohort. Our finding that the largest difference in residual lifetime risk of DM was observed with adiposity is consistent with the data from the National Health Interview Survey on 780,694 US subjects (1997–2004) which showed a positive and graded relation between severity of adiposity and residual lifetime risk of DM[20]. In addition, our results are in line with the Look AHEAD trial reporting beneficial effects of intensive lifestyle intervention on weight loss and cardiometabolic factors as well as glycemic control[21]. Other randomized control trials reported favorable effects of healthy diet or exercise on the risk of DM. The Indian Diabetes Prevention Program showed that a lifestyle modification (diet and exercise) resulted in a reduced risk of DM compared with the control group (they needed to treat 6 people in order to prevent a case of DM)[4]. Furthermore, the US Diabetes Prevention Program showed that lifestyle intervention centered on weight loss, physical activity, and proper diet led to a 34% reduction in incident DM after 10 years of follow up compared to placebo[10]. Likewise, the China Da Qing Diabetes Prevention Study showed that an intervention based on exercise, increased intake of vegetables and decreased consumption of sugar and alcohol led to a 43% reduction in DM risk compared to placebo after 20 years of follow up[8]. An intervention with a Mediterranean diet led to a 50% reduction in DM risk compared with the control group after 4 years of follow up[22] and after 7 years of follow up, the number needed to treat by lifestyle intervention (diet and exercise) to prevent one case of DM was 22 per year in obese subjects with impaired glucose tolerance test[23]. The fact that moderate drinkers had a lower lifetime risk of DM than never drinkers or abusers and male smokers had a higher risk of DM than never smokers suggest that these 2 modifiable factors could add incremental benefit to exercise, diet, and weight control. This hypothesis is consistent with the lowest risk of DM in the group with the most number of desirable factors.

All factors examined in our study (physical activity, smoking, diet, moderate drinking, and adiposity) have been individually related to diabetes in previous studies and numerous biologic mechanisms that may explain these benefits have been proposed. Improvement of weight and insulin resistance and glucose transport, attenuation of inflammation, modulation of adiponectin, reduction in hemoglobin A1c[24], and lowering of free fatty acids[25] appear to be major paths by which these modifiable factors may lower the lifetime risk of DM. Exercise has been associated with lower A1c[24], increased insulin sensitivity[26]. A 12-week trial reported weight loss with a comprehensive lifestyle intervention[27]. Human randomized trials have demonstrated that moderate alcohol consumption improved insulin sensitivity[28] and increased plasma levels of adiponectin[28]. Likewise, weight reduction[29] and dietary intervention[30] have been associated with improved insulin sensitivity.

Our study has several limitations that merit discussion. First, DM ascertainment in this study was primarily achieved through self-report. Despite excellent agreement in validation studies in both PHS I and WHS, we cannot exclude the possibility of case misclassification.

In particular, under-reporting of impaired glucose metabolism due to the lack of frequent regular blood tests may have led to an underestimation of the lifetime risk in this population. In addition, we may have missed some cases of DM, especially among older subjects with several chronic conditions where diagnoses may carry different weight and may not appear on the discharge summary. We were unable to distinguish between type 1 and type 2 diabetes, although the majority of our cases are more likely to be type 2 DM given their age at onset. Second, we relied on self-reported data to ascertain modifiable lifestyle factors. However, since we used this information for ranking, it is less likely that a self-report bias may have led to misclassification in ranking (for example, so that one person moves from one extreme to another). Third, we did not have repeated measures on the food frequency questionnaire in women to update dietary habits over time. Since the cumulative update of other factors had no effects except for stronger results with exercise, it is reasonable to infer that our effect measure with dietary factors in women is conservative. In particular, we did not have details on dietary information in men at baseline for a comprehensive evaluation of diet. Fourth, given the fact that our study population was mostly Caucasians from a highly selective group of male physicians or female healthcare professionals, the generalizability of our findings is limited. Lastly, our participants were members of two completed randomized trials, suggesting that we cannot exclude volunteer bias in our data.

On the other hand, the large sample size, the lengthy follow-up period, the availability of repeated measures on several lifestyle factors to allow cumulative exposure assessment, the standardized methods for data collection in both cohorts, wide range of body mass index and non-exclusion of subjects with normal glucose tolerance test, and the robustness of the findings in sensitivity analyses are major strengths of this paper.

