

## SUPPLEMENTAL MATERIAL

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## **Supplemental Methods**

### **Alternate Healthy Eating Index (AHEI) score**

Diet quality in NHS, HPFS and NHANES was assessed using the AHEI score, which is based on foods and nutrients predictive of chronic disease risk. Briefly, points were assigned for intake of each component on a scale from 0 to 10, with 10 indicating adherence to the recommended levels of servings per day. We included 10 components of the index in our diet score: high intakes of vegetables, fruit, nuts, whole grains, polyunsaturated fatty acids, and long-chain omega-3 fatty acids and low intakes of red and processed meats, sugar sweetened beverages, *trans* fat, and sodium. In this analysis, AHEI was divided in quintiles.

### **Statistical Method Used for Estimating Years of Life Gained**

We applied three pieces of information to estimate the gained life expectancy associated with adherence to a healthy lifestyle (henceforth “exposure groups”).<sup>1</sup>

- (1) Sex- and age-specific hazard ratios for all-cause in each exposure group versus the reference derived from the Nurses’ Health Study (NHS) and the Health Professionals Follow-up Study (HPFS);
- (2) Population all-cause and cause-specific mortality rates derived from the CDC WONDER database of the US Centers for Disease Control and Prevention;
- (3) Prevalence of exposure groups in the US population derived from the NHANES (2013-2014).

The lifetables for each of the 6 exposure groups in male and female, separately, were built on the estimated population mortality rates in each exposure group, and the later was estimated using sex specific hazard ratios for mortality by exposure groups in the NHS and HPFS,

prevalence of exposure groups from NHANES 2013-2014 and the overall population mortality rates by single-year age intervals and sex. We estimated gained life-expectancy as differences in expectation of life at any given age between any two lifetables compared.

Population all-cause (and cause-specific) mortality rates per 100,000 per sex and per single-year age group were obtained for the US population of 2014 from the Center for Disease Control (CDC) WONDER online database (<https://wonder.cdc.gov/ucd-icd10.html>). Because the mortality rates were provided only up to age 84 years old, but we desired to estimate the overall population survival curves until 105 years, we used a Poisson regression model with both linear and quadratic terms for the midpoints of single-year age groups minus age 50.5 years to extrapolate the mortality rates for each single year of age after 84 years (eFigure 1).

We fitted multivariable-adjusted Cox regression models for each gender separately to calculate the age specific hazard ratios for mortality by the number of low-risk factors as compared with zero low-risk factors. The model specification included linear and quadratic terms for the age variable (every 5-years, up to 85 years), and the interactions between the number of low-risk factors with linear and quadratic terms of age variable. The age specific hazard ratios for mortality were obtained as linear combinations of the relevant estimated coefficients, with age fixed at values corresponding to midpoints of 5-year age-groups from age 50 onwards to age 85. The HR of age above 85 was assumed to be the same as that in the 85 years age group. Then we applied the age- and sex- specific HRs to estimate the life expectancy at different age of female and male separately.

We built the life table starting at age 50 years and ending at 105 years by single-year age intervals. Survival probability was set of 1 at age 50 years and probability of survival between ages  $x$  and  $x + 1$  was calculated based on probability of dying (mortality rate) between ages  $x$

and  $x+1$  assuming that survivor function declines linearly between ages  $x$  and  $x + 1$ .<sup>2,3</sup> The life expectancy at any given age was derived by dividing the total person-years that would be lived beyond age  $x$  by the number of persons who survived to that age interval.<sup>2</sup>

Sex-specific prevalence of exposure groups in the US population was derived from the NHANES (2013-2014). We inferred the age-specific mortality rates appropriate for our reference group  $IR_{a0}$  as:<sup>4</sup>

$$IR_{a0} = \frac{IR_a}{(p_{a0} + \sum_{j=1}^5 p_{aj} \times RR_{aj})}$$

Where  $IR_a$  is the population mortality rate for age group  $a$ ,  $p_{aj}$  is the age-specific prevalence of exposure group  $j$ , and  $RR_{aj}$  is the age-specific hazard ratio in comparison of exposure group  $j$  versus reference group ( $j = 0$ ). The age-specific mortality rates in each of the non-reference exposure groups were then inferred in turn by multiplying the age-specific mortality rate for the reference group  $IR_{a0}$  by the age-specific hazard ratios  $RR_{aj}$ .

Finally, life table for each exposure group was built based on each sex- and age-specific  $IR_{aj}$  and the gain in life expectancy according to different exposure groups (number of low-risk lifestyle factor) was estimated as difference in the life expectancy at any given age between the reference group and each of the low-risk group (Figure 1B in the manuscript).

### **Supplemental References**

1. Emerging Risk Factors Collaboration, Di Angelantonio E, Kaptoge S, et al. Association of Cardiometabolic Multimorbidity With Mortality. JAMA. 2015;314(1):52-60.
2. Arias E. United States life tables, 2008. Natl Vital Stat Rep. 2012 Sep 24;61(3):1-63.

3. Chiang CL, World Health Organization. Life table and mortality analysis. 1979. Publisher:  
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4 Woloshin S, Schwartz LM, Welch HG. The risk of death by age, sex, and smoking status in the  
United States: putting health risks in context. *J Natl Cancer Inst* 2008;100(12):845-53.

**Supplemental Table 1 Hazard ratios (95% CIs) of total and cause-specific mortality among participants prior to 75 years according to individual lifestyle risk factors\***

