

## Supplementary Appendix

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

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Table 1: Selected characteristics for each prospective study

Study <sup>ref</sup>	Females	Males	Study entry	Follow-up Median (max)	Age at entry Median (range)	BMI (kg/m <sup>2</sup> ) Mean (SD)	% ever smokers	% C-M	Deaths
NIH-AARP Diet and Health Study (AARP) <sup>7,20</sup>	194960	306224	1995-97	10 (11) yrs	62 (50-71) yrs	27.0 (4.6)	64%	22%	58472
Adventist Health Study 1 (AHS-1) <sup>21</sup>	17693	12249	1976-80	12 (22) yrs	53 (25-83) yrs	24.6 (4.2)	25%	10%	3846
Agricultural Health Study (AHS) <sup>22</sup>	27888	38215	1993-97	10 (14) yrs	46 (19-83) yrs	26.9 (4.4)	39%	8%	3274
Breast Cancer Detection Demonstration Project Follow-up Study (BCDDP) <sup>23,24</sup>	41076	0	1987-89	17 (19) yrs	61 (40-83) yrs	25.0 (4.4)	45%	26%	7587
California Teachers Study (CTS) <sup>25</sup>	107846	0	1995-96	9 (9) yrs	52 (22-83) yrs	24.8 (4.9)	35%	27%	5027
CLUE I & II (CLUE) <sup>26</sup>	12413	8863	1989	14 (19) yrs	52 (19-83) yrs	26.2 (4.7)	47%	5%	4506
Cohort of Swedish Men (COSM) <sup>27</sup>	0	43125	1998	10 (10) yrs	59 (45-79) yrs	25.8 (3.3)	64%	38%	6004
Health Professionals Follow-up Study (HPFS) <sup>10</sup>	0	45382	1986-87	17 (23) yrs	54 (39-78) yrs	25.5 (3.2)	54%	34%	10542
Iowa Women's Health Study (IWHS) <sup>28</sup>	40623	0	1986	19 (19) yrs	62 (52-71) yrs	26.1 (4.8)	35%	17%	11565
Melbourne Collaborative Cohort Study (MCCS) <sup>18</sup>	24396	16956	1990-94	15 (18) yrs	56 (28-81) yrs	26.9 (4.4)	43%	8%	4765
Nurses' Health Study (NHS) <sup>11,12</sup>	90975	0	1976-78	26 (28) yrs	43 (29-56) yrs	24.4 (4.4)	57%	12%	16597
NYU Women's Health Study (NYUWHS) <sup>29</sup>	9683	0	1985-91	19 (20) yrs	52 (31-70) yrs	24.6 (4.4)	56%	8%	1038
Physicians' Health Study I & II (PHS) <sup>13</sup>	0	24381	1981-00	22 (26) yrs	53 (39-83) yrs	25.2 (3.0)	46%	6%	3014
Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) <sup>30-32</sup>	66278	63756	1993-01	9 (13) yrs	62 (50-78) yrs	27.3 (4.7)	54%	13%	12783
Swedish Mammography Cohort (SMC) <sup>33</sup>	36198	0	1998	10 (10) yrs	60 (48-83) yrs	25.1 (3.9)	46%	35%	3176
US Radiologic Technicians Cohort (USRT) <sup>34</sup>	64213	18197	1994-98	6 (7) yrs	46 (31-83) yrs	25.6 (4.9)	47%	9%	1450
VITamins and Lifestyle (VITAL) Study <sup>35</sup>	34386	33163	2000-02	6 (7) yrs	61 (50-76) yrs	27.4 (5.0)	53%	22%	3453
Women's Health Study (WHS) <sup>36-38</sup>	36654	0	1993-96	13 (15) yrs	52 (38-83) yrs	26.0 (5.0)	50%	1%	1908
Women's Lifestyle and Health Study (WLHS) <sup>39</sup>	47165	0	1991-92	15 (15) yrs	40 (30-50) yrs	23.5 (3.6)	59%	10%	1080
<b>Total</b>	<b>852447</b>	<b>610511</b>	<b>1976-02</b>	<b>10 (28) yrs</b>	<b>58 (19-83) yrs</b>	<b>26.2 (4.7)</b>	<b>53%</b>	<b>19%</b>	<b>160087</b>

\*C-M: co-morbidities (cancer and heart disease). Information on heart disease was not collected in CLUE II or MCCS.

