Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplementary Appendix

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- Table S8. Pooled Hazard Ratios (95% Confidence Intervals) for Association between Smoking Cessation and Type 2 Diabetes Incidence, Cardiovascular Disease Mortality, and All-Cause Mortality with Missing Covariates Imputed Using Multiple Imputation Procedures.

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Text 1. Study Population.

The Nurses' Health Study (NHS) was established in 1976 when 121,700 female registered nurses aged 30-55 were recruited. The NHSII cohort was initiated in 1989 and included 116,340 women aged 25-42 years. The Health Professionals Follow-Up Study (HPFS) began in 1986 and enrolled 51,529 male health professionals aged 40-75 years. The response rates exceeded 90% in each two-year cycle in all three cohorts.

Text 2. Defining the Time Window for Weight Gain upon Smoking Cessation.

We performed a multivariate-adjusted linear mixed-effect model to calculate the least squares means of biennial weight change by smoking cessation duration (Figure attached below). In this analysis, participants were censored at 65 years or older. On average, quitters gained 2.74 kg in the first 2 years, 1.33 kg by 4 years, and 0.98 kg by 6 years, and the weight gain trajectory largely overlapped with that of never smokers thereafter. Based on these results, we chose 6 years as a conservative cutoff point to define the time period of weight change relevant to smoking cessation.

Figure. Weight Change Trajectories among Incident Smoking Quitters and Never Smokers
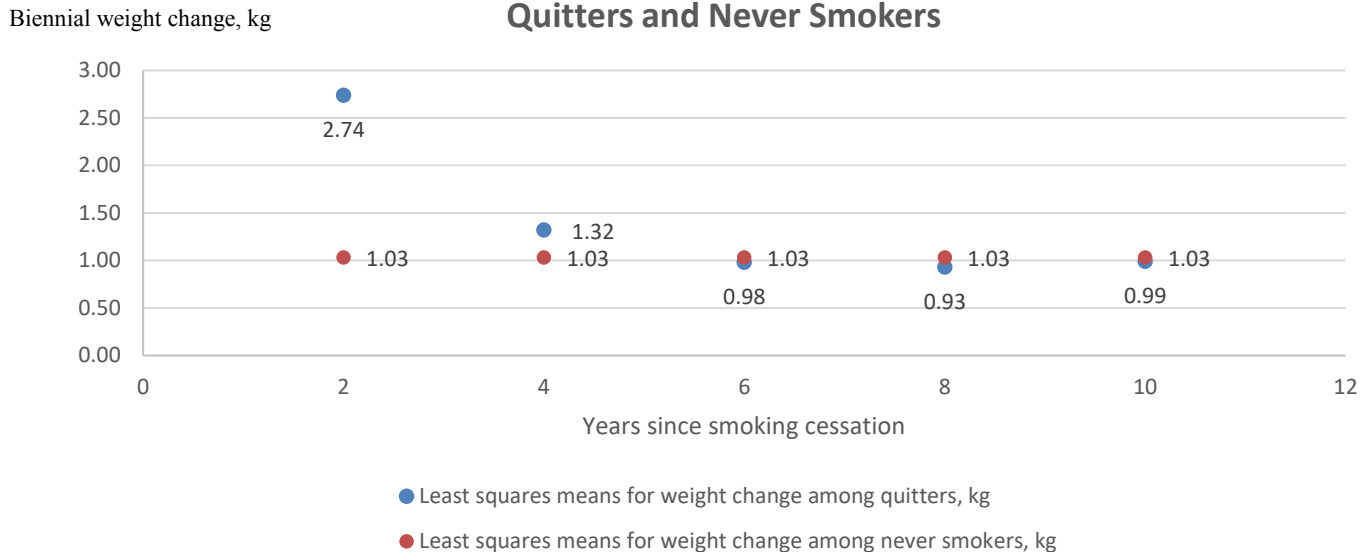
Text 3. The Confirmation of Self-Reported Type 2 Diabetes Diagnoses.

Participants who reported a diabetes diagnosis were mailed a supplementary questionnaire regarding symptoms, diagnostic tests, and hypoglycemic therapy. For cases diagnosed before 1998, type 2 diabetes (T2D) was confirmed if participants met at least one of the following National Diabetes Data Group criteria[1]: (1) an elevated glucose concentration (fasting plasma glucose of 7.8 mmol/l, random plasma glucose of 11.1 mmol/l, or plasma glucose 11.1 mmol/l after an oral glucose load), and at least one symptom related to diabetes (excessive thirst, polyuria, weight loss, or hunger); (2) no symptoms, but elevated glucose concentrations on two occasions; and (3) treatment with insulin or other hypoglycemic medication. For cases of T2D identified after 1998, the cutoff point for elevated fasting plasma glucose concentrations was lowered to 7.0 mmol/l according to the American Diabetes Association (ADA) criteria. We further considered HbA1c ≥6.5% in the

diagnosis criteria for confirming T2D cases identified after January, 2010.[2] Validation studies in the NHS and HPFS demonstrated the validity of using our supplementary questionnaire to adjudicate T2D diagnosis: in the NHS, 61 of the 62 (98.4%) T2D cases confirmed by the questionnaire were reconfirmed through medical record review by an endocrinologist blinded to questionnaire information,[3] and in the HPFS, 57 of 59 (97%) cases were reconfirmed.[4]

Text 4. Multiple Imputation Procedure for Imputing Missing Values of Covariates.

We used the Markov Chain Monte Carlo (MCMC)-based method to impute missing values for four covariates: total energy, alcohol intake, alternative healthy eating index, and physical activity, before making categories of these variables. There were 3.0%-17.4% data with missing values in the type 2 diabetes analyses, and 3.0%-13.3% data with missing values in the mortality analyses. Balancing the computational capacity and relative efficiency, we imputed 4 times for the type 2 diabetes analyses and 3 times for the mortality analyses to achieve both relative efficiencies > 95%. To account for heterogeneity among three cohorts and between follow-up cycles, the imputation was stratified by both follow-up cycles and cohort origins. Variables, including age in months, smoking status (never smokers, past smokers, or current smokers), hypertension (yes or no), hypercholesterolemia (yes or no), family history of diabetes (yes or no), multivitamin use (yes or no), and baseline BMI (continuous and quadratic), were included as covariates in the multiple imputation models. The beta coefficients estimated from imputed datasets were averaged and exponentiated to calculate the hazard ratios, and 95% confidence intervals were derived as well.

Text 5. Tests for Proportional Hazards Assumption.

We tested the proportional hazards assumption for two main exposure variables: smoking cessation by duration (current smoker, recent quitter, long-term quitter, and never smoker) and smoking cessation by both duration and weight changes in recent quitters (current smoker, recent quitter in the following weight change categories: ≤0 kg, 0.1-5.0 kg, 5.1-10.0 kg, and >10.0 kg, long-term quitter, and never smoker). For each study outcome, the product terms between each exposure indicator and log-transformed follow-up time were simultaneously included in the models. We did not detect any evidence of violations of this assumption, as P values from the Wald tests for the product terms were all greater than 0.05.

Text 6. Analyses of Associations of Diet Quality and Physical Activity Changes after Quitting in Relation to Biennial Weight Changes.

A linear mixed-effect model with an unstructured correlation matrix was used to estimate the associations between changes in diet quality and physical activities after quitting and biennial weight change. The changes in diet quality and physical activities were categorized as decreased, no change, and increased, and we also estimated the biennial weight change per 10 points increase of AHEI or 10 METs increment of physical activities. The models were adjusted for age (in months, continuous), cohort (NHS, NHSII, or HPFS), sex (men or women), race (White, African American, Asian, or Other), baseline BMI (continuous and quadratic), alcohol intake (0, <5.0, 5.0-9.9, 10.0-14.9, 15.0-29.9, ≥30.0 g/d), hypertension (yes or no), hypercholesterolemia (yes or no), family history of diabetes (yes or no), multivitamin use (yes or no), and total energy intake (quintiles), and physical activity and AHEI were mutually adjusted for in all models. To avoid impacts of outliers, the data were truncated at 0.5th to 99.5th percentile of change of AHEI (-18 – 24 points), physical activities (-72 – 78 METs), and weight change (-17 – 18 kg). To minimize the influence of aging on weight change, participants ≥65 years old were excluded from this analysis.

Text 7. Test for Mediation Effects.

When estimating the mediating effects of 6-year weight change on the association between smoking cessation status and type 2 diabetes risk, we included smokers quitted for 6 consecutive years and current smokers. We

first fitted a model without weight change to examine the association between quitting status and type 2 diabetes risk. We then fitted a model with the adjustment of weight change variable. The mediation effects of weight change are estimated as the proportion of treatment effect explained: $(\hat{\beta}_1^* - \hat{\beta}_1)/\hat{\beta}_1^*$, where $\hat{\beta}_1^*$ and $\hat{\beta}_1$ are the estimates for the quitting status before and after adjustment for the weight change. Proportional hazards assumption was tested by including a product term between binary quitting status and log-transformed follow-up time. We did not find any evidence of violations of the proportional hazards assumption in the mediation analysis.

Text 8. Adjustment of Multiplicity Using False Discovery Rate.

