Supplementary Table 1. Demographic and lifestyle characteristics of participants with available dietary data in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial[a]

Weight change across the adult life course	age 20y to 50y					age 20y to study enrollment				
	Loss ≤-5 kg	Stable -5 to < 5 kg	Gain 5 to < 10 kg	Gain 10 to < 20 kg	Gain ≥20 kg	Loss ≤-5 kg	Stable -5 to < 5 kg	Gain 5 to < 10 kg	Gain 10 to < 20 kg	Gain ≥20 kg
No. of participants	3104	37738	34661	41614	21805	3536	24414	24627	44536	41809
Age at study enrollment, years	62.3 (5.2)	63.2 (5.3)	62.9 (5.3)	62.3 (5.3)	61.0 (5.1)	63.3 (5.4)	62.9 (5.4)	62.7 (5.3)	62.5 (5.3)	62.2 (5.2)
Sex										
Men	47.5	45.1	45.6	53.4	55.0	55.8	50.3	50.1	50.8	46.2
Women	51.0	54.0	51.4	46.3	44.9	43.1	48.5	49.0	49.1	51.5
Race and ethnicity										
Hispanic	1.9	1.5	1.7	2.0	2.0	1.7	1.5	1.8	2.0	2.1
Non-Hispanic Black	5.5	3.2	3.2	4.5	7.7	5.9	3.3	4.3	5.4	8.4
Non-Hispanic White	87.2	89.0	89.0	88.9	88.0	88.0	89.3	88.8	88.7	87.0
Other[b]	5.5	6.4	6.1	4.7	2.3	4.5	6.1	5.2	3.9	2.7
Hypertension	27.8	24.3	31.2	37.8	48.7	29.1	23.7	27.1	32.7	45.7
Diverticulitis	5.9	5.9	6.9	7.2	7.4	5.6	5.6	6.2	6.8	7.8
Diabetes mellitus	6.5	3.4	5.1	8.4	17.9	9.1	4.7	5.1	6.6	11.7
Liver cirrhosis[c]	4.5	3.5	3.6	3.7	3.8	4.4	3.7	3.3	3.7	3.7
Family history of liver cancer	2.1	2.1	2.0	2.1	1.9	1.8	2.1	1.9	2.0	2.1
Family history of biliary tract cancer	0.3	0.2	0.2	0.2	0.3	0.3	0.2	0.3	0.2	0.3
Gall bladder stones or inflammation[c]	10.7	8.3	10.3	12.1	16.4	10.1	7.4	8.6	10.8	15.7
Alcohol intake										
Never	7.2	9.6	9.9	9.7	10.5	8.6	9.6	9.2	9.6	10.8
Former	17.1	12.6	12.9	15.1	18.9	16.5	13.2	12.3	13.7	17.4
Current	72.2	74.1	73.7	71.4	66.1	71.5	73.6	75.2	73.1	67.6
Unknown	3.5	3.7	3.5	3.8	4.5	3.4	3.6	3.3	3.6	4.2
Education										
Less than high school	8.6	6.1	6.7	7.6	8.9	9.1	5.8	5.7	6.8	9.3
High school	21.6	21.2	22.8	24.0	24.2	21.5	19.6	21.4	23.8	24.9
Post high school training other than college	12.6	11.7	12.2	13.2	13.7	12.5	11.4	11.9	12.8	13.5
Some college	20.7	20.7	21.6	22.3	23.4	19.4	20.4	20.8	21.9	23.3
College graduate	16.9	18.8	17.4	16.2	15.3	17.4	19.9	18.9	16.8	14.5
Postgraduate	19.6	21.5	19.3	16.7	14.5	20.1	22.9	21.3	17.9	14.5
Smoking status										
Never	37.8	47.7	47.3	45.5	44.3	38.5	48.5	48.4	46.3	44.2
Former	20.1	12.1	10.2	9.6	9.1	22.8	14.5	11.0	9.8	7.9
Current	42.1	40.2	42.5	44.9	46.6	38.7	37.0	40.6	43.9	47.9
Job status										
Homemaker	9.5	12.2	11.8	10.6	9.8	8.1	11.0	11.6	11.2	11.4
Working	41.2	37.5	39.1	40.9	44.3	37.6	39.5	40.8	40.5	39.6