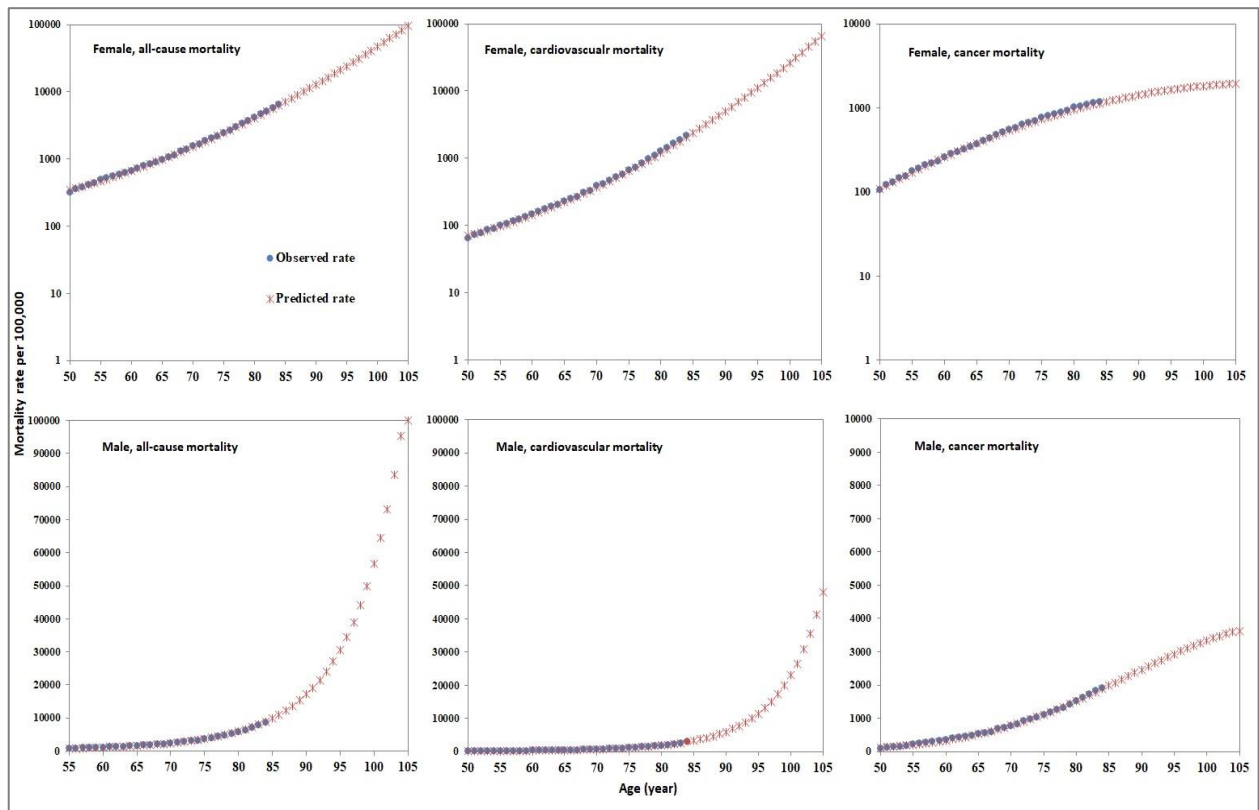
	Person Years	<u>Deaths from any cause</u>		<u>Cancer deaths</u>		<u>Cardiovascular deaths</u>	
		Cases	RR (95% CI)	Cases	RR (95% CI)	Cases	RR (95% CI)
<b>Body mass index (kg/m<sup>2</sup>)</b>							
18.5-22.9	562354	2664	1.15 (1.09-1.21)	1290	1.02 (0.94-1.09)	476	1.22 (1.08-1.38)
23-24.9	583042	2949	1.0(ref.)	1522	1.0(ref.)	555	1.0(ref.)
25-29.9	1150992	7156	1.09 (1.04-1.13)	3360	1.02 (0.96-1.08)	1722	1.35 (1.23-1.49)
30-34.9	434413	3385	1.35 (1.29-1.42)	1433	1.12 (1.04-1.20)	915	2.12 (1.90-2.36)
≥35	215683	2244	1.87 (1.77-1.98)	831	1.32 (1.21-1.44)	613	3.40 (3.02-3.83)
<b>Cigarette smoking</b>							
Never	1290489	5521	1.0(ref.)	2587	1.0(ref.)	1186	1.0(ref.)
Past	1240208	9254	1.51 (1.46-1.56)	4235	1.52 (1.45-1.60)	2206	1.60 (1.49-1.72)
Current 1-14/day	160682	1418	2.14 (2.02-2.27)	602	1.86 (1.71-2.04)	355	2.62 (2.33-2.95)
Current 15-24/day	157531	1286	2.46 (2.31-2.61)	584	2.13 (1.95-2.34)	335	3.32 (2.94-3.76)
Current ≥25/day	97576	919	3.22 (3.00-3.46)	428	2.82 (2.54-3.13)	199	3.60 (3.09-4.19)
<b>Alcohol consumption (g/day)</b>							
0	848882	6633	1.34 (1.29-1.40)	2656	1.04 (0.98-1.10)	1711	1.81 (1.66-1.97)
1-4.9	960473	5038	1.03 (0.98-1.07)	2522	0.98 (0.92-1.04)	1118	1.17 (1.07-1.29)
5-14.9	669556	3577	1.0(ref.)	1800	1.0(ref.)	754	1.0(ref.)
15-29.9	289685	1642	0.99 (0.93-1.05)	793	0.98 (0.90-1.06)	354	0.96 (0.84-1.09)
≥30	177888	1508	1.38 (1.30-1.46)	665	1.26 (1.15-1.38)	344	1.33 (1.17-1.52)
<b>Physical activity (hours/week)</b>							
0	845324	9126	1.0(ref.)	3805	1.0(ref.)	2232	1.0(ref.)
0.1-0.9	811380	4165	0.62 (0.60-0.65)	2037	0.70 (0.66-0.74)	964	0.62 (0.58-0.68)
1.0-3.4	462343	1928	0.53 (0.50-0.55)	994	0.63 (0.59-0.68)	403	0.46 (0.41-0.51)
3.5-5.9	330135	1331	0.47 (0.45-0.50)	672	0.57 (0.52-0.62)	281	0.40 (0.35-0.45)
≥6	497302	1848	0.44 (0.42-0.46)	928	0.54 (0.50-0.58)	401	0.37 (0.33-0.41)
<b>Alternative healthy eating index</b>							
Fifth 1	636924	4988	1.0(ref.)	2165	1.0(ref.)	1116	1.0(ref.)
Fifth 2	599813	3910	0.81 (0.78-0.85)	1797	0.87 (0.82-0.92)	889	0.80 (0.73-0.88)
Fifth 3	588706	3560	0.74 (0.71-0.77)	1647	0.79 (0.74-0.85)	836	0.74 (0.68-0.81)
Fifth 4	572043	3150	0.66 (0.63-0.69)	1469	0.71 (0.67-0.76)	769	0.68 (0.62-0.74)
Fifth 5	548998	2790	0.58 (0.55-0.60)	1358	0.66 (0.61-0.70)	671	0.58 (0.52-0.64)
<b>Number of 5 low-risk factors**</b>							
Zero	379007	4141	1.0(ref.)	1681	1.0(ref.)	1103	1.0(ref.)
One	926243	7046	0.74 (0.71-0.77)	3171	0.82 (0.77-0.87)	1662	0.65 (0.60-0.70)
Two	906085	4678	0.54 (0.52-0.56)	2294	0.65 (0.61-0.69)	1002	0.41 (0.38-0.45)
Three	521881	1927	0.40 (0.38-0.42)	961	0.49 (0.46-0.53)	406	0.29 (0.26-0.33)
Four	183975	544	0.32 (0.30-0.35)	294	0.44 (0.39-0.50)	98	0.20 (0.16-0.24)
Five	29294	62	0.23 (0.18-0.29)	35	0.33 (0.24-0.47)	10	0.12 (0.06-0.22)
<b>For not having five low-risk factors vs. all others (95% CI)</b>		<b>HRs</b>	0.37 (0.29-0.48)		0.48 (0.34-0.67)		0.23 (0.12-0.42)
		<b>PAR<sup>§</sup> (%)</b>	62.7 (52.1-71.0)		51.7 (32.3-65.5)		76.8 (56.7-87.6)