Although our study had a pre-specified goal to examine the role of body weight change following smoking cessation in type 2 diabetes risk and mortality, a potential multiplicity issue may originate through examining multiple exposure categories and three correlated disease outcomes in one analysis. We estimated that there were altogether 22 comparisons (eight smoking status categories for type 2 diabetes analysis and seven smoking status categories for both cardiovascular and all-cause mortality analyses) needed to be adjusted for multiplicity. Due to the close relationships among type 2 diabetes, cardiovascular and total mortality, we choose the Benjamini-Hochberg method,[5] a less conservative approach to adjusting for multiple comparisons. We rejected the null hypothesis with false discovery rate (FDR) < 0.05, i.e., to find the largest k such that $P_{(k)} \leq \frac{k}{m}\alpha$ in each model, where m=22 and α=0.05. The statistically-significant associations after multiple comparison adjustment were marked in all tables.

References for supplementary text

1. Group NDD. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 1979;28(12):1039–57.
2. Committee PP, Classification A. Standards of medical care in diabetes—2010. Diabetes Care 2010;33(S1):S11–61.
3. Manson JE, Stampfer MJ, Colditz GA, et al. Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. Lancet 1991;338(8770):774–8.
4. Hu FB, Leitzmann MF, Stampfer MJ, Colditz G a, Willett WC, Rimm EB. Physical activity and television watching in relation to risk for type 2 diabetes mellitus in men. Arch Intern Med 2001;161(12):1542–8.
5. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J. R. Stat. Soc. B. 1995;57(1):289–300.

Figure S1. Prevalence (%) of Current, Past, and Never Smokers during Follow-Up in Nurses' Health Study (1984-2012), Nurses' Health Study II (1991-2013) and Health Professionals Follow-Up Study (1988-2012).

Nurses' Health Study

Current smokers Past smokers Never smokers Trend of past smokers prevalence Calender year

Nurses' Health Study II

Legend: Current smokers, Past smokers, Never smokers, Trend of past smokers prevalence, Calender year