Unemployed	1.6	0.9	0.9	1.1	1.3	1.6	1.0	0.8	1.0	1.2
Retired	40.1	45.4	44.4	43.1	38.0	45.7	44.3	43.1	43.3	42.0
Extended sick leave and Disabled	4.9	1.7	1.7	2.2	4.4	4.7	0.1	0.2	0.2	0.3
Other	2.7	2.3	2.1	2.1	2.2	2.3	2.4	2.1	2.2	2.1
HEI-2010 score	65.2 (11.8)	66.7 (11.0)	54.8 (10.6)	64.4 (10.7)	63.1 (10.5)	65.4 (12.1)	67.0 (11.1)	66.4 (10.7)	65.1 (10.6)	63.5 (10.5)
Coffee, g/day	809 (95)	647 (70)	627 (71)	631 (73)	597 (77)	782 (90)	667 (87)	634 (77)	633 (74)	601 (76)
Aspirin use[d]	45.7	45.1	46.8	48.2	49.2	46.3	45.1	46.5	47.2	48.6
BMI at age 20, kg/m^2	27.2 (4.8)	22.3 (2.8)	21.9 (2.6)	21.6 (2.8)	21.9 (3.3)	26.8 (4.8)	22.6 (2.9)	22.0 (2.6)	21.7 (2.7)	21.6 (3.0)
BMI at age 50, kg/m^2	23.3 (3.7)	23.0 (2.8)	24.6 (2.6)	26.5 (2.9)	31.5 (5.0)	24.5 (4.4)	23.5 (3.4)	24.3 (3.1)	25.5 (3.3)	28.5 (4.8)
BMI at study enrollment, kg/m^2	24.7 (4.6)	24.3 (3.5)	26.3 (3.5)	28.3 (3.9)	32.3 (5.6)	23.0 (3.9)	23.2 (2.9)	24.7 (2.6)	26.8 (2.8)	31.9 (4.8)

[a]All data reported as percentage (%) or mean (SD), unless noted otherwise. BMI = body mass index; HEI-2010 = Healthy Eating Index-2010; SD = standard deviation.
[b]"Other" race category includes Asian, Pacific Islander, American Indian, and unknown.
[c]Variables were self-reported.
[d]Aspirin use for more than 12 months.

Supplementary Table 2. Hazard ratios and 95% confidence intervals for incident liver and biliary tract cancers according to body mass index in a sub-cohort with available dietary data in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial

Model	BMI category (kg/m^2)				BMI (per 5 kg/m^2) [h]
	BMI < 18.5	BMI 18.5 to <25	BMI 25 to <30	BMI ≥30	
Liver cancer					
BMI, age 20y, kg/m^2					
No. of cases/person-years	9/144,825	66/1,370,974	19/232,655	3/30,130	-
Age-adjusted HR (95% CI)	1.29 (0.64-2.59)	1 (reference)	1.79 (1.07-2.99)	2.29 (0.72-7.32)	1.40 (1.05-1.86)
MV, HR (95% CI) [a]	1.04 (0.56-1.94)	1 (reference)	1.35 (0.92-1.99)	2.54 (1.18-5.46)	1.37 (1.10-1.72)
MV, HR (95% CI) [b]	1.28 (0.64-2.61)	1 (reference)	1.29 (0.76-2.17)	1.56 (0.48-5.05)	1.14 (0.83-1.55)
MV, HR (95% CI) [c]	1.30 (0.64-2.63)	1 (reference)	1.29 (0.76-2.18)	1.54 (0.47-5.00)	1.13 (0.83-1.55)
MV+ Average BMI during age 50y to study enrollment, HR (95% CI) [d]	1.20 (0.64-2.25)	1 (reference)	0.99 (0.65-1.50)	1.60 (0.73-3.54)	1.37 (1.10-1.72)
BMI, age 50y, kg/m^2					
No. of cases/person-years	0/12,565	36/844,164	36/692,256	25/229,599	-
Age-adjusted HR (95% CI)	-	1 (reference)	1.29 (0.81-2.06)	3.05 (1.81-5.13)	1.49 (1.25-1.79)
MV, HR (95% CI) [a]	-	1 (reference)	1.40 (0.98-2.01)	2.58 (1.69-3.96)	1.45 (1.24-1.70)
MV, HR (95% CI) [b]	-	1 (reference)	0.93 (0.57-1.51)	1.88 (1.06-3.32)	1.28 (1.02-1.60)
MV, HR (95% CI) [c]	-	1 (reference)	0.93 (0.57-1.50)	1.87 (1.05-3.32)	1.28 (1.02-1.60)
BMI, age at study enrollment					
No. of cases/person-years	0/10,549	28/603,197	41/764,236	28/400,602	-
Age-adjusted HR (95% CI)	-	1 (reference)	1.17 (0.72-1.90)	1.62 (0.95-2.74)	1.17 (0.96-1.42)
MV, HR (95% CI) [a]	1.18 (0.16-8.64)	1 (reference)	1.14 (0.78-1.68)	1.91 (1.26-2.89)	1.32 (1.14-1.54)
MV, HR (95% CI) [b]	-	1 (reference)	0.91 (0.55-1.49)	1.16 (0.66-2.06)	1.03 (0.82-1.29)
MV, HR (95% CI) [c]	-	1 (reference)	0.90 (0.55-1.48)	1.15 (0.65-2.04)	1.03 (0.82-1.29)
Average BMI during age 20 to 50y					
No. of cases/person-years	0/21,973	58/1,214,666	30/461,119	9/80,825	-
Age-adjusted HR (95% CI)	-	1 (reference)	1.47 (0.94-2.29)	2.75 (1.35-5.61)	1.64 (1.28-2.10)
MV, HR (95% CI) [a]	-	1 (reference)	1.46 (1.05-2.04)	2.29 (1.29-4.06)	1.58 (1.29-1.95)
MV, HR (95% CI) [b]	-	1 (reference)	1.09 (0.68-1.72)	1.72 (0.81-3.62)	1.30 (0.97-1.74)