Table 2: Prevalence of potential confounders by BMI category

		BMI (kg/m <sup>2</sup> )									
		15-18.4	18.5-19.9	20-22.4	22.5-24.9	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9	All
Male participants	Median BMI	17.6	19.5	21.7	23.8	26.2	28.7	31.6	36.6	42.3	
Female participants	Median BMI	17.9	19.4	21.3	23.6	26.1	28.6	31.9	36.9	42.6	
Male participants	All	0.5%	1%	8%	23%	30%	19%	15%	3%	1%	100%
	Healthy never-smokers*	0.4%	1%	10%	26%	30%	17%	13%	3%	1%	100%
Female participants	All	2%	6%	22%	25%	19%	11%	11%	4%	2%	100%
	Healthy never-smokers*	2%	6%	22%	24%	18%	11%	12%	4%	2%	100%
Smoking status	Never	48%	51%	51%	48%	45%	44%	45%	47%	48%	47%
	Former	27%	28%	32%	38%	43%	45%	45%	44%	44%	40%
	Current	25%	20%	17%	14%	12%	11%	10%	9%	8%	13%
Co-morbidities	Cancer	10%	8%	8%	8%	8%	8%	8%	8%	9%	8%
	Heart disease	11%	8%	10%	13%	15%	17%	17%	17%	17%	14%
	Emphysema	5%	3%	2%	2%	2%	2%	2%	3%	3%	2%
	Stroke	2%	1%	1%	2%	2%	2%	2%	2%	2%	2%
Alcohol	0 g/day	36%	30%	27%	26%	26%	28%	32%	38%	44%	28%
	>0 g/day	64%	70%	73%	74%	74%	72%	68%	62%	56%	72%
Physical activity	Low	35%	30%	28%	29%	31%	35%	41%	50%	58%	33%
	Medium	29%	31%	31%	30%	29%	29%	28%	26%	23%	29%
	High	37%	39%	40%	41%	40%	36%	31%	24%	19%	38%
Education	High school	25%	22%	23%	27%	30%	32%	33%	33%	32%	28%
	Some college	23%	22%	23%	23%	26%	27%	30%	31%	33%	25%
	College+	53%	57%	54%	50%	45%	41%	37%	36%	35%	46%
Marital status	Married	67%	72%	76%	78%	80%	80%	77%	71%	64%	78%
	Not married	33%	28%	25%	22%	20%	20%	23%	29%	36%	22%

\*No cancer or heart disease at baseline

Table 3: Estimated hazard ratios<sup>†</sup> (and 95% CI) for death from any cause according to BMI category: impact of excluding smokers and those with co-morbidities\*

a) Female participants

		BMI (kg/m <sup>2</sup> )								
		15-18.4	18.5-19.9	20-22.4	22.5-24.9	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9
No. of deaths	All	2345	4541	15099	17576	14499	9196	10489	4060	2010
ASR		734	486	389	362	376	408	463	581	785
Adjusted HR		2.02	1.34	1.06	1.00	1.03	1.11	1.25	1.59	1.99
95% CI		[1.94-2.11]	[1.30-1.38]	[[1.04-1.09]	-	[1.01-1.06]	[1.08-1.14]	[1.22-1.28]	[1.53-1.64]	[1.90-2.09]
No. of deaths	Never and former-smokers	1268	2654	9783	12257	10838	7127	8462	3387	1736
ASR		558	372	316	302	327	359	419	543	756
Adjusted HR		1.81	1.23	1.04	1.00	1.07	1.16	1.35	1.75	2.28
95% CI		[1.71-1.91]	[1.18-1.29]	[1.01-1.06]	-	[1.04-1.10]	[1.13-1.20]	[1.31-1.38]	[1.68-1.82]	[2.17-2.40]
No. of deaths	Never-smokers	699	1471	5487	7129	6417	4220	4985	1932	913
ASR		471	324	284	276	306	326	389	507	686
Adjusted HR		1.60	1.16	1.00	1.00	1.09	1.17	1.39	1.83	2.39
95% CI		[1.48-1.73]	[1.09-1.22]	[0.97-1.04]	-	[1.05-1.13]	[1.13-1.22]	[1.34-1.44]	[1.74-1.93]	[2.23-2.57]
No. of deaths	Healthy never-smokers	426	1016	3877	5044	4474	2933	3515	1323	623
ASR		368	278	249	239	264	281	347	450	610
Adjusted HR		1.47	1.14	1.00	1.00	1.09	1.19	1.44	1.88	2.51
95% CI		[1.33-1.62]	[1.07-1.22]	[0.96-1.04]	-	[1.05-1.14]	[1.14-1.24]	[1.38-1.50]	[1.77-2.00]	[2.30-2.73]