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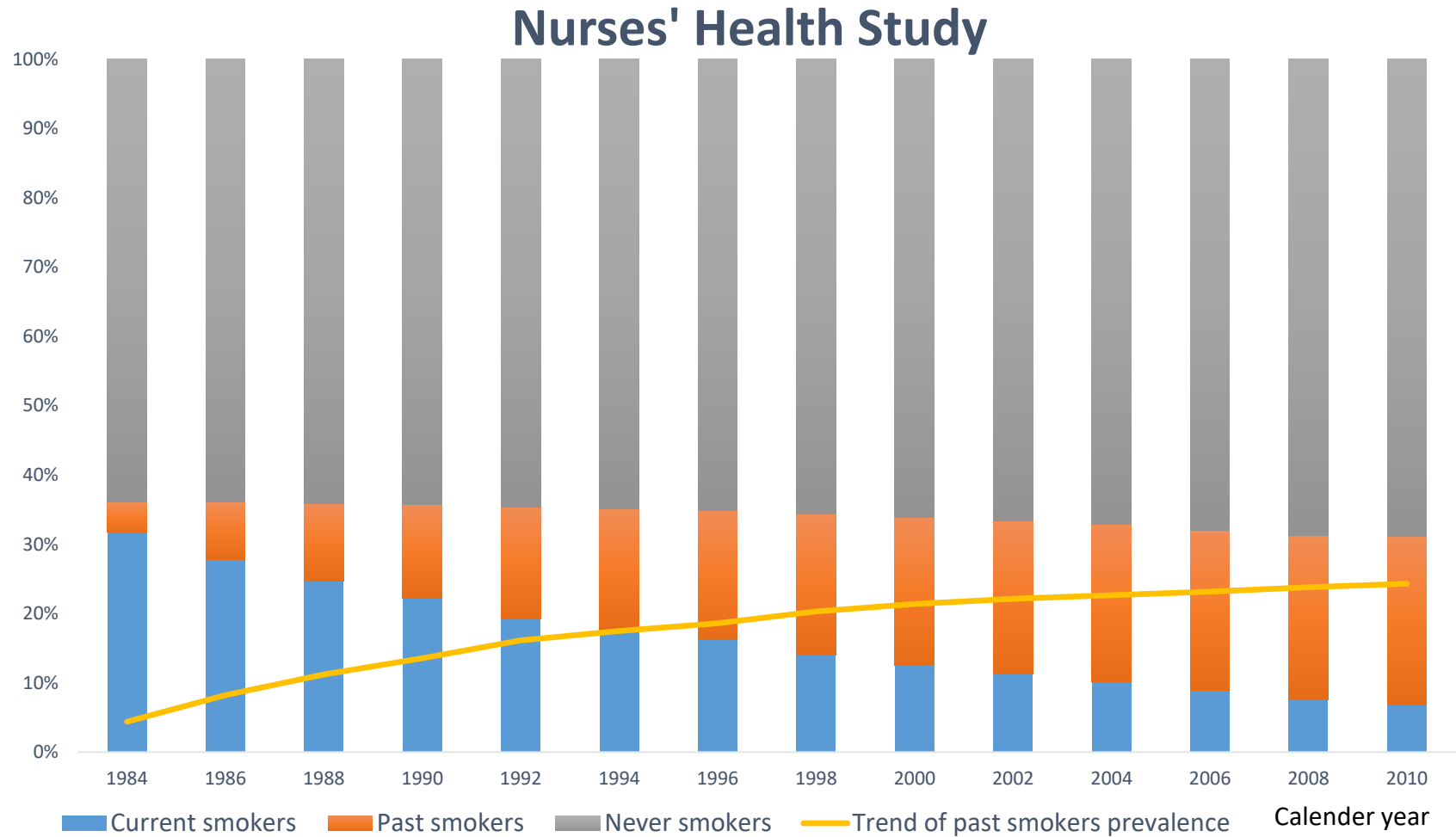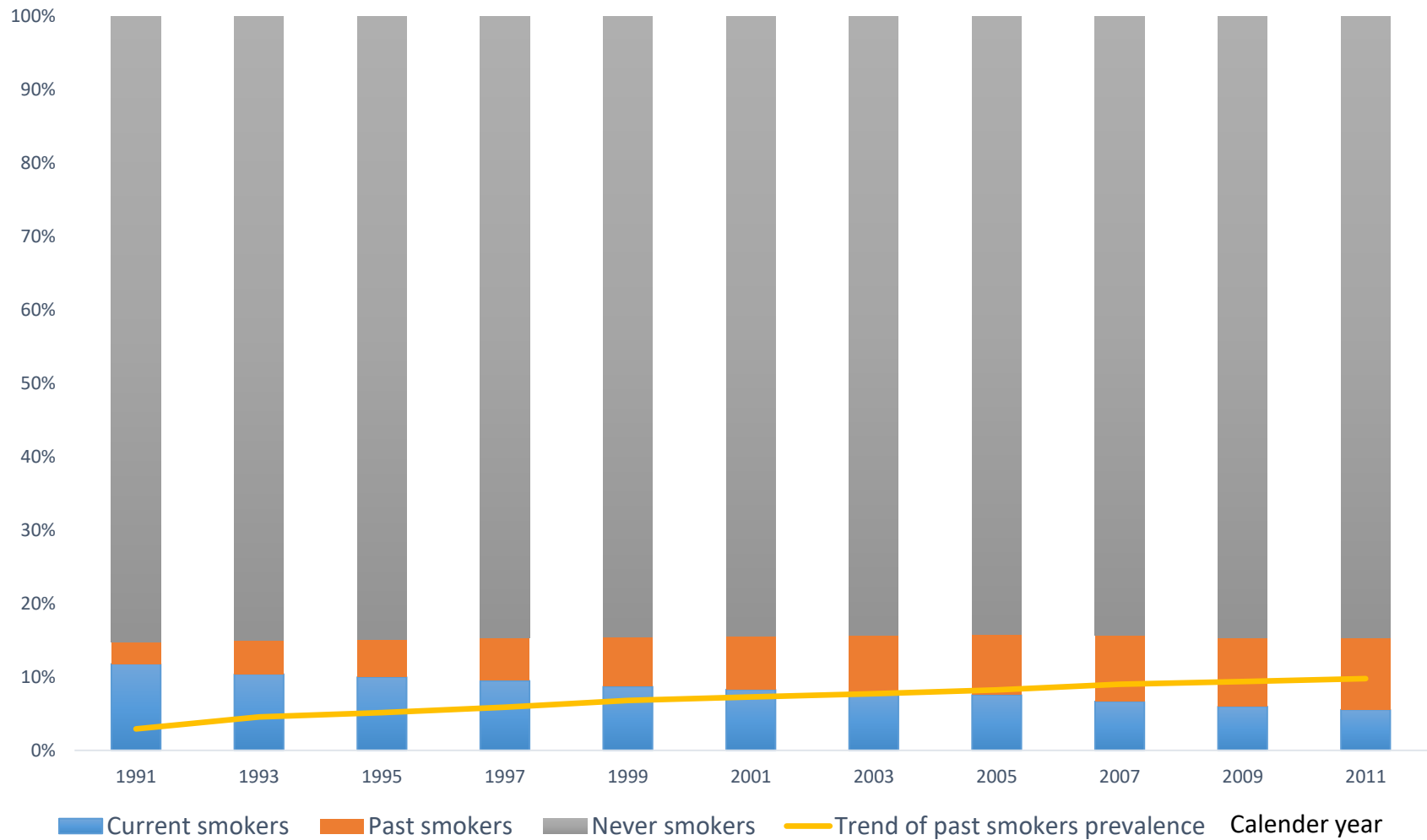
Health Professionals Follow-Up Study
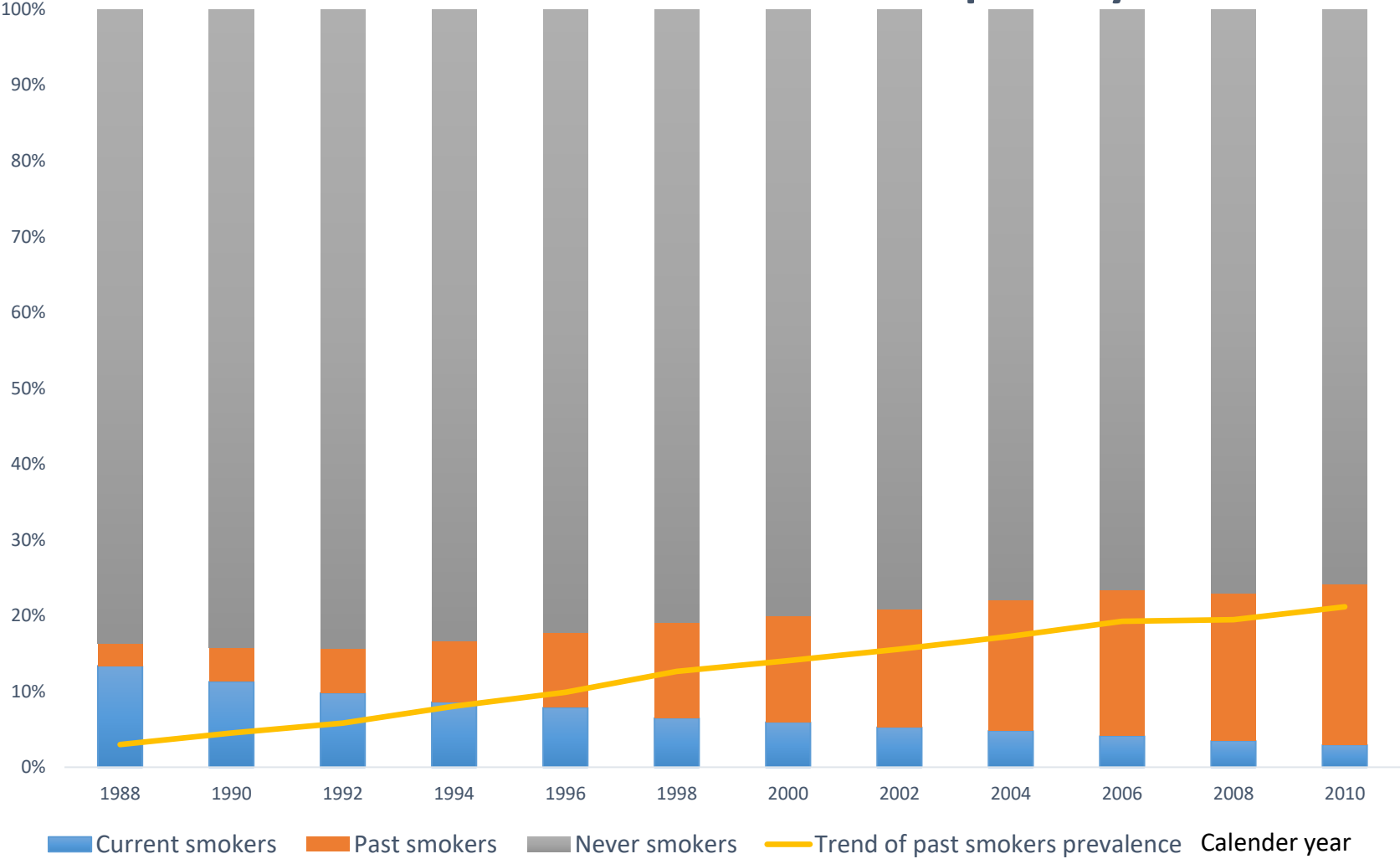
Figure S2. Associations between Smoking Cessation Duration and Risk of Type 2 Diabetes in Nurses' Health Study.
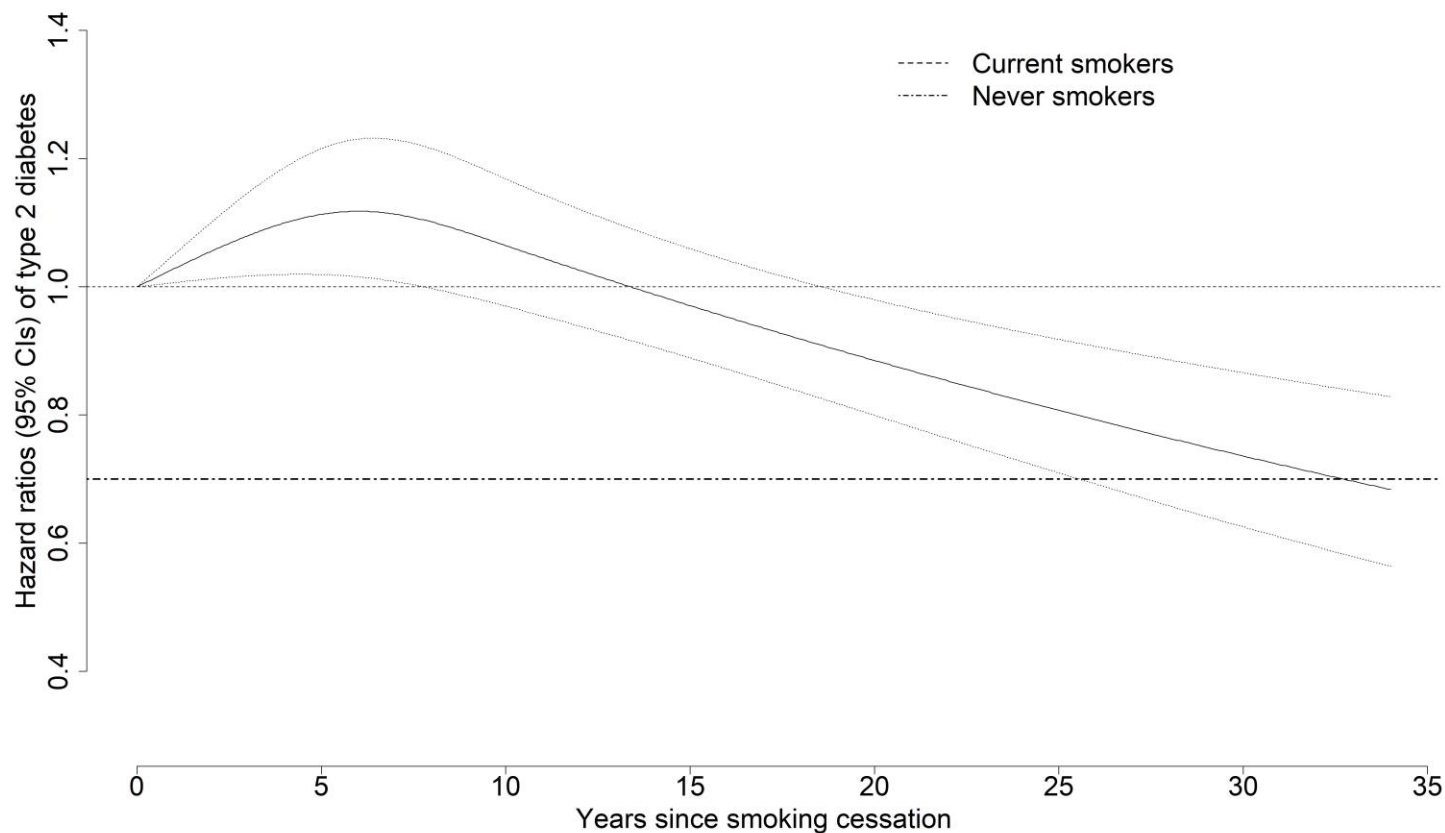
Multivariate analyses were adjusted for age (in months, continuous), race (White, African American, Asian, Other), physical activity (quintiles), baseline BMI (continuous and quadratic), alcohol intake (0, <5.0, 5.0-9.9,10.0-14.9,15.0-29.9, ≥30.0 g/d), history of hypertension (yes or no), history of hypercholesterolemia (yes or no), family history of diabetes (yes or no), multivitamin use (yes or no), Alternative Healthy Eating Index (quintiles), and total energy intake (quintiles).
Dotted lines represented 95% confidence intervals (CIs).