HR: Hazard ratio; PAR: Population-Attributable-Risk

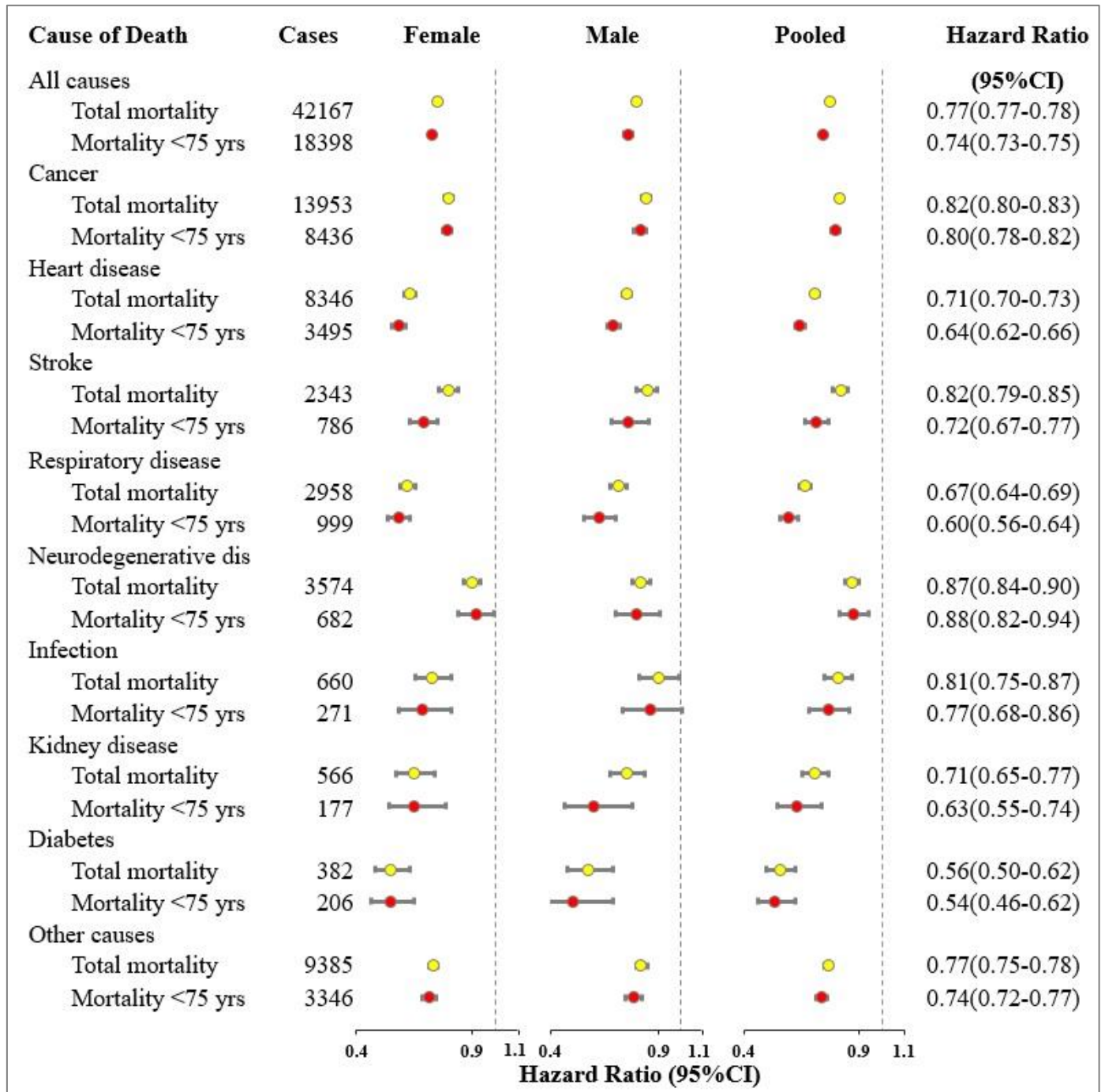
\* Multivariable adjusted hazard ratio adjusted for age, sex, ethnicity, current multivitamin use, current aspirin use, family history of diabetes mellitus, myocardial infarction, or cancer, and menopausal status and hormone use (for female).

\*\*Low-risk lifestyle factors included: cigarette smoking (never smoking), physical active (≥3.5 hours/week moderate to vigorous intensity activity), high diet quality (upper 40% of alternative healthy eating index (AHEI), moderate alcohol intake of 5-15 g/day (female) or 5-30 g/day (male), and normal weight (body mass index 18.5-24.9 kg/m<sup>2</sup>).

§ Estimation of PAR was based on the prevalence of not having five low-risk factors among American adults from NHANES data.



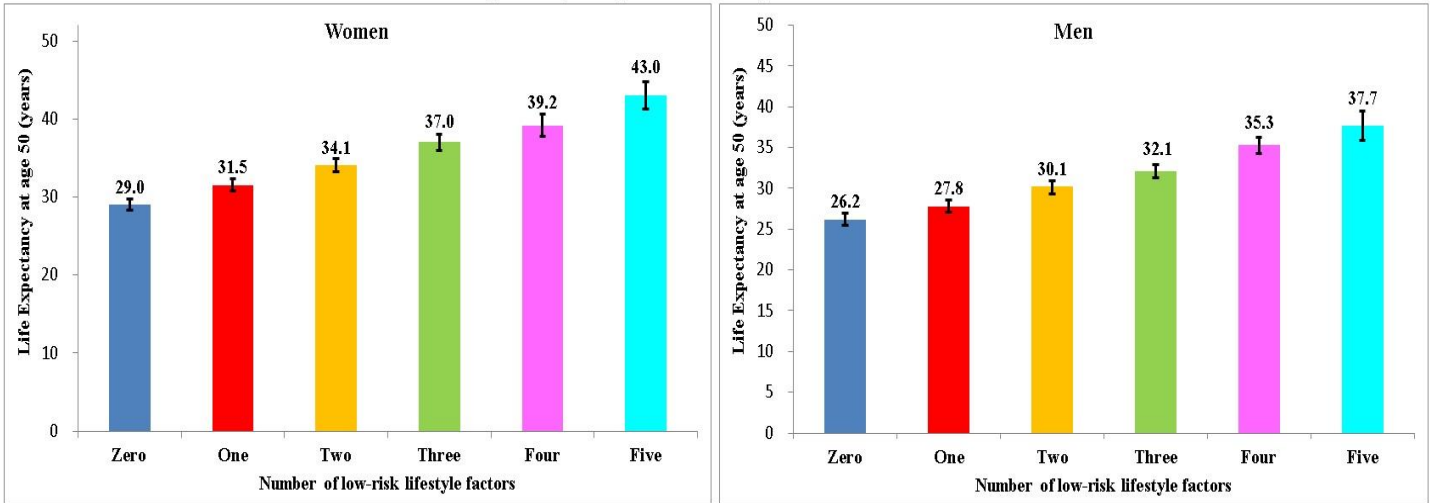
**Supplemental Figure 1** Observed and predicted rate of US population mortality rates of 2014.