MV, HR (95% CI) [c]	-	1 (reference)	1.08 (0.68-1.72)	1.70 (0.81-3.61)	1.30 (0.97-1.74)
Average BMI during age 20y to study enrollment					
No. of cases/person-years	0/13,234	49/1,063,962	42/585,090	6/116,298	-
Age-adjusted HR (95% CI)	-	1 (reference)	1.62 (1.07-2.44)	1.26 (0.53-2.95)	1.35 (1.03-1.77)
MV, HR (95% CI) [a]	-	1 (reference)	1.56 (1.13-2.16)	1.86 (1.06-3.26)	1.50 (1.22-1.85)
MV, HR (95% CI) [b]	-	1 (reference)	1.28 (0.83-1.97)	0.86 (0.35-2.07)	1.09 (0.81-1.48)
MV, HR (95% CI) [c]	-	1 (reference)	1.27 (0.83-1.96)	0.85 (0.35-2.06)	1.09 (0.80-1.48)
Average BMI during age 50y to study enrollment					
No. of cases/person-years	0/8,317	29/702,346	46/770,876	22/297,045	-
Age-adjusted HR (95% CI)	-	1 (reference)	1.48 (0.93-2.36)	2.02 (1.16-3.54)	1.36 (1.11-1.67)
MV, HR (95% CI) [a]	-	1 (reference)	1.34 (0.92-1.93)	2.35 (1.54-3.60)	1.44 (1.15-1.80)
MV, HR (95% CI) [b]	-	1 (reference)	1.11 (0.69-1.80)	1.31 (0.71-2.42)	1.16 (0.92-1.48)
MV, HR (95% CI) [c]	-	1 (reference)	1.10 (0.68-1.78)	1.30 (0.71-2.41)	1.16 (0.91-1.48)
Biliary tract cancer					
BMI, age 20y, kg/m^2					
No. of cases/person-years	6/144,825	67/1,370,974	14/232,655	3/30,130	-
Age-adjusted HR (95% CI)	0.84 (0.36-1.95)	1 (reference)	1.28 (0.71-2.27)	2.17 (0.68-6.91)	1.22 (0.88-1.68)
MV, HR (95% CI) [c]	0.82 (0.36-1.91)	1 (reference)	1.23 (0.68-2.24)	2.02 (0.63-6.52)	1.20 (0.86-1.67)
MV, HR (95% CI) [e]	0.90 (0.47-1.72)	1 (reference)	1.32 (0.83-2.08)	2.15 (0.87-5.31)	1.28 (0.99-1.64)
MV, HR (95% CI) [f]	0.82 (0.35-1.90)	1 (reference)	1.24 (0.68-2.25)	2.03 (0.63-6.55)	1.20 (0.86-1.68)
BMI, age 50y, kg/m^2					
No. of cases/person-years	0/12,565	36/44,164	38/692,256	16/229,599	-
Age-adjusted HR (95% CI)	-	1 (reference)	1.34 (0.85-2.12)	1.83 (1.01-3.33)	1.26 (1.02-1.57)
MV, HR (95% CI) [c]	-	1 (reference)	1.34 (0.83-2.17)	1.90 (1.00-3.59)	1.28 (1.01-1.62)
MV, HR (95% CI) [e]	1.13 (0.16-8.18)	1 (reference)	1.46 (0.99-2.14)	2.15 (1.33-3.47)	1.35 (1.14-1.59)
MV, HR (95% CI) [f]	-	1 (reference)	1.34 (0.83-2.17)	1.89 (1.00-3.59)	1.28 (1.01-1.62)
BMI, age at study enrollment					
No. of cases/person-years	0/10,549	24/603,197	36/764,236	30/400,602	-
Age-adjusted HR (95% CI)	-	1 (reference)	1.19 (0.71-2.00)	1.96 (1.14-3.36)	1.14 (0.93-1.40)