Figure S3. Three-Dimensional Illustrations of Type 2 Diabetes Risk, Cardiovascular Disease Mortality, and Total Mortality by Smoking Cessation Duration and Post-Cessation Weight Change in Comparison with Current Smokers.
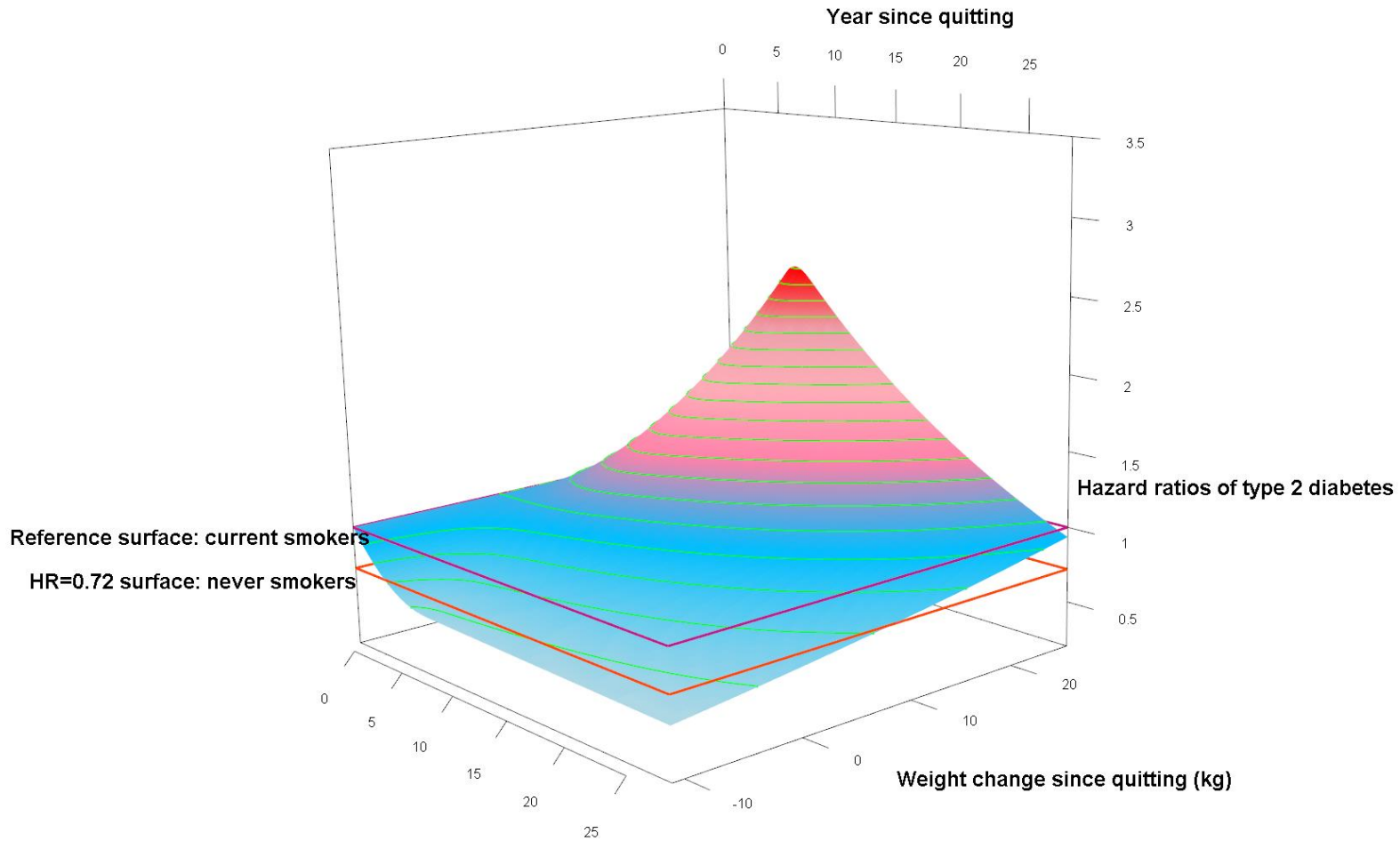
Panel A. Type 2 diabetes risk trajectory by smoking cessation duration and weight change. The blue-colored region maps the lower risk area, and the red-colored area stands for higher risk area. Green contour lines are used to enhance the visual perception of the relative altitude.

For type 2 diabetes analyses, weight change data were truncated at 1th percentile (-11 kg) and 99th (26 kg) percentile.

Multivariate analyses were adjusted for age (in months, continuous), cohort (NHS, NHSII, or HPFS), sex (men or women), race (White, African American, Asian, Other), physical activity (quintiles), baseline BMI (continuous and quadratic), alcohol intake (0, <5.0, 5.0-9.9, 10.0-14.9, 15.0-29.9, ≥30.0 g/d), history of hypertension (yes or no), history of hypercholesterolemia (yes or no), family history of diabetes (yes or no), multivitamin use (yes or no), Alternative Healthy Eating Index (quintiles), and total energy intake (quintiles).
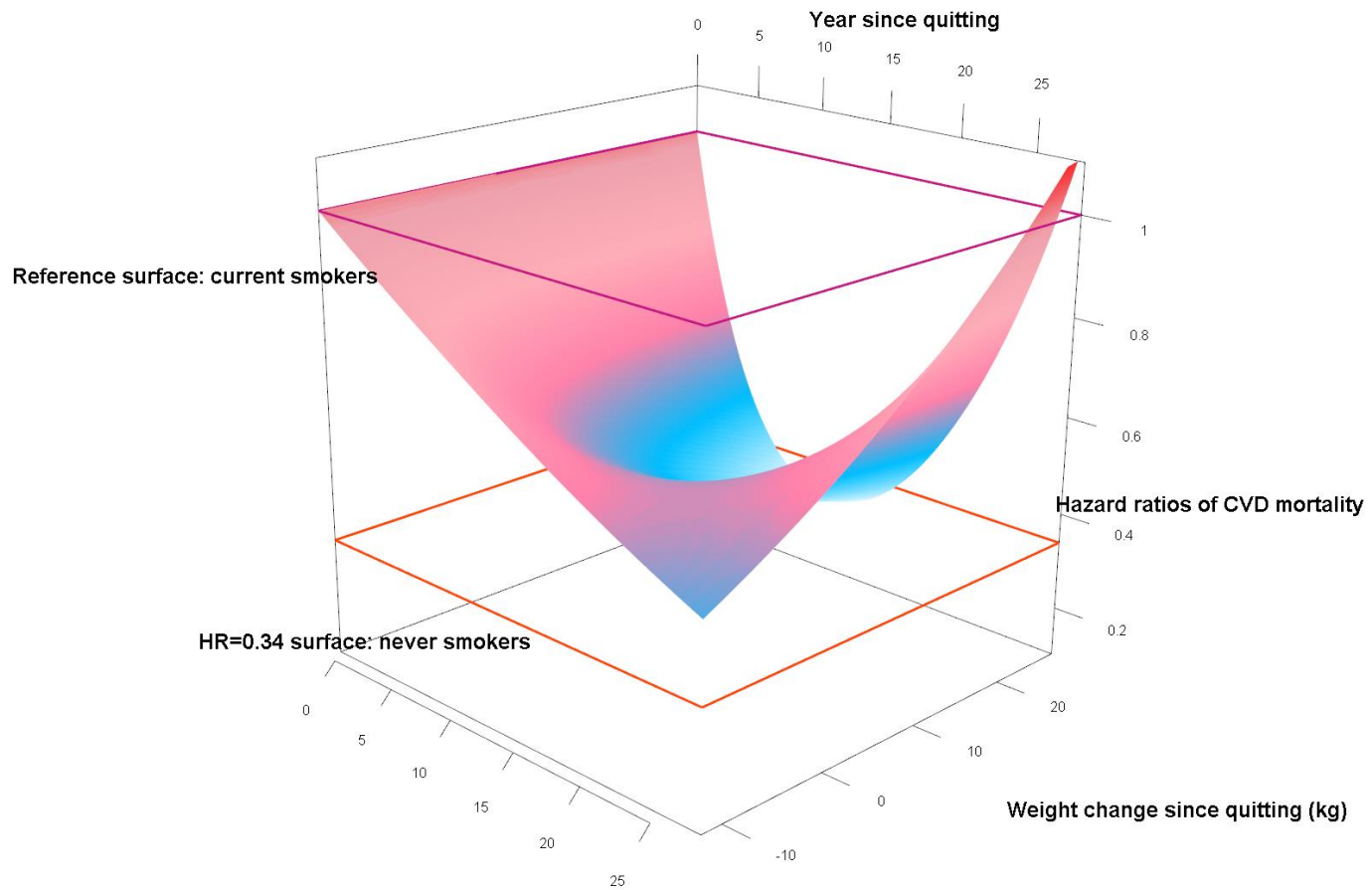
Panel B: Cardiovascular disease mortality by smoking cessation duration and weight change. The blue-colored region maps the lower risk area, and the red-colored area stands for higher risk area.
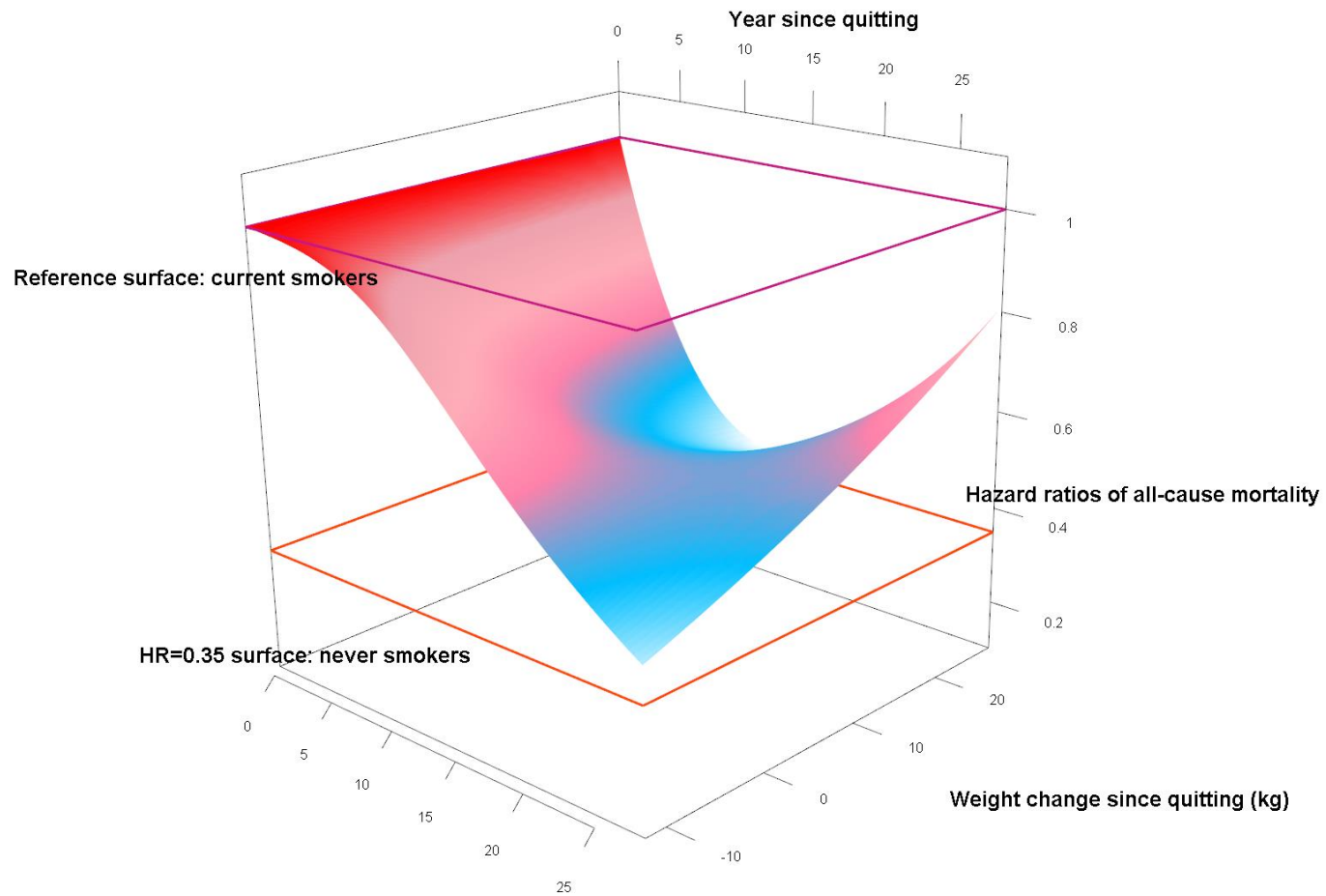
Panel C. Total mortality by smoking cessation and weight change. The blue-colored region maps the lower risk area, and the red-colored area stands for higher risk area.