b) Male participants

		BMI (kg/m <sup>2</sup> )								
		15-18.4	18.5-19.9	20-22.4	22.5-24.9	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9
No. of deaths	All	700	1245	7425	17714	22497	14239	12382	3039	1031
ASR		1273.95	833.47	610.2	510.99	540.95	569.3	670.57	857.39	1127.67
Adjusted HR		1.98	1.60	1.18	1.00	0.97	1.03	1.16	1.44	1.93
95% CI		[1.83-2.13]	[1.51-1.69]	[1.15-1.21]	-	[0.95-0.99]	[1.01-1.06]	[1.13-1.19]	[1.39-1.50]	[1.81-2.06]
No. of deaths	Never and former-smokers	427	761	5187	13454	17978	11604	10158	2559	880
ASR		1025.02	662.17	504.29	439.35	474.89	519.11	621.70	811.99	1062.31
Adjusted HR		1.77	1.48	1.12	1.00	1.01	1.10	1.25	1.60	2.20
95% CI		[1.61-1.95]	[1.37-1.59]	[1.09-1.16]	-	[0.99-1.03]	[1.07-1.13]	[1.22-1.28]	[1.54-1.68]	[2.05-2.36]
No. of deaths	Never-smokers	124	236	1869	4632	5528	3241	2734	673	247
ASR		769.84	413.82	401.12	360.28	388.73	428.51	534.08	692.74	1015.36
Adjusted HR		1.42	1.11	1.04	1.00	1.04	1.17	1.43	1.95	2.86
95% CI		[1.18-1.69]	[0.97-1.26]	[0.99-1.10]	-	[1.00-1.08]	[1.12-1.23]	[1.36-1.50]	[1.79-2.12]	[2.51-3.25]
No. of deaths	Healthy never-smokers	78	136	1160	2941	3509	2040	1692	424	158
ASR		637.84	316.06	324.75	299.68	327.2	369.35	437.02	570.48	881.76
Adjusted HR		1.37	1.01	1.00	1.00	1.06	1.21	1.44	2.06	2.93
95% CI		[1.09-1.71]	[0.85-1.20]	[0.93-1.07]	-	[1.01-1.12]	[1.14-1.28]	[1.35-1.53]	[1.85-2.28]	[2.49-3.45]

†Hazard ratio calculated with age as the underlying time scale, stratified by study and adjusted for alcohol (g/day), education, marital status and overall physical activity. \*No cancer or heart disease at baseline. ASR/100,000- age-standardized rate, standardized using the US general population.



Table 4: Estimated hazard ratios<sup>†</sup> (and 95% CI) for death from any cause according to BMI category: impact of excluding additional co-morbidities in never smokers\*