MV, HR (95% CI) [c]	-	1 (reference)	1.21 (0.71-2.06)	2.12 (1.19-3.76)	1.16 (0.93-1.45)
MV, HR (95% CI) [e]	-	1 (reference)	1.24 (0.81-1.90)	2.20 (1.41-3.43)	1.24 (1.06-1.45)
MV, HR (95% CI) [f]	-	1 (reference)	1.21 (0.71-2.06)	2.12 (1.19-3.77)	1.16 (0.93-1.45)
Average BMI during age 20 to 50y					
No. of cases/person-years	1/21,973	59/1,214,666	26/461,119	4/80,825	-
Age-adjusted HR (95% CI)	0.93 (0.12-6.71)	1 (reference)	1.22 (0.76-1.94)	1.12 (0.40-3.12)	1.33 (0.99-1.78)
MV, HR (95% CI) [c]	0.93 (0.13-6.74)	1 (reference)	1.20 (0.74-1.95)	1.08 (0.38-3.06)	1.34 (0.98-1.83)
MV, HR (95% CI) [e]	1.23 (0.30-5.03)	1 (reference)	1.32 (0.91-1.94)	2.22 (1.20-4.11)	1.44 (1.22-1.69)
MV, HR (95% CI) [f]	0.93 (0.13-6.74)	1 (reference)	1.21 (0.74-1.96)	1.08 (0.38-3.06)	1.34 (0.98-1.83)
Average BMI during age 20y to study enrollment					
No. of cases/person-years	0/13,234	49/1,063,962	35/585,090	6/116,298	-
Age-adjusted HR (95% CI)	-	1 (reference)	1.32 (0.86-2.05)	1.20 (0.51-2.81)	1.24 (0.93-1.66)
MV, HR (95% CI) [c]	-	1 (reference)	1.34 (0.86-2.11)	1.21 (0.50-2.91)	1.25 (0.92-1.70)
MV, HR (95% CI) [e]	1.01 (0.14-7.31)	1 (reference)	1.38 (0.96-1.98)	2.01 (1.14-3.54)	1.37 (1.09-1.71)
MV, HR (95% CI) [f]	-	1 (reference)	1.35 (0.86-2.12)	1.21 (0.51-2.92)	1.25 (0.92-1.70)
Average BMI during age 50y to study enrollment					
No. of cases/person-years	0/8,317	29/702,346	42/770,876	19/297,045	-
Age-adjusted HR (95% CI)	-	1 (reference)	1.33 (0.83-2.14)	1.67 (0.93-2.99)	1.22 (0.97-1.53)
MV, HR (95% CI) [c]	-	1 (reference)	1.35 (0.82-2.20)	1.74 (0.93-3.25)	1.24 (0.98-1.59)
MV, HR (95% CI) [e]	-	1 (reference)	1.49 (1.00-2.20)	1.91 (1.18-3.07)	1.33 (1.12-1.58)
MV, HR (95% CI) [f]	-	1 (reference)	1.35 (0.82-2.20)	1.74 (0.93-3.25)	1.24 (0.98-1.58)

[a]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, and family history of liver cancer. BMI = body mass index; CI = confidence interval; HR = hazard ratio.

[b]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, family history of liver cancer, the Healthy Eating Index-2010 scores, and alcohol.

[c]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, gallbladder stones or inflammation, the Healthy Eating Index-2010 scores, and alcohol.

[d]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, family history of liver cancer, the Healthy Eating Index-2010 scores, alcohol, and average BMI during age 50y to study enrollment.

[e]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, and family history of biliary tract cancer.

[f]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, liver cirrhosis, gallbladder stones or inflammation, and family history of biliary tract cancer, the Healthy Eating Index-2010 scores, and alcohol.

[g]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, liver cirrhosis, gallbladder stones or inflammation, and family history of biliary tract cancer, the Healthy Eating Index-2010 scores, alcohol, and average BMI during age 50y to study enrollment.

[h]The trend tests were conducted using BMI as a continuous variable.

Supplementary Table 3. Hazard ratios and 95% confidence intervals for incident liver and biliary tract cancers according to timing of being first overweight in a sub-cohort with available dietary data in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial

Model	Time when body mass index first exceeded 25 kg/m^2			
	Never	By age 20y	By age 50y	By age at study enrollment
Liver cancer				
No. of cases	22	22	39	14
Person-years	545,121	262,785	679,922	290,756
MV, HR (95% CI) [a]	1 (reference)	2.03 (1.26-3.28)	1.63 (1.06-2.49)	1.34 (0.78-2.29)
MV, HR (95% CI) [b]	1 (reference)	1.31 (0.70-2.47)	1.02 (0.59-1.77)	1.06 (0.54-2.09)
MV, HR (95% CI) [c]	1 (reference)	1.30 (0.69-2.46)	1.01 (0.58-1.76)	1.05 (0.53-2.07)
Biliary tract cancer				
No. of cases	19	17	38	16
Person-years	545,121	262,785	679,922	290,756
MV, HR (95% CI) [d]	1 (reference)	1.99 (1.16-3.39)	1.67 (1.06-2.61)	1.30 (0.74-2.26)
MV, HR (95% CI) [f]	1 (reference)	1.97 (0.98-3.96)	1.68 (0.95-3.00)	1.53 (0.78-3.01)
MV, HR (95% CI) [c]	1 (reference)	1.96 (0.98-3.94)	1.68 (0.95-3.00)	1.53 (0.78-2.99)

[a]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, and family history of liver cancer. CI = confidence interval; HR = hazard ratio.
[b]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, family history of liver cancer, the Healthy Eating Index-2010 scores, and alcohol.
[c]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, gallbladder stones or inflammation, the Healthy Eating Index-2010 scores, and alcohol.
[d]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, and family history of biliary tract cancer.
[f]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, liver cirrhosis, gallbladder stones or inflammation, family history of biliary tract cancer, the Healthy Eating Index-2010 scores, and alcohol.