For mortality analyses, weight change data were truncated at 1th percentile (-12 kg) and 99th (27 kg) percentile.

Multivariate analyses were adjusted for age (in months, continuous), cohort (NHS, NHSII, or HPFS), sex (men or women), race (White, African American, Asian, Other), physical activity (quintiles), baseline BMI (continuous and quadratic), alcohol intake (0, <5.0, 5.0-9.9, 10.0-14.9, 15.0-29.9, ≥30.0 g/d), history of hypertension (yes or no), history of hypercholesterolemia (yes or no), family history of diabetes (yes or no), family history of myocardial infarction (yes or no), multivitamin use (yes or no), Alternative Healthy Eating Index (quintiles), and total energy intake (quintiles).

Table S1. Illustration of Definition of Smoking Status and Smoking Cessation Status during Follow-Up.

	Follow-up cycles											Smoking cessation starting cycles	Smoking cessation duration, years	Recent quitting periods	Long-term quitting periods
	1	2	3	4	5	6	7	8	9	10	11				
Never smokers	N	N	N	N	N	N	N	N	N	N	N	-	-	-	-
Quitters who never relapsed	C	C	C	P	P	P	P	P	P	P	P	3	16	4-5	6-18
Quitters who relapsed	C	P	P	C	C	P	P	P	P	C	C	1 & 5	4 & 8	2-3 & 6-7	8-9
Transient quitters	C	C	C	C	P	C	C	P	C	C	C	-	-	-	-
Never smokers to smokers	N	N	N	N	C	C	C	C	C	C	C	-	-	-	-
Never smokers to smokers, and then to quitters who never relapsed	N	N	N	N	N	N	C	C	P	P	P	8	6	9-11	11
Never smokers to smokers, and then to quitters who relapsed	N	N	C	P	P	C	C	P	P	P	P	3 & 7	4 & 8	4-5 & 8-9	10-11
Current smokers	C	C	C	C	C	C	C	C	C	C	C	-	-	-	-

The letter C indicates current smokers, P for past smokers, and N for never smokers.
For the simplicity of illustration, all types of participants were assumed to be followed until the end of study.

Table S2. Age-Standardized Characteristics of Study Participants in Nurses' Health Study, Nurses' Health Study II, and Health Professionals Follow-Up Study for All-Cause Mortality Analyses.

		Recent quitters by weight change within 6 years of quitting						
	Current smokers	≤ 0 kg	0.1-5.0 kg	5.1-10.0 kg	>10.0 kg	Long-term quitters	Transient quitters	Never smokers
Person-years	519,569	39,386	53,815	30,826	20,616	253,822	11,927	2,994,849
Age (years)	56.0±11.5	56.0±11.2	54.3±10.9	53.9±10.5	51.9±10.3	63.5±10.8	50.5±10.6	54.2±12.6
Baseline body mass index (kg/m²)	24.5±4.6	24.8±4.8	23.5±3.8	24.5±4.2	26.4±5.4	24.7±4.9	24.1±4.2	24.9±4.9
Race								
- White, %	97.5	96.7	97.2	97.3	97.5	97.1	96.8	95.5
- African American, %	1.4	1.9	1.5	1.7	1.7	1.6	1.6	1.9
- Asian, %	0.6	0.5	0.7	0.6	0.3	0.6	0.8	1.3
- Others, %	0.6	0.8	0.6	0.5	0.4	0.7	0.7	1.3
Self-reported hypertension, %	27.3	28.2	24.4	27.9	33.8	33.6	22.5	28.9
Self-reported hypercholesterolemia, %	34.8	33.9	32.9	37.4	39.9	43.9	32.1	36.4
Family history of MI, %	30.3	28.6	28.1	29.6	30.5	30.2	29.9	31.3
Family history of diabetes	29.9	27.0	27.0	30.4	32.3	29.1	27.7	29.9
Multivitamin use, %	37.8	40.7	41.7	40.9	39.7	45.5	42.2	43.6
Physical activity (MET-h/wk)†	7.9(2.4-20.9)	12.5(4.0-28.7)	12.7(4.4-28.4)	10.2(3.4-23.7)	8.1(2.8-19.8)	12.2(3.9-27.8)	10.9(3.7-25.2)	12.9(4.4-28.7)
Alternative healthy eating index	47.8±9.6	51.0±9.9	50.7±9.9	49.6±9.6	49.0±9.4	51.9±9.5	49.9±9.7	51.0±10.2
Alcohol consumption (g/day)†	2.9(0.5-11.0)	3.4(0.7-10.4)	3.8(0.9-10.9)	2.8(0.6-9.2)	1.9(0.4-6.4)	3.3(0.7-9.8)	3.4(0.9-9.8)	1.0(0-4.2)
Total energy intake (Kcal/d)	1761±509	1746±494	1755±499	1749±496	1766±508	1779±477	1742±507	1819±504

Abbreviations: MI, myocardial infarction; MET, metabolic equivalent tasks.

Values are mean±SD for continuous variables or percentages for categorical variables. All values are standardized to the age distribution of the study population.

Person-years are based on all-cause mortality analyses.

†Values are median (interquartile range).

Table S3. Associations of Changes in Diet Quality and Physical Activity with 2-year Weight Changes (kg) after Smoking Cessation.

	No change	Decreased	Increased	Per 10 units increase
Alternative Healthy Eating Index	0 (Ref)	-0.05 (-0.14 to 0.04)	-0.41 (-0.51 to -0.32)	-0.26 (-0.32 to -0.21)
Physical activity, METs hours/week	0 (Ref)	0.10 (0.01 to 0.19)	-0.49 (-0.59 to -0.40)	-0.13 (-0.15 to -0.11)

Data were analyzed using mixed-effect models with unstructured correlations matrix.

Multivariate models were adjusted for age (in months, continuous), cohort (NHS, NHSII, or HPFS), sex (men or women), race (White, African American, Asian, Other), baseline BMI (continuous and quadratic), alcohol intake (0, <5.0, 5.0-9.9, 10.0-14.9, 15.0-29.9, ≥30.0 g/d), hypertension (yes or no), hypercholesterolemia (yes or no), family history of diabetes (yes or no), family history of myocardial infarction (yes or no), multivitamin use (yes or no), and total energy intake (quintiles).

Alternative Healthy Eating Index and physical activity levels were mutually adjusted.