a) Female participants

Co-morbidity exclusion		BMI (kg/m <sup>2</sup> )								
		15-18.4	18.5-19.9	20-22.4	<u>22.5-24.9</u>	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9
Adjusted HR	None	1.67	1.22	1.04	1.00	1.09	1.13	1.29	1.62	2.1
95% CI		[1.48-1.88]	[1.12-1.33]	[0.99-1.10]	-	[1.03-1.15]	[1.07-1.20]	[1.22-1.36]	[1.50-1.75]	[1.90-2.32]
Adjusted HR	Excluding cancer	1.63	1.24	1.06	1.00	1.08	1.14	1.33	1.68	2.28
95% CI		[1.42-1.87]	[1.13-1.37]	[1.00-1.13]	-	[1.02-1.15]	[1.07-1.22]	[1.25-1.42]	[1.54-1.84]	[2.04-2.54]
Adjusted HR	Additionally excluding heart disease	1.57	1.27	1.06	1.00	1.10	1.19	1.36	1.67	2.16
95% CI		[1.34-1.85]	[1.14-1.42]	[0.99-1.14]	-	[1.03-1.18]	[1.10-1.28]	[1.26-1.46]	[1.51-1.84]	[1.90-2.46]
Adjusted HR	Additionally excluding emphysema	1.56	1.26	1.06	1.00	1.10	1.19	1.36	1.67	2.14
95% CI		[1.32-1.84]	[1.13-1.41]	[0.98-1.13]	-	[1.03-1.17]	[1.10-1.28]	[1.26-1.46]	[1.51-1.84]	[1.88-2.44]
Adjusted HR	Additionally excluding stroke	1.56	1.24	1.05	1.00	1.10	1.18	1.35	1.67	2.14
95% CI		[1.32-1.84]	[1.11-1.39]	[0.98-1.13]	-	[1.02-1.17]	[1.09-1.27]	[1.26-1.46]	[1.50-1.85]	[1.87-2.44]

b) Male participants

Co-morbidity exclusion		BMI (kg/m <sup>2</sup> )								
		15-18.4	18.5-19.9	20-22.4	22.5-24.9	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9
Adjusted HR	None	1.51	1.17	1.06	1.00	1.02	1.16	1.38	1.83	2.83
95% CI		[1.23-1.87]	[0.99-1.37]	[0.99-1.13]	-	[0.97-1.07]	[1.10-1.22]	[1.31-1.46]	[1.67-2.01]	[2.46-3.25]
Adjusted HR	Excluding cancer	1.60	1.16	1.04	1.00	1.04	1.20	1.43	1.94	3.01
95% CI		[1.28-1.99]	[0.97-1.37]	[0.97-1.12]	-	[0.99-1.09]	[1.13-1.27]	[1.34-1.51]	[1.76-2.14]	[2.60-3.49]
Adjusted HR	Additionally excluding heart disease	1.61	1.00	1.01	1.00	1.06	1.23	1.44	1.96	2.91
95% CI		[1.23-2.11]	[0.80-1.25]	[0.93-1.10]	-	[1.00-1.13]	[1.15-1.31]	[1.34-1.55]	[1.75-2.20]	[2.44-3.47]
Adjusted HR	Additionally excluding emphysema	1.60	0.98	1.01	1.00	1.06	1.23	1.45	1.97	2.93
95% CI		[1.22-2.10]	[0.78-1.23]	[0.93-1.10]	-	[1.00-1.13]	[1.15-1.32]	[1.35-1.57]	[1.75-2.21]	[2.45-3.49]
Adjusted HR	Additionally excluding stroke	1.57	0.98	1.01	1.00	1.06	1.24	1.45	1.96	2.95
95% CI		[1.19-2.08]	[0.77-1.23]	[0.92-1.10]	-	[1.00-1.13]	[1.15-1.33]	[1.35-1.56]	[1.74-2.21]	[2.47-3.53]

†Hazard ratio calculated with age as the underlying time scale, stratified by study and adjusted for alcohol (g/day), education, marital status and overall physical activity. \*Analyses were restricted to the 9 cohorts including females and 7 cohorts including males that had all four co-morbidity variables.

Table 5: Estimated hazard ratios<sup>†</sup>(and 95% CI) for death from any cause according to BMI category: impact of adjustment for potential confounding variables in healthy never smokers\*