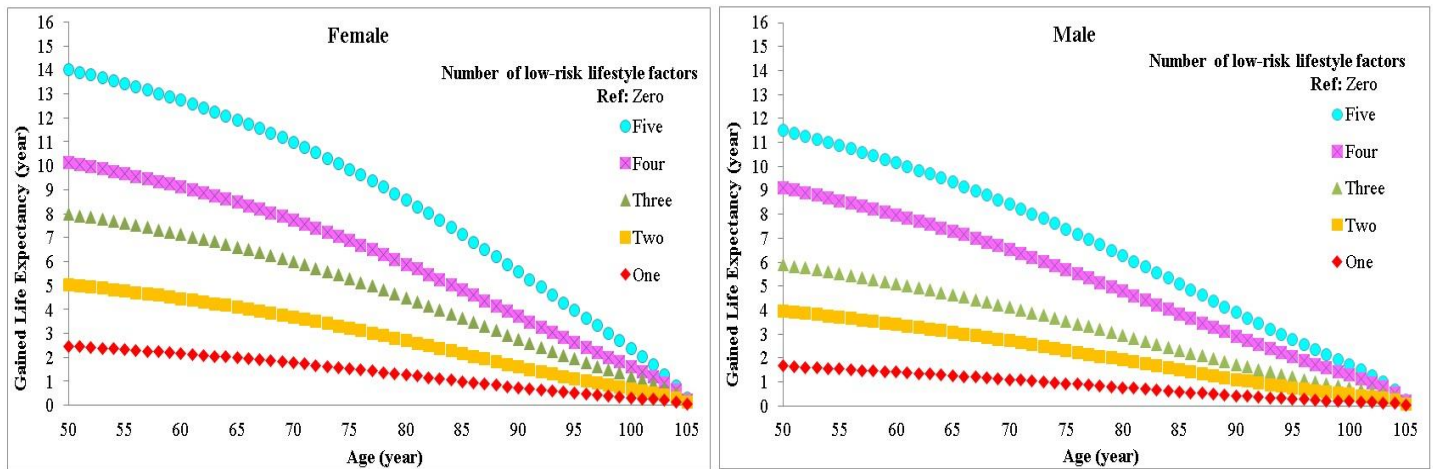
**Supplemental Figure 2 Hazard ratios for total and cause-specific death associated with an increment of each low-risk lifestyle factor.** Hazard ratios adjusted for age, sex, ethnicity, current multivitamin use, current aspirin use, family history of diabetes mellitus, myocardial infarction, or cancer, and menopausal status and hormone (for female only). Low-risk lifestyle factors included: cigarette smoking (never smoking), physical active ( $\geq 3.5$  hours/week moderate to vigorous intensity activity), high diet quality (upper 40% of alternative healthy eating index (AHEI), moderate alcohol intake of 5-15 g/day (female) or 5-30 g/day (male), and normal weight (body mass index 18.5-24.9 kg/m<sup>2</sup>).



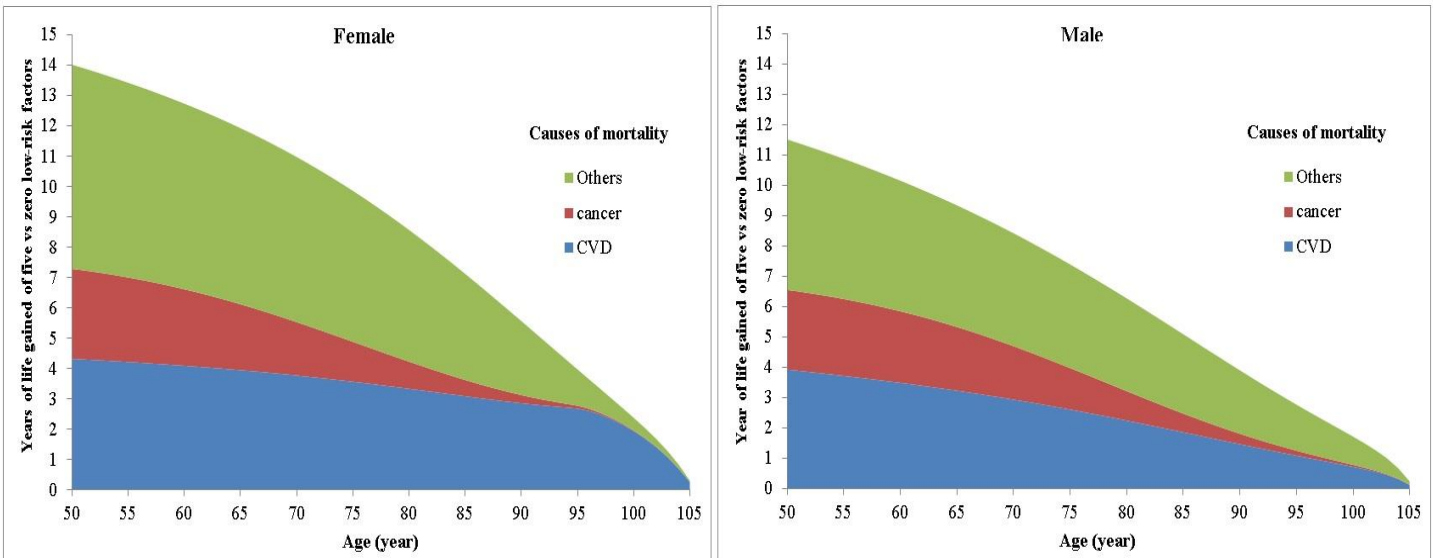
**A: Estimated life expectancy at age 50 according to the number of low-risk factors**



**B: Estimated gained life expectancy at different age by applying healthy lifestyle as compared to zero low-risk factor**