Table S4. Pooled Hazard Ratios (95% CIs) for the Association between Smoking Cessation and Type 2 Diabetes Incidence, Cardiovascular Disease Mortality, and All-Cause Mortality Restricted to Participants with Complete Data of Smoking Status.

	Case/person-year	Age-adjusted	Baseline BMI-adjusted	Multivariable-adjusted
		Type 2 diabetes incidence		
Current smokers	1350/355,918	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤6 y)†	734/131,782	1.39 (1.27 to 1.53)§	1.30 (1.19 to 1.42)§	1.27 (1.16 to 1.39)§
- No weight gain	183/35,859	1.25 (1.07 to 1.46)§	1.07 (0.91 to 1.25)	1.06 (0.91 to 1.24)
- Weight gain 0.1-5.0 kg	192/49,327	0.98 (0.84 to 1.14)	1.17 (1.00 to 1.36)§	1.18 (1.01 to 1.37)§
- Weight gain 5.1-10.0 kg	176/28,153	1.56 (1.33 to 1.82)§	1.47 (1.25 to 1.72)§	1.39 (1.19 to 1.63)§
- Weight gain >10.0 kg	183/18,444	2.60 (2.23 to 3.04)§	1.67 (1.43 to 1.96)§	1.59 (1.36 to 1.87)§
Long-term quitters (>6 y)	1090/173,273	1.18 (1.09 to 1.28)§	1.06 (0.97 to 1.15)	1.04 (0.96 to 1.13)
Transient quitters	45/11,842	1.05 (0.77 to 1.41)	1.02 (0.76 to 1.39)	1.02 (0.75 to 1.38)
Never smokers	8535/2,390,937	0.93 (0.88 to 0.99)§	0.78 (0.73 to 0.83)§	0.73 (0.69 to 0.77)§
		Cardiovascular disease mortality‡		
Current smokers	1,257/467,270	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤6 y)†	85/137,239	0.30 (0.24 to 0.38)§	0.31 (0.25 to 0.38)§	0.34 (0.27 to 0.42)§
- No weight gain	38/36,245	0.42 (0.31 to 0.59)§	0.42 (0.30 to 0.58)§	0.46 (0.33 to 0.64)§
- Weight gain 0.1-5.0 kg	28/50,873	0.27 (0.18 to 0.39)§	0.28 (0.20 to 0.41)§	0.32 (0.22 to 0.47)§
- Weight gain 5.1-10.0 kg	9/29,142	0.17 (0.09 to 0.32)§	0.17 (0.09 to 0.32)§	0.18 (0.09 to 0.35)§
- Weight gain >10.0 kg	10/19,552	0.35 (0.19 to 0.66)§	0.32 (0.17 to 0.59)§	0.33 (0.17 to 0.61)§
Long-term quitters (>6 y)	560/237,343	0.46 (0.42 to 0.51)§	0.46 (0.41 to 0.51)§	0.50 (0.45 to 0.56)§
Never smokers	2,752/2,914,921	0.34 (0.32 to 0.37)§	0.31 (0.29 to 0.33)§	0.34 (0.32 to 0.36)§
		All-cause mortality‡		
Current smokers	5,571/463,424	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤6 y)†	549/136,842	0.43 (0.39 to 0.47)§	0.43 (0.40 to 0.47)§	0.48 (0.44 to 0.52)§
- No weight gain	232/36,077	0.57 (0.50 to 0.65)§	0.57 (0.50 to 0.65)§	0.62 (0.54 to 0.71)§
- Weight gain 0.1-5.0 kg	163/50,763	0.34 (0.29 to 0.40)§	0.36 (0.30 to 0.42)§	0.40 (0.35 to 0.47)§
- Weight gain 5.1-10.0 kg	87/29,069	0.35 (0.28 to 0.43)§	0.35 (0.28 to 0.44)§	0.38 (0.31 to 0.47)§
- Weight gain >10.0 kg	62/19,510	0.45 (0.35 to 0.58)§	0.43 (0.33 to 0.55)§	0.45 (0.35 to 0.57)§
Long-term quitters (>6 y)	2,855/235,263	0.51 (0.48 to 0.53)§	0.50 (0.48 to 0.53)§	0.57 (0.54 to 0.59)§
Never smokers	11,868/2,906,802	0.33 (0.32 to 0.34)§	0.32 (0.31 to 0.33)§	0.36 (0.34 to 0.37)§

Hazard ratios and 95% confidence intervals were estimated using the Cox proportional hazards model with adjustment for age (in months, continuous), cohort (NHS, NHSII, or HPFS), sex (men or women), race (White, African American, Asian, Other), physical activity (quintiles), baseline BMI (continuous and quadratic), alcohol intake (0, <5.0, 5.0-9.9, 10.0-14.9, 15.0-29.9, ≥30.0 g/d), hypertension (yes or no),

hypercholesterolemia (yes or no), family history of diabetes (yes or no), multivitamin use (yes or no), Alternative Healthy Eating Index (quintiles) and total energy intake (quintiles).

For cardiovascular disease mortality and all-cause mortality, both family history of diabetes (yes or no) and myocardial infarction (yes or no) were further adjusted.

†Stratification by weight changes among recent quitters. In this analysis stratified by weight change since quitting, 0.2% (n=5) cases and 0.4% person-time in all-cause mortality with missing data of weight change were removed from the stratified analyses, and therefore the total number of cases and person-time across weight change categories was smaller than that in the analyses of total recent quitters, in which subsequent weight change was not considered.

‡No cases among transient quitters for mortality analyses.

§FDR<0.05.

Table S5. Pooled Hazard Ratios (95% CIs) for the Association between Smoking Cessation and Type 2 Diabetes Incidence, Cardiovascular Disease Mortality, and All-Cause Mortality by Defining the Start of Cessation as the Cycle that Participants First Reported as Past Smokers.

	Case/person-year	Age-adjusted	Baseline BMI-adjusted	Multivariable-adjusted
		Type 2 diabetes incidence		
Current smokers	1,547/395,872	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤6 y)†	969/172,955	1.30 (1.20 to 1.42)§	1.21 (1.11 to 1.31)§	1.18 (1.08 to 1.28)§
- No weight gain	214/46,670	1.01 (0.88 to 1.17)	0.91 (0.78 to 1.05)	0.89 (0.77 to 1.03)
- Weight gain 0.1-5.0 kg	180/42,145	0.96 (0.82 to 1.12)	1.08 (0.93 to 1.27)	1.07 (0.92 to 1.26)
- Weight gain 5.1-10.0 kg	126/16,113	1.77 (1.48 to 2.13)§	1.56 (1.29 to 1.87)§	1.53 (1.27 to 1.84)§
- Weight gain >10.0 kg	91/7,898	2.78 (2.24 to 3.44)§	1.57 (1.26 to 1.95)§	1.43 (1.15 to 1.78)§
Long-term quitters (>6 y)	1,035/160,963	1.17 (1.08 to 1.27)§	1.04 (0.96 to 1.13)	1.03 (0.94 to 1.11)
Transient quitters	54/12,853	1.12 (0.85 to 1.48)	1.11 (0.84 to 1.46)	1.10 (0.84 to 1.45)
Never smokers	8,779/2,451,805	0.91 (0.86 to 0.96)§	0.77 (0.72 to 0.81)§	0.72 (0.68 to 0.76)§
		Cardiovascular disease mortality‡		
Current smokers	1,487/520,439	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤6 y)†	224/197,238	0.43 (0.37 to 0.49)§	0.43 (0.37 to 0.49)§	0.47 (0.40 to 0.54)§
- No weight gain	88/56,758	0.53 (0.43 to 0.66)§	0.52 (0.42 to 0.65)§	0.58 (0.46 to 0.72)§
- Weight gain 0.1-5.0 kg	44/49,182	0.35 (0.26 to 0.48)§	0.37 (0.28 to 0.51)§	0.42 (0.31 to 0.57)§
- Weight gain 5.1-10.0 kg	17/20,017	0.38 (0.24 to 0.62)§	0.38 (0.23 to 0.61)§	0.39 (0.24 to 0.63)§
- Weight gain >10.0 kg	9/10,372	0.51 (0.26 to 0.98)§	0.42 (0.22 to 0.82)§	0.43 (0.22 to 0.83)§
Long-term quitters (>6 y)	599/212,983	0.47 (0.43 to 0.52)§	0.46 (0.42 to 0.51)§	0.51 (0.46 to 0.56)§
Never smokers	3,181/3,003,966	0.34 (0.32 to 0.36)§	0.31 (0.29 to 0.33)§	0.34 (0.32 to 0.37)§
		All-cause disease mortality‡		
Current smokers	6,532/515,829	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤6 y)†	1,223/196,381	0.54 (0.50 to 0.57)§	0.54 (0.50 to 0.57)§	0.59 (0.55 to 0.63)§
- No weight gain	547/56,344	0.75 (0.69 to 0.82)§	0.75 (0.68 to 0.81)§	0.82 (0.76 to 0.90)§
- Weight gain 0.1-5.0 kg	227/49,019	0.41 (0.36 to 0.47)§	0.42 (0.37 to 0.48)§	0.48 (0.42 to 0.54)§
- Weight gain 5.1-10.0 kg	92/19,947	0.45 (0.37 to 0.56)§	0.45 (0.37 to 0.56)§	0.48 (0.39 to 0.59)§
- Weight gain >10.0 kg	53/10,337	0.63 (0.48 to 0.82)§	0.57 (0.43 to 0.75)§	0.60 (0.45 to 0.78)§
Long-term quitters (>6 y)	2,908/210,853	0.50 (0.48 to 0.52)§	0.49 (0.47 to 0.52)§	0.56 (0.53 to 0.58)§
Never smokers	13,198/2,994,849	0.32 (0.31 to 0.33)§	0.31 (0.30 to 0.32)§	0.35 (0.34 to 0.36)§

Hazard ratios and 95% confidence intervals were estimated using the Cox proportional hazards model with adjustment for age (in months, continuous), cohort (NHS, NHSII, or HPFS), sex (men or women), race (White, African American, Asian, Other), physical activity (quintiles), baseline BMI (continuous and quadratic), alcohol intake (0, <5.0, 5.0-9.9, 10.0-14.9, 15.0-29.9, ≥30.0 g/d), hypertension (yes or no), hypercholesterolemia (yes or no), family history of diabetes (yes or no), multivitamin use (yes or no), Alternative Healthy Eating Index (quintiles)

and total energy intake (quintiles).