a)Female participants

Adjustment factor	BMI (kg/m <sup>2</sup> )									
	15-18.4	18.5-19.9	20-22.4	22.5-24.9	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9	
Unadjusted HR [95% CI]	-	1.49 [1.35-1.65]	1.15 [1.07-1.23]	0.99 [0.95-1.04]	1.00 -	1.11 [1.06-1.15]	1.22 [1.17-1.28]	1.51 [1.44-1.57]	2.02 [1.90-2.15]	2.74 [2.52-2.98]
Adjusted HR [95% CI]	Alcohol	1.48 [1.34-1.63]	1.15 [1.07-1.23]	1.00 [0.96-1.04]	1.00 -	1.10 [1.05-1.14]	1.20 [1.15-1.26]	1.47 [1.41-1.53]	1.95 [1.84-2.08]	2.63 [2.41-2.86]
Adjusted HR [95% CI]	Education	1.50 [1.36-1.66]	1.16 [1.08-1.24]	1.00 [0.96-1.04]	1.00 -	1.10 [1.06-1.15]	1.21 [1.16-1.27]	1.49 [1.43-1.56]	2.00 [1.88-2.12]	2.70 [2.48-2.93]
Adjusted HR [95% CI]	Marital status	1.48 [1.34-1.63]	1.14 [1.07-1.22]	0.99 [0.95-1.04]	1.00 -	1.11 [1.06-1.15]	1.22 [1.17-1.28]	1.50 [1.44-1.57]	2.01 [1.89-2.14]	2.71 [2.49-2.94]
Adjusted HR [95% CI]	Physical activity	1.49 [1.35-1.65]	1.15 [1.07-1.23]	1.00 [0.95-1.04]	1.00 -	1.10 [1.06-1.15]	1.21 [1.16-1.27]	1.49 [1.42-1.55]	1.97 [1.86-2.10]	2.65 [2.44-2.88]

b)Male participants

Adjustment factor		BMI (kg/m <sup>2</sup> )								
		15-18.4	18.5-19.9	20-22.4	22.5-24.9	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9
Unadjusted HR [95% CI]	-	1.48 [1.18-1.85]	1.06 [0.89-1.26]	1.01 [0.94-1.08]	1.00 -	1.07 [1.02-1.13]	1.24 [1.17-1.31]	1.52 [1.43-1.61]	2.25 [2.03-2.49]	3.29 [2.80-3.87]
Adjusted HR [95% CI]	Alcohol	1.44 [1.15-1.81]	1.04 [0.88-1.24]	1.01 [0.94-1.08]	1.00 -	1.07 [1.02-1.12]	1.23 [1.17-1.31]	1.50 [1.41-1.59]	2.21 [2.00-2.45]	3.21 [2.73-3.77]
Adjusted HR [95% CI]	Education	1.48 [1.18-1.86]	1.06 [0.89-1.26]	1.01 [0.95-1.09]	1.00 -	1.07 [1.01-1.12]	1.22 [1.16-1.30]	1.49 [1.40-1.58]	2.18 [1.96-2.42]	3.19 [2.71-3.75]
Adjusted HR [95% CI]	Marital status	1.41 [1.12-1.76]	1.03 [0.86-1.22]	1.00 [0.93-1.07]	1.00 -	1.08 [1.03-1.13]	1.25 [1.18-1.32]	1.52 [1.43-1.62]	2.22 [2.00-2.46]	3.22 [2.74-3.78]
Adjusted HR [95% CI]	Physical activity	1.47 [1.17-1.84]	1.05 [0.89-1.25]	1.01 [0.95-1.09]	1.00 -	1.06 [1.01-1.12]	1.22 [1.15-1.29]	1.47 [1.39-1.57]	2.15 [1.94-2.39]	3.12 [2.66-3.67]

†Hazard ratios calculated with age as the underlying time scale, stratified by study. \*No cancer or heart disease at baseline.

Table 6: Estimated hazard ratios<sup>†</sup> (and 95% CI) for death from any cause according to BMI category in healthy\* never smokers: impact of adjustment for reporting error using external data from NHANES\*\*