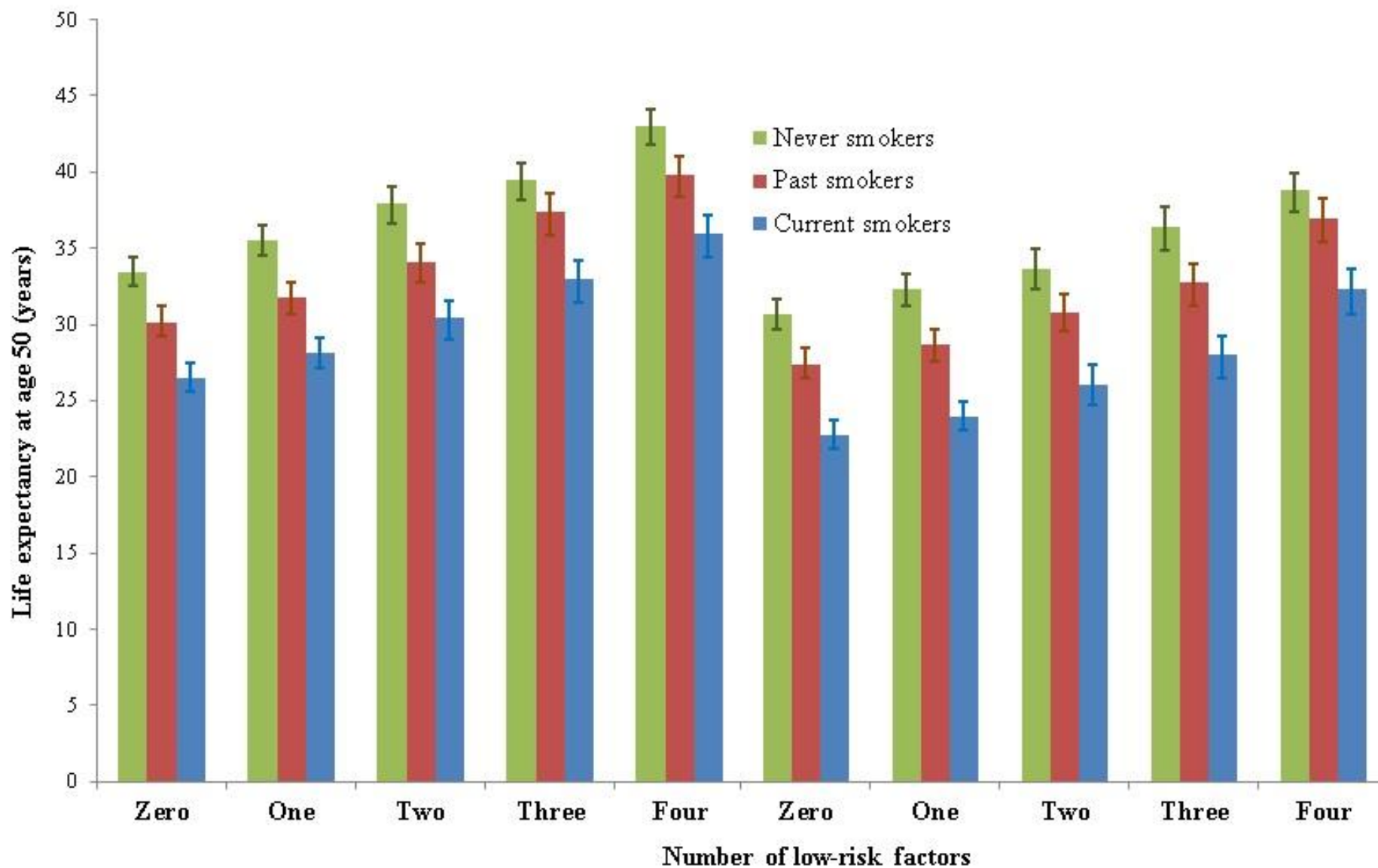
**C: Estimated future years of life gained from adopting five versus zero low-risk factors attributable to less CVD, cancer and other mortality causes**



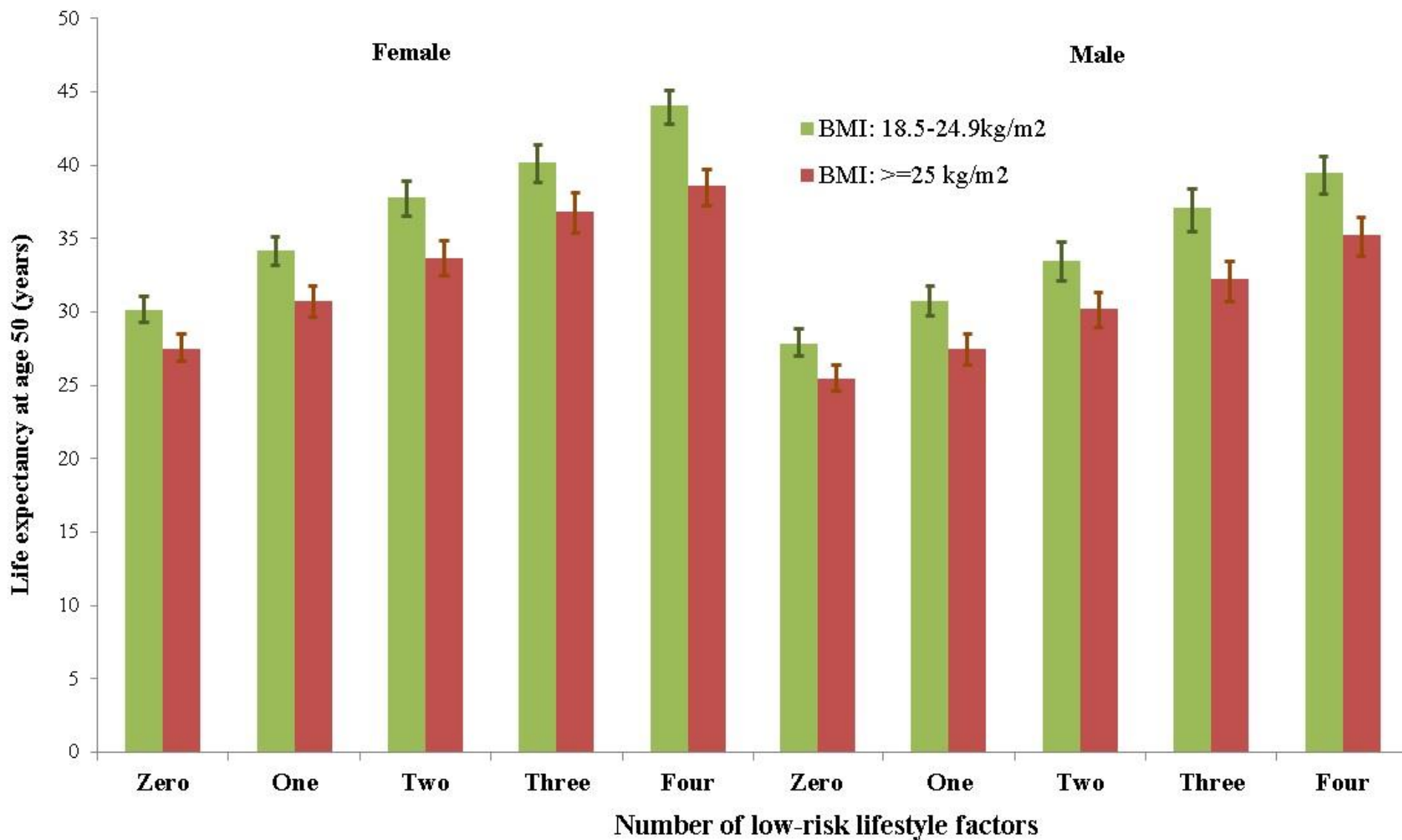
**Supplemental Figure 3: Life expectancy estimated based on overall mortality rate of Americans (CDC report) and the prevalence of lifestyle factors using NHANES data 2013-2014 and sex-specific Harvard Ratios (A: life expectancy at age 50; B: life expectancy by age; C: attributable life expectancy) <sup>\*</sup>, <sup>†</sup>**

\* Low-risk lifestyle factors included: cigarette smoking (never smoking), physically active ( $\geq 3.5$  hours/week moderate to vigorous intensity activity), high diet quality (upper 40% of alternative healthy eating index (AHEI), moderate alcohol intake of 5-15 g/day (female) or 5-30 g/day (male), and normal weight (body mass index  $< 25$  kg/m<sup>2</sup>).