Supplementary Table 4. Hazard ratios and 95% confidence intervals for incident liver and biliary tract cancers according to weight change in a sub-cohort with available dietary data in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial

Model	Loss	Stable weight	Gain	Gain	Gain	P_{trend} [h]
	≤-5 kg	-5 to < 5 kg	5 to < 10 kg	10 to < 20 kg	≥20 kg	
Liver cancer						
Weight change during early-to-mid adulthood (age 20 to 50y)						
No. of cases/person-years	2/37,985	19/495,005	17/452,912	33/528,546	26/264,135	-
Median (IQR)	-9.1 (-12.7, -6.8)	2.2 (0, 4.5)	7.7 (6.8, 9.1)	13.6 (11.3, 15.8)	24.9 (22.7, 31.7)	-
Age-adjusted HR (95% CI)	1.47 (0.34-6.34)	1 (reference)	0.99 (0.51-1.92)	1.73 (0.98-3.05)	3.03 (1.66-5.52)	<0.001
MV, HR (95% CI) [a]	0.60 (0.15-2.51)	1 (reference)	0.96 (0.59-1.55)	1.60 (1.06-2.43)	1.99 (1.25-3.17)	0.002
MV, HR (95% CI) [b]	1.15 (0.26-4.97)	1 (reference)	0.92 (0.48-1.78)	1.39 (0.78-2.47)	1.88 (1.00-3.53)	0.07
MV, HR (95% CI) [c]	1.14 (0.26-4.95)	1 (reference)	0.91 (0.47-1.76)	1.38 (0.77-2.46)	1.86 (0.99-3.51)	0.07
MV+BMI at 20 age, HR (95% CI) [d]	0.94 (0.21-4.21)	1 (reference)	0.95 (0.49-1.84)	1.48 (0.82-2.65)	2.02 (1.06-3.83)	0.04
Weight change across the adult life course (age 20y to study enrollment)						
No. of cases/person-years	2/40,764	19/315,334	17/327,537	33/578,276	26/516,673	-
Median (IQR)	-9.1 (-12.2, -6.8)	2.2 (0, 4.1)	7.7 (6.8, 9.1)	14.5 (12.2, 17.2)	27.2 (22.7, 34.1)	-
Age-adjusted HR (95% CI)	0.90 (0.21-3.94)	1 (reference)	0.80 (0.39-1.62)	1.21 (0.68-2.15)	1.01 (0.55-1.86)	0.54
MV, HR (95% CI) [b]	0.75 (0.17-3.24)	1 (reference)	0.79 (0.39-1.61)	1.08 (0.60-1.93)	0.78 (0.42-1.47)	0.72
MV, HR (95% CI) [c]	0.76 (0.18-3.32)	1 (reference)	0.79 (0.39-1.60)	1.07 (0.60-1.91)	0.78 (0.41-1.47)	0.71
MV+BMI at 20 age, HR (95% CI) [d]	0.67 (0.15-2.98)	1 (reference)	0.81 (0.40-1.66)	1.12 (0.62-2.02)	0.83 (0.43-1.58)	0.90
Weight change across the adult life course (age 50y to study enrollment)						
No. of cases/person-years	16/117,331	52/1,035,174	20/345,663	9/219,455	0/60,960	
Median (IQR)	-9.1 (-12.7-6.8)	1.8 (0.0-3.6)	6.8 (6.8-9.1)	13.6 (11.4-15.9)	25.0 (21.8-29.5)	
Age-adjusted HR (95% CI)	2.60 (1.48-4.56)	1 (reference)	1.09 (0.65-1.82)	0.75 (0.37-1.52)	-	<0.001
MV, HR (95% CI) [b]	1.74 (0.97-3.11)	1 (reference)	1.11 (0.66-1.87)	0.73 (0.36-1.50)	-	0.006
MV, HR (95% CI) [c]	1.73 (0.96-3.10)	1 (reference)	1.11 (0.66-1.88)	0.72 (0.35-1.49)	-	0.006
MV+BMI at 20 age, HR (95% CI) [d]	1.71 (0.95-3.07)	1 (reference)	1.12 (0.66-1.88)	0.73 (0.36-1.51)	-	0.008
Biliary tract cancer						
Weight change during early-to-mid adulthood (age 20 to 50y)						
No. of cases/person-years	1/37,985	20/495,005	29/452,912	23/528,546	17/264,135	-