For cardiovascular disease mortality and all-cause mortality, both family history of diabetes (yes or no) and myocardial infarction (yes or no) were further adjusted.

†Stratification by weight changes among recent quitters. In this analysis stratified by weight change since quitting, 2.9% (n=358) cases and 1.9% person-time in type 2 diabetes analysis, 1.2% (n=66) cases and 0.2% person-time in cardiovascular mortality analysis, and 1.3% (n=304) cases and 1.5% person time in all-cause mortality with missing data of weight change were removed from the stratified analyses, and therefore the total number of cases and person-time across weight change categories was smaller than that in the analyses of total recent quitters, in which subsequent weight change was not considered.

‡No cases among transient quitters for mortality analyses.

§FDR<0.05.

Table S6. Pooled Hazard Ratios (95% CIs) for the Association between Smoking Cessation and Type 2 Diabetes Incidence, Cardiovascular Disease Mortality, and All-Cause Mortality by Defining Recent Quitters as Quitting for Consecutive 2-8 years Rather than 2-6 years.

	Case/person-year	Age-adjusted	Baseline BMI-adjusted	Multivariable-adjusted
		Type 2 diabetes incidence		
Current smokers	1,547/395,872	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤8 y)†	1,037/184,988	1.29 (1.19 to 1.40)§	1.19 (1.10 to 1.29)§	1.16 (1.07 to 1.26)§
- No weight gain	233/44,123	1.19 (1.03 to 1.36)§	1.01 (0.88 to 1.16)	1.00 (0.87 to 1.15)
- Weight gain 0.1-5.0 kg	237/62,835	0.89 (0.77 to 1.02)	1.06 (0.93 to 1.22)	1.07 (0.93 to 1.23)
- Weight gain 5.1-10.0 kg	234/38,641	1.40 (1.22 to 1.61)§	1.35 (1.18 to 1.56)§	1.29 (1.12 to 1.49)§
- Weight gain >10.0 kg	286/27,979	2.44 (2.14 to 2.77)§	1.62 (1.42 to 1.84)§	1.53 (1.35 to 1.74)§
Long-term quitters (>8 y)	967/148,931	1.17 (1.08 to 1.27)§	1.04 (0.96 to 1.13)	1.03 (0.95 to 1.12)
Transient quitters	54/12,853	1.12 (0.85 to 1.47)	1.09 (0.83 to 1.44)	1.09 (0.83 to 1.44)
Never smokers	8,779/2,451,805	0.91 (0.86 to 0.96)§	0.77 (0.72 to 0.81)§	0.72 (0.68 to 0.76)§
		Cardiovascular disease mortality‡		
Current smokers	1488/524,182	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤8 y)†	224/197,305	0.43 (0.37 to 0.49)§	0.43 (0.37 to 0.49)§	0.47 (0.40 to 0.54)§
- No weight gain	89/47,970	0.61 (0.50 to 0.76)§	0.60 (0.49 to 0.75)§	0.67 (0.54 to 0.83)§
- Weight gain 0.1-5.0 kg	59/66,257	0.37 (0.28 to 0.48)§	0.40 (0.30 to 0.51)§	0.45 (0.34 to 0.58)§
- Weight gain 5.1-10.0 kg	27/41,072	0.31 (0.21 to 0.45)§	0.31 (0.21 to 0.45)§	0.33 (0.22 to 0.48)§
- Weight gain >10.0 kg	17/30,591	0.34 (0.21 to 0.54)§	0.30 (0.19 to 0.49)§	0.31 (0.19 to 0.50)§
Long-term quitters (>8 y)	599/213,148	0.47 (0.43 to 0.52)§	0.46 (0.42 to 0.51)§	0.51 (0.46 to 0.56)§
Never smokers	3181/3,003,966	0.34 (0.32 to 0.36)§	0.31 (0.29 to 0.33)§	0.34 (0.32 to 0.37)§
		All-cause disease mortality‡		
Current smokers	6537/519,569	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤8 y)†	1223/196,447	0.54 (0.50 to 0.57)§	0.54 (0.50 to 0.57)§	0.59 (0.56 to 0.63)§
- No weight gain	478/47,622	0.75 (0.68 to 0.82)§	0.74 (0.68 to 0.81)§	0.82 (0.74 to 0.90)§
- Weight gain 0.1-5.0 kg	318/66,052	0.45 (0.40 to 0.50)§	0.46 (0.41 to 0.52)§	0.53 (0.47 to 0.59)§
- Weight gain 5.1-10.0 kg	181/40,935	0.45 (0.39 to 0.52)§	0.46 (0.39 to 0.53)§	0.50 (0.43 to 0.58)§
- Weight gain >10.0 kg	129/30,498	0.53 (0.44 to 0.63)§	0.50 (0.42 to 0.60)§	0.52 (0.44 to 0.62)§
Long-term quitters (>8 y)	2909/211,018	0.50 (0.48 to 0.52)§	0.49 (0.47 to 0.52)§	0.56 (0.53 to 0.59)§
Never smokers	13,198/2,994,849	0.32 (0.31 to 0.33)§	0.31 (0.30 to 0.32)§	0.35 (0.34 to 0.37)§

Hazard ratios and 95% confidence intervals were estimated using the Cox proportional hazards model with adjustment for age (in months, continuous), cohort (NHS, NHSII, or HPFS), sex (men or women), race (White, African American, Asian, Other), physical activity (quintiles), baseline BMI (continuous and quadratic), alcohol intake (0, <5.0, 5.0-9.9, 10.0-14.9, 15.0-29.9, ≥30.0 g/d), hypertension (yes or no),

hypercholesterolemia (yes or no), family history of diabetes (yes or no), multivitamin use (yes or no), Alternative Healthy Eating Index (quintiles) and total energy intake (quintiles).

For cardiovascular disease mortality and all-cause mortality, both family history of diabetes (yes or no) and myocardial infarction (yes or no) were further adjusted.

†Stratification by weight changes among recent quitters. In this analysis stratified by weight change since quitting, 0.4% (n=42) cases and 0.4% person-time in type 2 diabetes analysis, 0.1% (n=28) cases and 0.3% person-time in cardiovascular mortality analysis, and 0.3% (n=93) cases and 0.3% person time in all-cause mortality with missing data of weight change were removed from the stratified analyses, and therefore the total number of cases and person-time across weight change categories was smaller than that in the analyses of total recent quitters, in which subsequent weight change was not considered.

‡No cases among transient quitters for mortality analyses.

§FDR<0.05.

Table S7. Pooled Hazard Ratios (95% CIs) for Association between Smoking Cessation and Type 2 Diabetes Incidence, Cardiovascular Disease Mortality, and All-Cause Mortality by Quartiles of Weight Change.