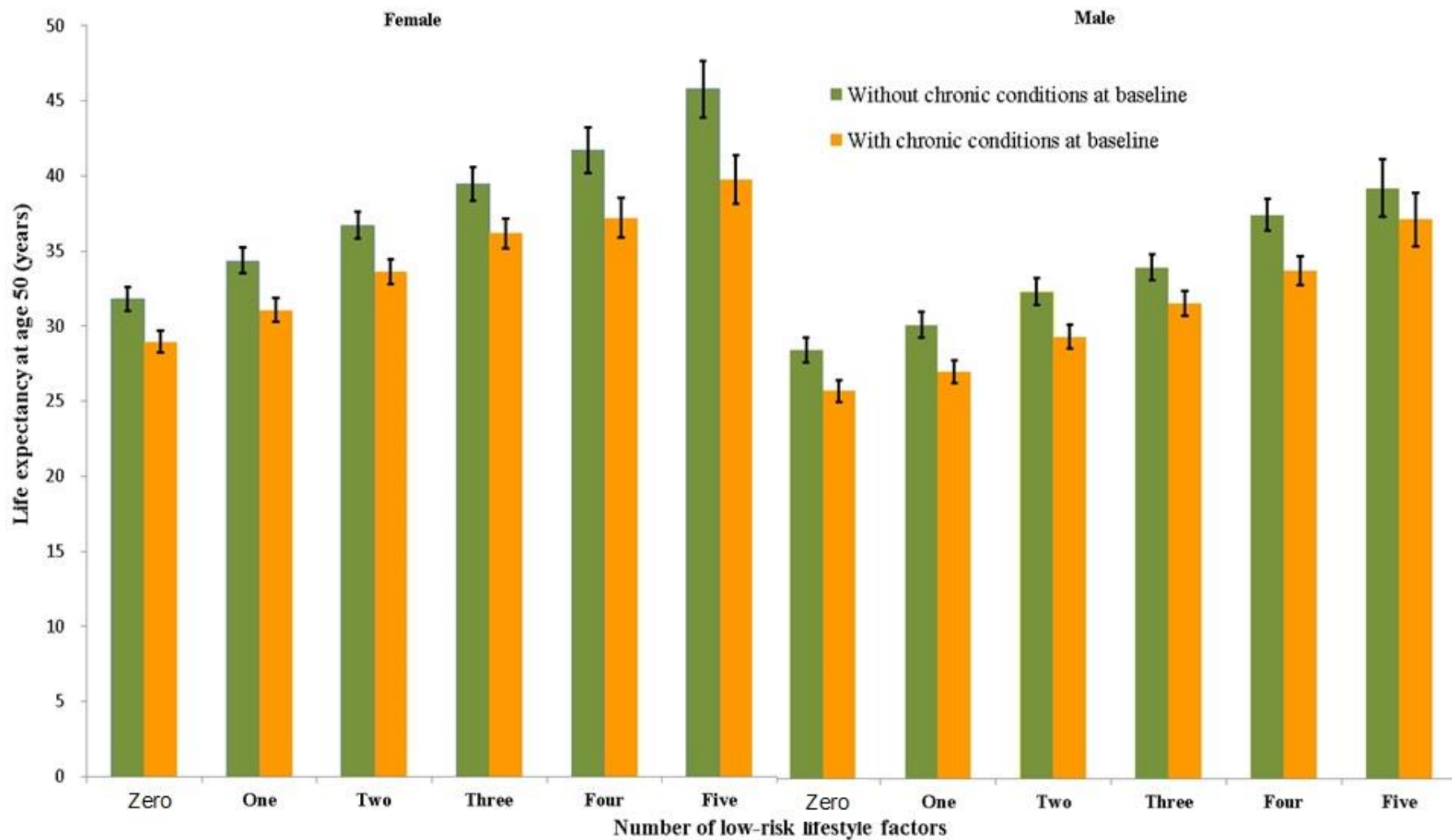
<sup>†</sup>The estimates of cumulative survival from 50 years of age onward among the 5 lifestyle risk factor groups were calculated by applying: (1) all-cause and cause-specific mortality rates were obtained from the US CDC WONDER database; (2) distribution of different numbers of low-risk lifestyles was based on the US NHANES 2013-2014; (3) multivariate-adjusted hazard ratios (gender-specific but same across age) for all-cause and cause-specific mortality associated with the 5 low-risk lifestyles as compared to those without any low-risk lifestyle factors, adjusted for age, ethnicity, current multivitamin use, current aspirin use, family history of diabetes mellitus, myocardial infarction, or cancer, and menopausal status and hormone use (females only), were based on data from the NHS and HPFS.