Median (IQR)	-9.1 (-12.7, -6.8)	2.2 (0, 4.5)	7.7 (6.8, 9.1)	13.6 (11.3, 15.8)	24.9 (22.7, 31.7)	-
Age-adjusted HR (95% CI)	0.68 (0.09-5.08)	1 (reference)	1.60 (0.90-2.82)	1.11 (0.61-2.04)	1.77 (0.92-3.40)	0.09
MV, HR (95% CI) [e]	0.37 (0.05-2.67)	1 (reference)	1.23 (0.78-1.96)	1.12 (0.71-1.78)	1.74 (1.05-2.89)	0.01
MV, HR (95% CI) [f]	0.65 (0.09-4.83)	1 (reference)	1.57 (0.89-2.79)	1.09 (0.59-2.01)	1.70 (0.86-3.37)	0.12
MV, HR (95% CI) [c]	0.64 (0.09-4.75)	1 (reference)	1.57 (0.89-2.79)	1.09 (0.59-2.01)	1.71 (0.86-3.38)	0.11
MV+BMI at 20 age, HR (95% CI) [g]	0.49 (0.06-3.81)	1 (reference)	1.63 (0.92-2.90)	1.17 (0.63-2.16)	1.83 (0.92-3.63)	0.07
Weight change across the adult life course (age 20y to study enrollment)						
No. of cases/person-years	1/40,764	20/315,334	29/327,537	23/578,276	17/516,673	-
Median (IQR)	-9.1 (-12.2, -6.8)	2.2 (0, 4.1)	7.7 (6.8, 9.1)	14.5 (12.2, 17.2)	27.2 (22.7, 34.1)	-
Age-adjusted HR (95% CI)	1.75 (0.50-6.16)	1 (reference)	0.89 (0.41-1.97)	1.31 (0.68-2.51)	1.48 (0.77-2.83)	0.43
MV, HR (95% CI) [f]	1.67 (0.47-5.88)	1 (reference)	0.90 (0.41-1.97)	1.34 (0.69-2.57)	1.52 (0.78-2.98)	0.44
MV, HR (95% CI) [c]	1.66 (0.47-5.86)	1 (reference)	0.90 (0.41-1.98)	1.34 (0.70-2.58)	1.52 (0.78-2.98)	0.44
MV+BMI at 20 age, HR (95% CI) [g]	1.39 (0.38-5.08)	1 (reference)	0.93 (0.42-2.05)	1.41 (0.73-2.73)	1.63 (0.82-3.22)	0.29
Weight change across the adult life course (age 50y to study enrollment)						
No. of cases/person-years	8/117,331	54/1,035,174	16/345,663	9/219,455	3/60,960	
Median (IQR)	-9.1 (-12.7-6.8)	1.8 (0.0-3.6)	6.8 (6.8-9.1)	13.6 (11.4-15.9)	25.0 (21.8-29.5)	
Age-adjusted HR (95% CI)	1.23 (0.58-2.58)	1 (reference)	0.83 (0.48-1.46)	0.71 (0.35-1.45)	0.84 (0.26-2.70)	0.39
MV, HR (95% CI) [f]	1.12 (0.52-2.38)	1 (reference)	0.83 (0.47-1.46)	0.70 (0.34-1.44)	0.82 (0.25-2.68)	0.49
MV, HR (95% CI) [c]	1.12 (0.52-2.38)	1 (reference)	0.83 (0.47-1.46)	0.70 (0.34-1.43)	0.81 (0.25-2.66)	0.48
MV+BMI at 20 age, HR (95% CI) [g]	1.07 (0.50-2.30)	1 (reference)	0.84 (0.48-1.47)	0.70 (0.34-1.44)	0.81 (0.25-2.65)	0.54

[a]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, and family history of liver cancer. BMI = body mass index; CI = confidence interval; HR = hazard ratio; IQR = interquartile range; MV = multivariable model.
[b]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, family history of liver cancer, the Healthy Eating Index-2010 scores, and alcohol.
[c]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, gallbladder stones or inflammation, the Healthy Eating Index-2010 scores, and alcohol.
[d]Models in liver cancer were further adjusted for the BMI at 20 ages.
[e]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, and family history of biliary tract cancer.
[f]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, liver cirrhosis, gallbladder stones or inflammation, and family history of biliary tract cancer, the Healthy Eating Index-2010 scores, and alcohol.
[g]Models in biliary tract cancer were further adjusted for the BMI at 20 ages.
[h]P values for trend were calculated using continuous BMI exposure variables.