	Case/person-year	Age-adjusted	Baseline BMI-adjusted	Multivariable-adjusted
		Type 2 diabetes incidence		
Current smokers	1547/395,872	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤6 y)†	836/148,082	1.35 (1.24 to 1.47)§	1.25 (1.14 to 1.36)§	1.22 (1.12 to 1.32)§
- Q1 (≤0.9 kg)	216/40,204	1.26 (1.09 to 1.45)§	1.10 (0.96 to 1.28)	1.10 (0.95 to 1.27)
- Q2 (1.0-4.5 kg)	133/37,217	0.87 (0.73 to 1.04)	1.11 (0.93 to 1.33)	1.13 (0.94 to 1.35)
- Q3 (4.6-8.2 kg)	173/32,801	1.27 (1.08 to 1.48)§	1.28 (1.10 to 1.51)§	1.22 (1.04 to 1.44)§
- Q4 (>8.2 kg)	272/28,560	2.39 (2.10 to 2.72)§	1.65 (1.44 to 1.88)§	1.56 (1.37 to 1.79)§
Long-term quitters (>6 y)	1,168/185,838	1.15 (1.07 to 1.25)§	1.03 (0.96 to 1.12)	1.02 (0.94 to 1.10)
Transient quitters	54/12,853	1.12 (0.85 to 1.47)	1.09 (0.83 to 1.44)	1.09 (0.83 to 1.44)
Never smokers	8,779/2,451,805	0.91 (0.86 to 0.96)§	0.77 (0.72 to 0.81)§	0.72 (0.68 to 0.76)§
		Cardiovascular disease mortality‡		
Current smokers	1488/524,182	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤6 y)†	167/154,259	0.44 (0.37 to 0.51)§	0.44 (0.37 to 0.51)§	0.48 (0.41 to 0.56)§
- Q1 (≤0.9 kg)	72/42,487	0.62 (0.49 to 0.79)§	0.63 (0.49 to 0.79)§	0.69 (0.54 to 0.87)§
- Q2 (1.0-4.5 kg)	32/38,401	0.37 (0.26 to 0.53)§	0.40 (0.28 to 0.57)§	0.46 (0.32 to 0.65)§
- Q3 (4.6-8.2 kg)	20/34,055	0.29 (0.19 to 0.45)§	0.30 (0.19 to 0.46)§	0.32 (0.21 to 0.50)§
- Q4 (>8.2 kg)	15/30,259	0.31 (0.19 to 0.52)§	0.29 (0.17 to 0.48)§	0.29 (0.18 to 0.49)§
Long-term quitters (>6 y)	656/256,194	0.46 (0.42 to 0.51)§	0.46 (0.42 to 0.50)§	0.51 (0.46 to 0.56)§
Never smokers	3181/3,003,966	0.34 (0.32 to 0.36)§	0.31 (0.29 to 0.33)§	0.34 (0.32 to 0.37)§
		All-cause mortality‡		
Current smokers	6537/519,569	1 (reference)	1 (reference)	1 (reference)
Recent quitters (≤6 y)†	880/153,642	0.53 (0.49 to 0.57)§	0.53 (0.49 to 0.57)§	0.58 (0.54 to 0.62)§
- Q1 (≤0.9 kg)	372/42,227	0.72 (0.65 to 0.80)§	0.72 (0.65 to 0.80)§	0.79 (0.71 to 0.88)§
- Q2 (1.0-4.5 kg)	171/38,293	0.44 (0.38 to 0.52)§	0.46 (0.40 to 0.54)§	0.53 (0.45 to 0.61)§
- Q3 (4.6-8.2 kg)	136/33,948	0.44 (0.37 to 0.52)§	0.45 (0.38 to 0.53)§	0.49 (0.41 to 0.58)§
- Q4 (>8.2 kg)	108/30,178	0.47 (0.39 to 0.57)§	0.45 (0.37 to 0.54)§	0.47 (0.39 to 0.57)§
Long-term quitters (>6 y)	3,252/253,822	0.50 (0.48 to 0.53)§	0.50 (0.48 to 0.52)§	0.57 (0.54 to 0.59)§
Never smokers	13,198/2,994,849	0.32 (0.31 to 0.33)§	0.31 (0.30 to 0.32)§	0.35 (0.34 to 0.37)§

Hazard ratios and 95% confidence intervals were estimated using the Cox proportional hazards model with adjustment for age (in months, continuous), cohort (NHS, NHSII, or HPFS), sex (men or women), race (White, African American, Asian, Other), physical activity (quintiles), baseline BMI (continuous and quadratic), alcohol intake (0, <5.0, 5.0-9.9, 10.0-14.9, 15.0-29.9, ≥30.0 g/d), hypertension (yes or no), hypercholesterolemia (yes or no), family history of diabetes (yes or no), multivitamin use (yes or no), Alternative Healthy Eating Index (quintiles) and total energy intake (quintiles).

For cardiovascular disease mortality and all-cause mortality, both family history of diabetes (yes or no) and myocardial infarction (yes or no) were further adjusted.

†Stratification by weight changes among recent quitters. In this analysis stratified by weight change since quitting, 0.3% (n=42) cases and 0.3% person-time in type 2 diabetes analysis, 0.1% (n=28) cases and 0.2% person-time in cardiovascular mortality analysis, and 0.4% (n=93) cases and 0.3% person time in all-cause mortality with missing data of weight change were removed from the stratified analyses, and therefore the total number of cases and person-time across weight change categories was smaller than that in the analyses of total recent quitters, in which subsequent weight change was not considered.

‡No cases among transient quitters for mortality analyses.

§FDR<0.05.

Table S8. Pooled Hazard Ratios (95% Confidence Intervals) for Associations between Smoking Cessation and Type 2 Diabetes Incidence, Cardiovascular Disease Mortality, and All-Cause Mortality with Missing Covariates Imputed Using Multiple Imputation Procedures.

	Case/person-year	Multivariable-adjusted,† original	Multivariable-adjusted,† multiple imputation
		Type 2 diabetes incidence	
Current smokers	1,547/395,872	1 (reference)	1 (reference)
Recent quitters (≤6 y)‡	836/148,082	1.22 (1.12 to 1.32)¶	1.21 (1.11 to 1.32)¶
- No weight gain	204/37,444	1.08 (0.93 to 1.26)	1.00 (0.87 to 1.15)
- Weight gain 0.1-5.0 kg	206/52,147	1.15 (0.99 to 1.33)	1.14 (0.98 to 1.32)
- Weight gain 5.1-10.0 kg	188/29,767	1.36 (1.16 to 1.58)¶	1.35 (1.16 to 1.58)¶
- Weight gain >10.0 kg	196/19,424	1.59 (1.36 to 1.85)¶	1.59 (1.36 to 1.85)¶
Long-term quitters (>6 y)	1,168/185,838	1.02 (0.94 to 1.10)	1.02 (0.94 to 1.10)
Transient quitters	54/12,853	1.09 (0.83 to 1.44)	1.08 (0.82 to 1.43)
Never smokers	8,779/2,451,805	0.72 (0.68 to 0.76)¶	0.72 (0.68 to 0.76)¶
		Cardiovascular disease mortality§	
Current smokers	1488/524,182	1 (reference)	1 (reference)
Recent quitters (≤6 y)‡	167/154,259	0.48 (0.41 to 0.56)¶	0.47 (0.40 to 0.55)¶
- No weight gain	68/39,637	0.69 (0.54 to 0.88)¶	0.68 (0.53 to 0.87)¶
- Weight gain 0.1-5.0 kg	46/53,969	0.47 (0.35 to 0.63)¶	0.45 (0.34 to 0.61)¶
- Weight gain 5.1-10.0 kg	14/30,926	0.25 (0.15 to 0.42)¶	0.25 (0.15 to 0.42)¶
- Weight gain > 10.0 kg	11/20,670	0.33 (0.18 to 0.60)¶	0.33 (0.18 to 0.59)¶
Long-term quitters (>6 y)	656/256,194	0.50 (0.46 to 0.55)¶	0.50 (0.45 to 0.55)¶
Never smokers	3,181/3,003,966	0.34 (0.32 to 0.37)¶	0.34 (0.32 to 0.37)¶
		All-cause mortality§	

Current smokers	6537/519,569	1 (reference)	1 (reference)
Recent quitters (≤6 y)‡	880/153,642	0.58 (0.54 to 0.62)¶	0.57 (0.53 to 0.62)¶
- No weight gain	360/39,386	0.81 (0.73 to 0.90)¶	0.81 (0.73 to 0.90)¶
- Weight gain 0.1-5.0 kg	236/53,815	0.52 (0.46 to 0.59)¶	0.51 (0.44 to 0.57)¶
- Weight gain 5.1-10.0 kg	115/30,826	0.46 (0.38 to 0.55)¶	0.45 (0.37 to 0.54)¶
- Weight gain > 10.0 kg	76/20,616	0.50 (0.40 to 0.63)¶	0.49 (0.39 to 0.62)¶
Long-term quitters (>6 y)	3,252/253,822	0.57 (0.54 to 0.59)¶	0.56 (0.53 to 0.58)¶
Never smokers	13,198/2,994,849	0.35 (0.34 to 0.37)¶	0.35 (0.34 to 0.36)¶

Markov Chain Monte Carlo (MCMC)-based method to impute missing values for four covariates: total energy, alcohol intake, alternative healthy eating index, and physical activity.

†Hazard ratios and 95% confidence intervals were estimated using the Cox proportional hazards model with adjustment for age (in months, continuous), cohort (NHS, NHSII, or HPFS), sex (men or women), race (White, African American, Asian, Other), physical activity (quintiles), baseline BMI (continuous and quadratic), alcohol intake (0, <5.0, 5.0-9.9, 10.0-14.9, 15.0-29.9, ≥30.0 g/d), hypertension (yes or no), hypercholesterolemia (yes or no), family history of diabetes (yes or no), multivitamin use (yes or no), Alternative Healthy Eating Index (quintiles) and total energy intake (quintiles).

For cardiovascular disease mortality and all-cause mortality, both family history of diabetes (yes or no) and myocardial infarction (yes or no) were further adjusted.

‡Stratification by weight changes among recent quitters. In this analysis stratified by weight change since quitting, 0.3% (n=42) cases and 0.3% person-time in type 2 diabetes analysis, 0.1% (n=28) cases and 0.2% person-time in cardiovascular mortality analysis, and 0.4% (n=93) cases and 0.3% person time in all-cause mortality with missing data of weight change were removed from the stratified analyses, and therefore the total number of cases and person-time across weight change categories was smaller than that in the analyses of total recent quitters, in which subsequent weight change was not considered.

§No cases among transient quitters for mortality analyses.

¶FDR<0.05.