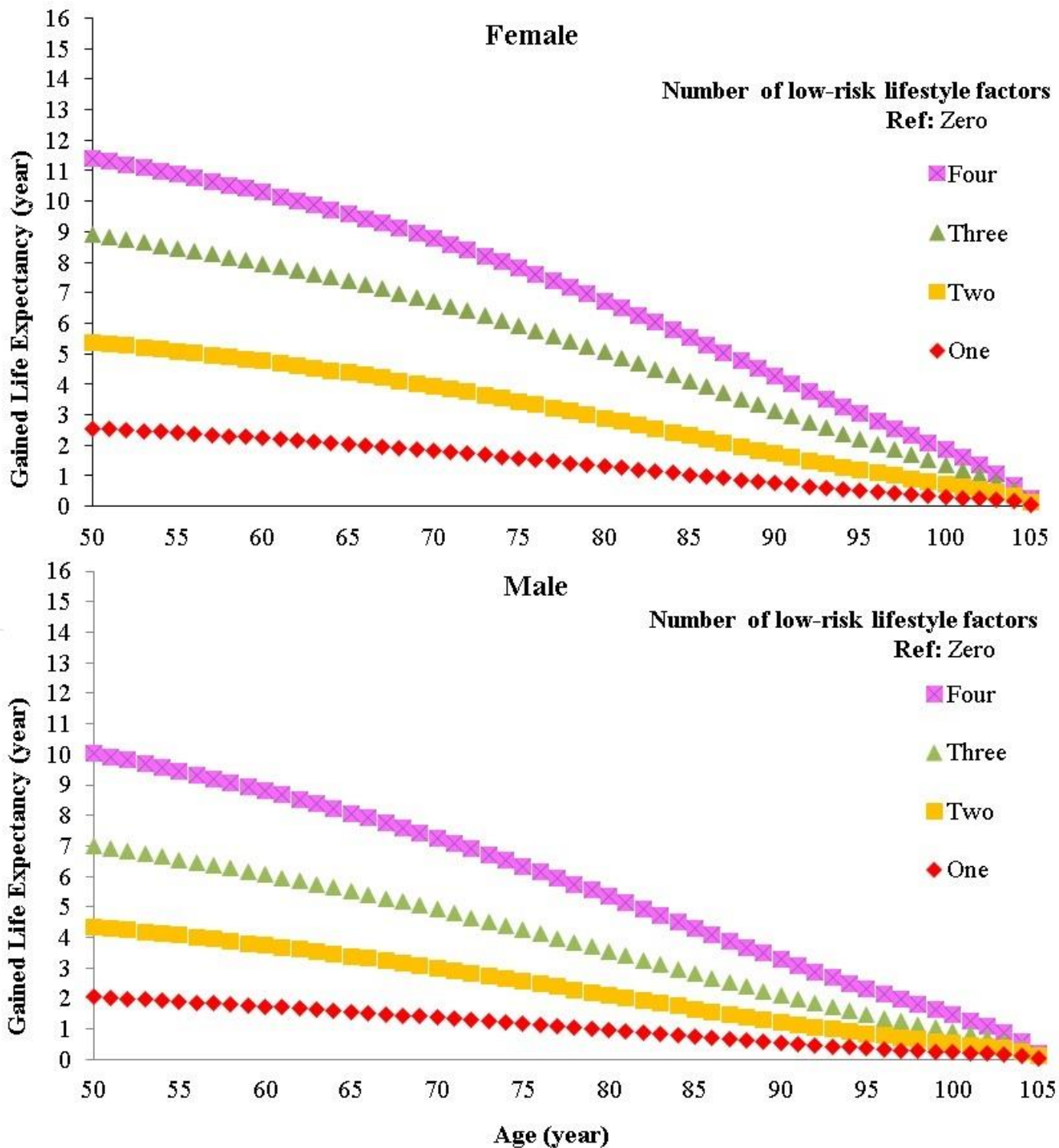
**Supplemental Figure 4** Estimated life expectancy at age 50 according to the number of low-risk factors stratified by smoking status (Low-risk lifestyle factors included: physical active ( $\geq 3.5$  hours/week moderate to vigorous intensity activity), high diet quality (upper 40% of alternative healthy eating index (AHEI), moderate alcohol intake of 5-15 g/day (female) or 5-30 g/day (male), and normal weight (body mass index 18.5-24.9 kg/m<sup>2</sup>).



**Supplemental Figure 5** Estimated life expectancy at age 50 according to the number of low low-risk factors stratified by BMI status (Low-risk lifestyle factors included: physical active ( $\geq 3.5$  hours/week moderate to vigorous intensity activity), high diet quality (upper 40% of alternative healthy eating index (AHEI), and never smoking)

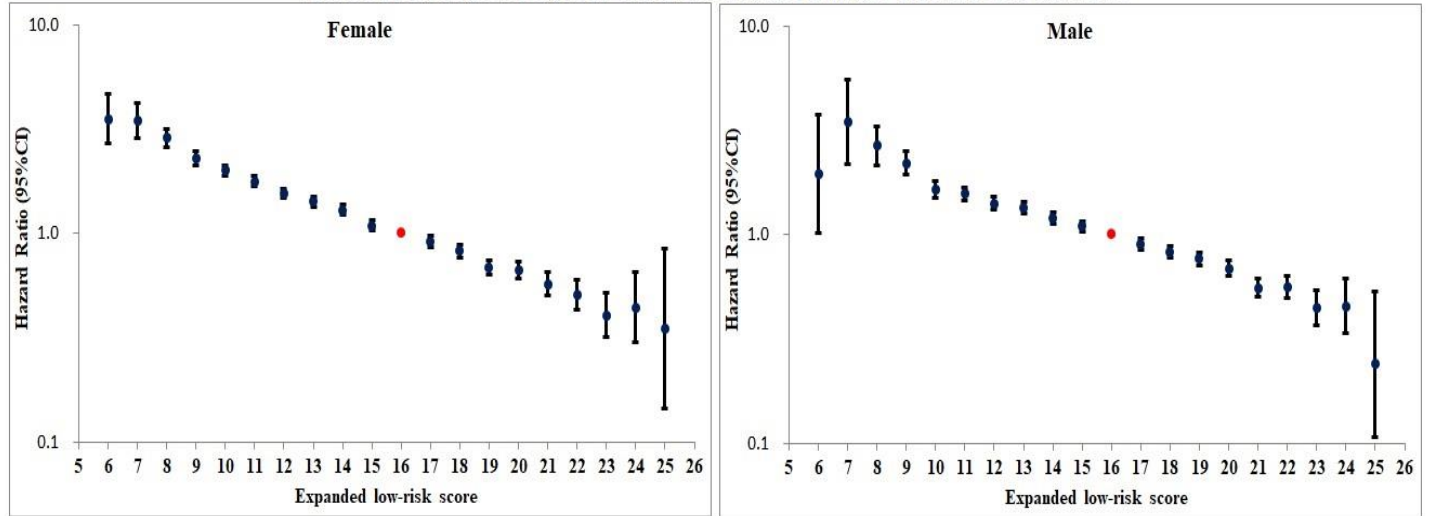


**Supplemental Figure 6** Estimated life expectancy at age 50 according to the number of low-risk factors stratified by the disease status at baseline