Supplementary Table 5. Hazard ratios and 95% confidence intervals for incident liver and biliary tract cancers according to weight change in a sub-cohort with available dietary data in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial

Model	Loss ≤-5 kg	Stable weight -5 to < 5 kg	Gain 5 to < 10 kg	Gain 10 to < 20 kg	Gain ≥20 kg	P_{trend}[f]
Liver cancer						
Weight change during early-to-mid adulthood (age 20 to 50y)						
No. of cases/person-years	2/37,928	18/494,710	17/452,634	29/528,132	25/263,876	-
Median (IQR)	-9.08 (-12.71,-6.81)	2.27 (0.00,4.54)	7.72 (6.81,9.08)	13.62 (11.35,15.89)	24.97 (22.70,31.78)	-
Age-adjusted HR (95% CI)	1.58 (0.37-6.79)	1 (reference)	1.06 (0.55-2.05)	1.63 (0.90-2.93)	3.16 (1.71-5.83)	<0.001
MV, HR (95% CI) [a]	1.23 (0.28-5.32)	1 (reference)	0.98 (0.50-1.90)	1.29 (0.70-2.35)	1.95 (1.02-3.73)	0.90
MV, HR (95% CI) [b]	1.26 (0.29-5.49)	1 (reference)	0.97 (0.50-1.88)	1.28 (0.70-2.33)	1.90 (0.99-3.64)	0.11
MV+BMI at 20 age, HR (95% CI) [c]	1.06 (0.24-4.77)	1 (reference)	1.00 (0.51-1.95)	1.35 (0.73-2.48)	2.06 (1.06-3.98)	0.06
Weight change across the adult life course (age 20y to study enrollment)						
No. of cases/person-years	2/40,764	15/315,121	12/327,298	37/577,950	25/516,218	-
Median (IQR)	-9.08 (-12.26,-6.81)	2.27 (0.00,4.09)	7.72 (6.81,9.08)	14.53 (12.26,17.25)	27.24 (22.70,34.05)	-
Age-adjusted HR (95% CI)	1.03 (0.24-4.52)	1 (reference)	0.78 (0.37-1.67)	1.38 (0.76-2.51)	1.07 (0.57-2.04)	0.45
MV, HR (95% CI) [a]	0.85 (0.19-3.73)	1 (reference)	0.78 (0.36-1.66)	1.24 (0.67-2.27)	0.83 (0.43-1.62)	0.83
MV, HR (95% CI) [b]	0.88 (0.20-3.85)	1 (reference)	0.76 (0.36-1.63)	1.21 (0.66-2.23)	0.81 (0.42-1.58)	0.76
MV+BMI at 20 age, HR (95% CI) [c]	0.79 (0.18-3.57)	1 (reference)	0.79 (0.37-1.69)	1.27 (0.69-2.35)	0.86 (0.44-1.71)	0.94
Weight change across the adult life course (age 50y to study enrollment)						
No. of cases/person-years	13/117,126	51/1,034,547	18/345,454	9/219,266	0/60,888	
Median (IQR)	-9.08 (-12.71,-6.81)	1.82 (0.00,3.63)	6.81 (6.81,9.08)	13.62 (11.35,15.89)	24.74 (22.25,29.51)	
Age-adjusted HR (95% CI)	2.15 (1.17-3.95)	1 (reference)	0.99 (0.58-1.69)	0.76 (0.37-1.54)	-	0.001
MV, HR (95% CI) [a]	1.39 (0.74-2.62)	1 (reference)	1.01 (0.58-1.73)	0.73 (0.35-1.49)	-	0.02
MV, HR (95% CI) [b]	1.39 (0.74-2.62)	1 (reference)	1.01 (0.59-1.74)	0.72 (0.35-1.49)	-	0.02
MV+BMI at 20 age, HR (95% CI) [c]	1.38 (0.73-2.60)	1 (reference)	1.01 (0.59-1.74)	0.73 (0.35-1.50)	-	0.02
Biliary tract cancer						
Weight change during early-to-mid adulthood (age 20 to 50y)						
No. of cases/person-years	1/37,928	18/494,710	29/452,634	21/528,132	14/263,876	-
Median (IQR)	-9.08 (-12.71,-6.81)	2.27 (0.00,4.54)	7.72 (6.81,9.08)	13.62 (11.35,15.89)	24.97 (22.70,31.78)	-
Age-adjusted HR (95% CI)	0.76 (0.10-5.72)	1 (reference)	1.78 (0.99-3.21)	1.14 (0.61-2.15)	1.65 (0.81-3.33)	0.58