In conclusion, our data suggest that desirable modifiable lifestyle factors such as regular exercise, normal body weight, healthy diet, moderate drinking, and not smoking are jointly associated with a lower residual lifetime risk of DM in a graded fashion for both men and women, regardless of adiposity and glucose tolerance status. Addition of not smoking and moderate drinking may have an incremental benefit beyond the effects of weight loss, exercise, and diet in preventing DM.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics--2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2009; 119:e21–181. [PubMed: 19075105]
2. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC Public Health*. 2009; 9:88. [PubMed: 19320986]
3. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002; 346:393–403. [PubMed: 11832527]

4. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia*. 2006; 49:289–97. [PubMed: 16391903]
5. Pietraszek A, Gregersen S, Hermansen K. Alcohol and type 2 diabetes. A review. *Nutr Metab Cardiovasc Dis*. 2010; 20:366–75. [PubMed: 20556883]
6. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA*. 2007; 298:2654–64. [PubMed: 18073361]
7. Mozaffarian D, Kamineni A, Carnethon M, Djousse L, Mukamal KJ, Siscovick D. Lifestyle risk factors and new-onset diabetes mellitus in older adults: the cardiovascular health study. *Arch Intern Med*. 2009; 169:798–807. [PubMed: 19398692]
8. Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet*. 2008; 371:1783–9. [PubMed: 18502303]
9. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N.Engl.J Med*. 2001; 344:1343–50. [PubMed: 11333990]
10. Knowler WC, Fowler SE, Hamman RF, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet*. 2009; 374:1677–86. [PubMed: 19878986]
11. Final report on the aspirin component of the ongoing Physicians' Health Study. Steering Committee of the Physicians' Health Study Research Group. *N.Engl.J Med*. 1989; 321:129–35. [PubMed: 2664509]
12. Lee IM, Cook NR, Gaziano JM, et al. Vitamin E in the primary prevention of cardiovascular disease and cancer: the Women's Health Study: a randomized controlled trial. *JAMA*. 2005; 294:56–65. [PubMed: 15998891]
13. Ding EL, Song Y, Manson JE, Pradhan AD, Buring JE, Liu S. Accuracy of administrative coding for type 2 diabetes in children, adolescents, and young adults. *Diabetes Care*. 2007; 30:e98. [PubMed: 17726188]
14. Lee, I-M.; Paffenbarger, RS, Jr.. Design of present-day epidemiologic studies of physical activity and health. In: Lee, I-M., editor. *Epidemiologic methods in physical activity studies*. Oxford University Press; New York, NY: 2009.
15. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol*. 1985; 122:51–65. [PubMed: 4014201]
16. Djousse L, Gaziano JM, Buring JE, Lee IM. Egg Consumption and Risk of Type 2 Diabetes in Men and Women. *Diabetes Care*. 2009; 32:295–300. [PubMed: 19017774]
17. Djousse L, Driver JA, Gaziano JM. Relation between modifiable lifestyle factors and lifetime risk of heart failure. *JAMA*. 2009; 302:394–400. [PubMed: 19622818]
18. Beiser A, D'Agostino RB Sr, Seshadri S, Sullivan LM, Wolf PA. Computing estimates of incidence, including lifetime risk: Alzheimer's disease in the Framingham Study. The Practical Incidence Estimators (PIE) macro. *Stat Med*. 2000; 19:1495–522. [PubMed: 10844714]
19. Narayan KM, Boyle JP, Thompson TJ, Sorensen SW, Williamson DF. Lifetime risk for diabetes mellitus in the United States. *JAMA*. 2003; 290:1884–90. [PubMed: 14532317]
20. Narayan KM, Boyle JP, Thompson TJ, Gregg EW, Williamson DF. Effect of BMI on lifetime risk for diabetes in the U.S. *Diabetes Care*. 2007; 30:1562–6. [PubMed: 17372155]
21. Wing RR. Long-term effects of a lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes mellitus: four-year results of the Look AHEAD trial. *Arch.Intern.Med*. 2010; 170:1566–75. [PubMed: 20876408]
22. Salas-Salvado J, Bullo M, Babio N, et al. Reduction in the incidence of type 2 diabetes with the Mediterranean diet: results of the PREDIMED-Reus nutrition intervention randomized trial. *Diabetes Care*. 2011; 34:14–9. [PubMed: 20929998]
23. Lindstrom J, Ilanne-Parikka P, Peltonen M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet*. 2006; 368:1673–9. [PubMed: 17098085]

24. Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. *JAMA*. 2001; 286:1218–27. [PubMed: 11559268]
25. O'Neill M, Watt MJ, Heigenhauser GJ, Spriet LL. Effects of reduced free fatty acid availability on hormone-sensitive lipase activity in human skeletal muscle during aerobic exercise. *J Appl.Physiol*. 2004; 97:1938–45. [PubMed: 15208282]
26. Kirwan JP, Solomon TP, Wojta DM, Staten MA, Holloszy JO. Effects of 7 days of exercise training on insulin sensitivity and responsiveness in type 2 diabetes mellitus. *Am J Physiol Endocrinol.Metab*. 2009; 297:E151–E156. [PubMed: 19383872]
27. Lim SS, Norman RJ, Clifton PM, Noakes M. The effect of comprehensive lifestyle intervention or metformin on obesity in young women. *Nutr Metab Cardiovasc Dis*. 2011; 21:261–8. [PubMed: 20163941]
28. Joosten MM, Beulens JW, Kersten S, Hendriks HF. Moderate alcohol consumption increases insulin sensitivity and ADIPOQ expression in postmenopausal women: a randomised, crossover trial. *Diabetologia*. 2008; 51:1375–81. [PubMed: 18504547]
29. Vitola BE, Deivanayagam S, Stein RI, et al. Weight loss reduces liver fat and improves hepatic and skeletal muscle insulin sensitivity in obese adolescents. *Obesity (Silver.Spring)*. 2009; 17:1744–8. [PubMed: 19498349]
30. Kim H, Stote KS, Behall KM, Spears K, Vinyard B, Conway JM. Glucose and insulin responses to whole grain breakfasts varying in soluble fiber, beta-glucan: a dose response study in obese women with increased risk for insulin resistance. *Eur.J Nutr*. 2009; 48:170–5. [PubMed: 19205780]

Fig 1.
Relation between baseline lifestyle factors and residual lifetime risk of diabetes at age 45

Table 1
 Characteristics of 20,915 men (Physicians' Health Study) by healthy lifestyle factors*

Characteristics	Number of healthy lifestyle factors				
	0 (N=1,465)	1 (N=4,745)	2 (N=6,988)	3 (N=5,432)	4+ (N=2,285)
Age (y)	53.4±8.6	53.3±8.9	53.6±9.5	53.5±9.8	53.8±10.0
Body mass index (kg/m ²)	27.6±2.5	26.2±2.8	24.7±2.6	23.6±2.0	23.0±1.5
Healthy diet (%)	0	6.1	16.8	38.3	78.9
Moderate drinking (%)	0	11.9	23.8	32.8	53.2
Never smokers (%)	0	28.2	48.2	67.6	87.0
Exercise 2+ times/week (%)	0	26.1	53.0	77.8	95.2

* Healthy lifestyle factors include never smoking, moderate alcohol consumption (1+ drink per day), regular exercise (2+ times per week of vigorous exercise), healthy diet, and normal weight (BMI below 25 kg/m²)

Table 2
 Characteristics of 36,594 women (Women's Health Study) by healthy lifestyle factors*

Characteristics	Number of healthy lifestyle factors				
	0 (N=2,639)	1 (N=8,746)	2 (N= 11,406)	3 (N=8,807)	4+ (N=4,996)
Age (y)	54.1±6.4	54.3±6.7	54.6±7.1	54.9±7.2	54.7±7.2
Body mass index (kg/m ²)	30.5±4.9	28.1±5.2	25.8±4.7	24.1±3.8	22.7±2.5
Postmenopausal (%)	53.7	54.3	53.5	55.3	54.0
Energy intake (kcal)	1703±544	1716±552	1722±532	1731±524	1761±509
Exercise (kcal/week)	247±226	483±793	864±1138	1338±1360	1822±1360
Healthy diet (%)	0	10.2	29.1	56.8	83.8
Moderate drinking (%)	0	14.9	32.9	49.0	73.9
Never smokers (%)	0	37.4	52.5	61.8	79.9

* Healthy lifestyle factors includes never smoking, moderate alcohol consumption (from 1 drink/week to 1 drink per day), regular exercise (upper 2 quintiles of MET-h/week), healthy diet score, and normal weight (BMI below 25 kg/m²)