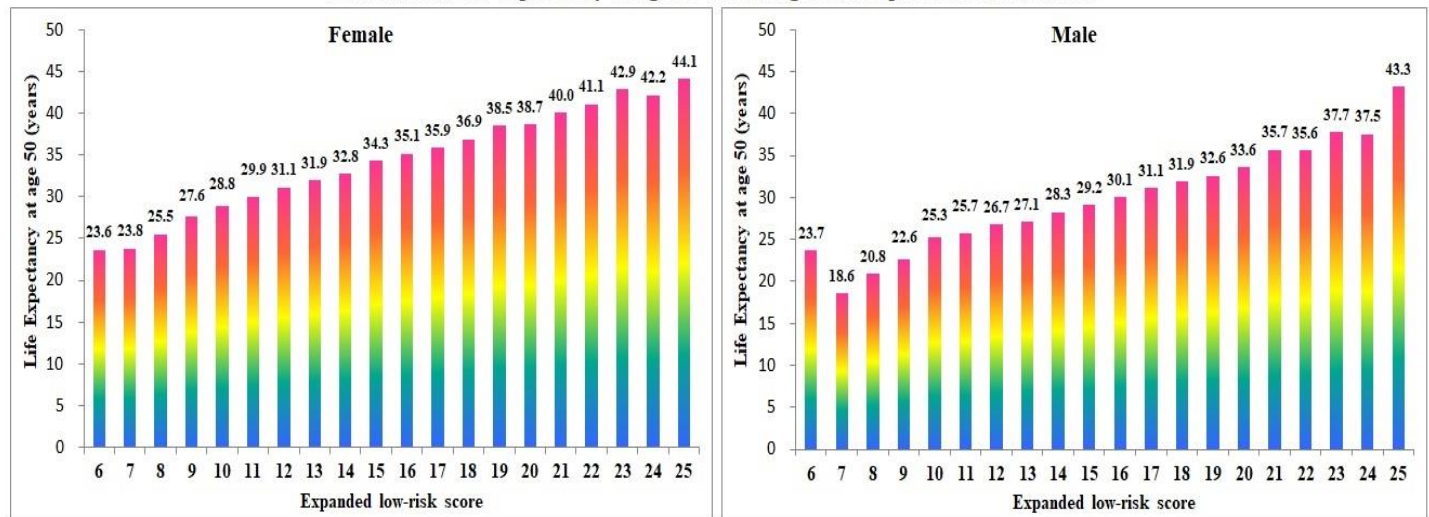


**Supplemental Figure 7 Sensitivity analysis of excluding moderate alcohol intake from the low-risk score**  
 (Estimated gained life expectancy at different age by applying one to four low-risk factors as compared to zero low-risk factor; low-risk lifestyle factors included: physical active ( $\geq 3.5$  hours/week moderate to vigorous intensity activity), high diet quality (upper 40% of alternative healthy eating index (AHEI), normal weight (body mass index 18.5-24.9 kg/m<sup>2</sup>), and cigarette smoking (never smoking)).

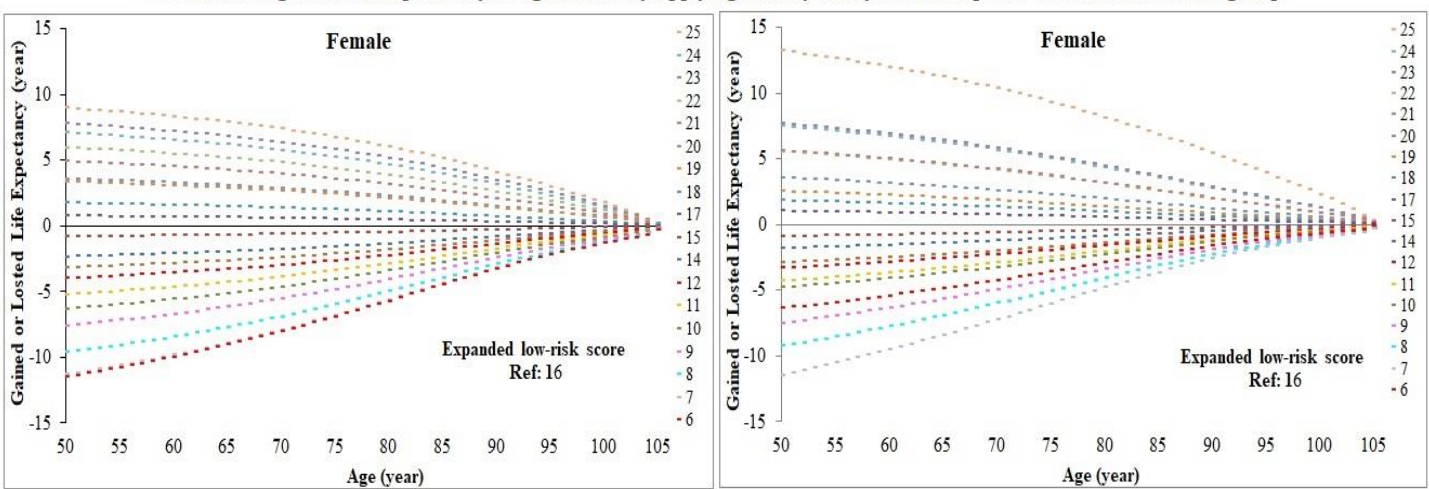
**A: Hazard Ratio (95% CI) of all-cause mortality according to expanded low-risk score**



**B: Estimated life expectancy at age 50 according to the expanded low-risk score**



**C: Estimated gained life expectancy at age-at-risk by applying healthy lifestyles as compared to the median score group**



**Supplemental Figure 8: Hazard Ratio of all-cause mortality and estimated life expectancy according to expanded low-risk score (A: hazard ratio; B: life expectancy at age 50; C: life expectancy by age) \*\*, \*\***

\* For expanded low-risk score, we assigned scores of 1 (least healthy) to 5 (most healthy) to the categories of the lifestyle factors and summed the points across all 5 factors as below (score for each category is listed in the bracket following:

- Body mass index (kg/m<sup>2</sup>): 18.5-22.9 (5), 23-24.9 (4), 25-29.9 (3), 30-34.9 (2), ≥35 (1)
- Cigarette smoking: never (5), past (4), current 1-14/day (3), Current 15-24/day (2), Current ≥25/day (1)
- Alcohol consumption (g/day): 0 (1), 1-4.9 (3), 5-14.9 (5), 15-29.9 (4), ≥30 (2)
- Physical activity (hours/week): 0 (1), 0.1-0.9 (2), 1.0-3.4 (3), 3.5-5.9 (4), ≥6 (5)
- Alternative healthy eating index: Fifth 1 (1), Fifth 2 (2), Fifth 3 (3), Fifth 4 (4), Fifth 5 (5)

Because too few participants classified in score=5, so the score 5 and 6 are combined as score 5-6, and the overall range of expanded low-risk score was 6-25; The cases of all-cause mortality according to the expanded low-risk score was score 5-6: 64 deaths; 7: 125; 8: 552; 9: 1393; 10: 2501; 11: 3652; 12: 4329; 13: 4982; 14: 5134; 15: 4628; 16: 4084; 17: 3393; 18: 2664; 19: 1883; 20: 1318; 21: 756; 22: 449; 23: 179; 24: 66, 25: 11.

\*\*The estimates of cumulative survival from 50 years of age onward among the 5 lifestyle risk factor groups were calculated by applying

- All-cause and cause-specific mortality rates were obtained from the US CDC WONDER database;
- Distribution of different numbers of low-risk lifestyles was based on the US NHANES 2013-2014; The proportion of the expanded low-risk score was: score 5-6: 0.14%; 7: 0.47%; 8: 1.30%; 9: 2.21%; 10: 2.30%; 11: 5.67%; 12: 6.51%; 13: 6.61%; 14: 9.56%; 15: 8.96%; 16: 12.29%; 17: 10.84%; 18: 8.41%; 19: 7.84%; 20: 6.06%; 21: 4.23%; 22: 2.65%; 23: 1.58%; 24: 1.42%; 25: 0.29%.
- Multivariate-adjusted hazard ratios (gender-specific) for all-cause and cause-specific mortality associated with the expanded low-risk score as compared to whose score equal 16 (median score), adjusted for age, ethnicity, current multivitamin use, current aspirin use, family history of diabetes mellitus, myocardial infarction, or cancer, and menopausal status and hormone use (females only), were based on data of NHS and HPFS.