MV, HR (95% CI) [d]	0.70 (0.09-5.25)	1 (reference)	1.75 (0.97-3.17)	1.12 (0.59-2.13)	1.64 (0.79-3.42)	0.59
MV, HR (95% CI) [b]	0.71 (0.09-5.32)	1 (reference)	1.74 (0.96-3.14)	1.11 (0.58-2.11)	1.61 (0.77-3.34)	0.63
MV+BMI at 20 age, HR (95% CI) [e]	0.56 (0.07-4.40)	1 (reference)	1.81 (1.00-3.28)	1.19 (0.62-2.27)	1.74 (0.83-3.65)	0.45
Weight change across the adult life course (age 20y to study enrollment)						
No. of cases/person-years	3/40,764	12/315,121	11/327,298	31/577,950	26/516,218	-
Median (IQR)	-9.08 (-12.26,-6.81)	2.27 (0.00,4.09)	7.72 (6.81,9.08)	14.53 (12.26,17.25)	27.24 (22.70,34.05)	-
Age-adjusted HR (95% CI)	1.91 (0.54-6.77)	1 (reference)	0.89 (0.39-2.03)	1.43 (0.73-2.78)	1.36 (0.68-2.69)	0.001
MV, HR (95% CI) [d]	1.79 (0.50-6.36)	1 (reference)	0.90 (0.40-2.04)	1.46 (0.74-2.86)	1.40 (0.69-2.86)	0.97
MV, HR (95% CI) [b]	1.82 (0.51-6.47)	1 (reference)	0.89 (0.39-2.01)	1.44 (0.74-2.83)	1.38 (0.68-2.81)	0.97
MV+BMI at 20 age, HR (95% CI) [e]	1.57 (0.42-5.80)	1 (reference)	0.92 (0.41-2.10)	1.52 (0.77-3.00)	1.48 (0.72-3.03)	0.82
Weight change across the adult life course (age 50y to study enrollment)						
No. of cases/person-years	7/117,126	50/1,034,547	14/345,454	9/219,266	3/60,888	
Median (IQR)	-9.08 (-12.71,-6.81)	1.82 (0.00,3.63)	6.81 (6.81,9.08)	13.62 (11.35,15.89)	24.74 (22.25,29.51)	
Age-adjusted HR (95% CI)	1.16 (0.53-2.56)	1 (reference)	0.78 (0.43-1.42)	0.77 (0.38-1.56)	0.90 (0.28-2.90)	0.48
MV, HR (95% CI) [d]	1.08 (0.48-2.42)	1 (reference)	0.78 (0.43-1.42)	0.75 (0.36-1.55)	0.89 (0.27-2.93)	0.55
MV, HR (95% CI) [b]	1.08 (0.48-2.42)	1 (reference)	0.78 (0.43-1.42)	0.75 (0.36-1.54)	0.89 (0.27-2.90)	0.54
MV+BMI at 20 age, HR (95% CI) [e]	1.05 (0.47-2.36)	1 (reference)	0.79 (0.43-1.43)	0.75 (0.36-1.55)	0.89 (0.27-2.91)	0.59

[a]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, family history of liver cancer, the Healthy Eating Index-2010 scores, and alcohol. BMI = body mass index; CI = confidence interval; HR = hazard ratio; IQR = interquartile range; MV = multivariable model.

[b]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, gallbladder stones or inflammation, the Healthy Eating Index-2010 scores, and alcohol.

[c]Models in liver cancer were further adjusted for the BMI at 20 ages.

[d]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, liver cirrhosis, gallbladder stones or inflammation, and family history of biliary tract cancer, the Healthy Eating Index-2010 scores, and alcohol.

[e]Models in biliary tract cancer were further adjusted for the BMI at 20 ages.

[f]P values for trend were calculated using continuous BMI exposure variables.

Supplementary Table 6. Hazard ratios and 95% confidence intervals for incident liver and biliary tract cancers according to body mass index trajectories across adulthood in a sub-cohort with available dietary data in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial

BMI trajectories	Liver cancer			Biliary tract cancer		
	No. of cases/ Person-years	HR (95% CI)[a]	HR (95% CI)[b]	No. of cases/ Person-years	HR (95% CI)[b]	HR (95% CI)[b]
Stable normal	18/485,387	1 (reference)	1 (reference)	14/485,387	1 (reference)	1 (reference)
Normal to overweight	47/901,870	1.09 (0.62-1.91)	1.07 (0.61-1.87)	52/901,870	2.10 (1.15-3.86)	2.10 (1.14-3.86)
Overweight to obese	4/75,594	1.01 (0.32-3.10)	0.99 (0.32-3.08)	5/75,594	2.85 (0.98-8.29)	2.85 (0.98-8.31)
Normal to obese	28/315,732	1.71 (0.91-3.24)	1.70 (0.89-3.22)	19/315,732	2.40 (1.16-4.98)	2.39 (1.16-4.95)

[a]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, family history of liver cancer, the Healthy Eating Index-2010 scores, and alcohol. BMI = body mass index; CI = confidence interval; HR = hazard ratio.

[b]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, education, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, diverticulitis, liver cirrhosis, gallbladder stones or inflammation, the Healthy Eating Index-2010 scores, and alcohol.

[c]Models were adjusted for age, sex, center, race and ethnicity, randomization arm, job status, aspirin use more than 12 months, smoking status, diabetes mellitus, hypertension, liver cirrhosis, gallbladder stones or inflammation, and family history of biliary tract cancer, the Healthy Eating Index-2010 scores, and alcohol.

Note: underweight, BMI <18.4 kg/m^2; normal weight, BMI 18.5-< 24.9 kg/m^2; overweight, BMI 25-< 29.9 kg/m^2; obese, BMI ≥30 kg/m^2.