	BMI (kg/m <sup>2</sup> )								
	15-18.4	18.5-19.9	20-22.4	22.5-24.9	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9
<i>Female participants</i>									
HR	1.47	1.14	1.00	1.00	1.09	1.19	1.44	1.88	2.51
95% CI	[1.33-1.62]	[1.07-1.22]	[0.96-1.04]	-	[1.05-1.14]	[1.14-1.24]	[1.38-1.50]	[1.77-2.00]	[2.30-2.73]
HR adjusted for reporting error <sup>‡</sup>	1.62	1.28	0.99	1.00	1.05	1.16	1.36	1.80	2.42
95% CI	[1.42-1.86]	[1.18-1.38]	[0.94-1.03]	-	[1.01-1.09]	[1.11-1.21]	[1.31-1.42]	[1.70-1.91]	[2.24-2.62]
<i>Male participants</i>									
HR	1.37	1.01	1.00	1.00	1.06	1.21	1.44	2.06	2.93
95% CI	[1.09-1.71]	[0.85-1.20]	[0.93-1.07]	-	[1.01-1.12]	[1.14-1.28]	[1.35-1.53]	[1.85-2.28]	[2.49-3.45]
HR adjusted for reporting error <sup>‡</sup>	1.36	1.11	0.98	1.00	1.03	1.17	1.39	1.98	2.82
95% CI	[1.01-1.84]	[0.90-1.37]	[0.90-1.06]	-	[0.98-1.08]	[1.10-1.23]	[1.30-1.47]	[1.79-2.19]	[2.41-3.31]

<sup>†</sup>Hazard ratios calculated with age as the underlying time scale, stratified by study and adjusted for alcohol (g/day), education, marital status and overall physical activity. \*No cancer or heart disease at baseline. \*\* Adjustment equations were estimated using NHANES survey data<sup>17</sup> by sex:  $BMI_{\text{measured}}=0.63+1.01BMI_{\text{self-reported}}+0.0006\text{Age}$  for females and  $BMI_{\text{measured}}=0.29+0.98BMI_{\text{self-reported}}+0.012\text{Age}$  for males.

Table 7: Estimated hazard ratios† (and 95% CI) for death from any cause according to BMI category: by physical activity level (male and female participants combined) in healthy\* never-smokers

Physical activity		BMI (kg/m <sup>2</sup> )								
		15-18.4	18.5-19.9	20-22.4	22.5-24.9	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9
Adjusted HR [95% CI]	Low	1.62 [1.38-1.91]	1.15 [1.02-1.29]	1.02 [0.95-1.09]	1.00 -	1.06 [1.00-1.12]	1.18 [1.10-1.26]	1.39 [1.31-1.48]	1.76 [1.62-1.92]	2.32 [2.07-2.59]
Adjusted HR [95% CI]	Medium	1.33 [1.09-1.62]	1.07 [0.92-1.22]	0.97 [0.90-1.04]	1.00 -	1.10 [1.04-1.18]	1.19 [1.11-1.29]	1.42 [1.32-1.53]	2.13 [1.90-2.37]	2.69 [2.27-3.18]
Adjusted HR [95% CI]	High	1.22 [1.02-1.46]	1.06 [0.94-1.19]	0.99 [0.93-1.05]	1.00 -	1.08 [1.02-1.15]	1.25 [1.17-1.34]	1.53 [1.42-1.64]	2.00 [1.78-2.26]	2.65 [2.20-3.19]

†Hazard ratios calculated with age as the underlying time scale, stratified by study and adjusted for gender, alcohol (g/day), education and marital status. \*No cancer or heart disease at baseline. p-trend across the categories of physical activity=0.14 for BMI<25 and 0.02 for BMI≥25 when estimated using a model for continuous BMI.

Table 8: Estimated hazard ratios† (and 95% CI) for death from any cause per 5 unit increase in BMI in healthy\* never-smokers: impact of omitting each study from the analysis

a) Female participants

Omitted study	BMI 15-<25 kg/m <sup>2</sup>		BMI 25-<50 kg/m <sup>2</sup>	
	HR	[95% CI]	HR	[95% CI]
AARP	0.86	[0.81-0.91]	1.30	[1.28-1.33]
AHS-1	0.84	[0.80-0.89]	1.29	[1.26-1.31]
AHS	0.85	[0.81-0.90]	1.29	[1.26-1.31]
BCDDP	0.85	[0.80-0.89]	1.29	[1.26-1.32]
CLUE	0.85	[0.80-0.89]	1.28	[1.25-1.30]
CTS	0.84	[0.81-0.90]	1.29	[1.26-1.31]
IWHS	0.85	[0.80-0.90]	1.28	[1.25-1.30]
MCCS	0.84	[0.80-0.90]	1.29	[1.26-1.32]
NHS	0.81	[0.77-0.86]	1.28	[1.25-1.30]
NYUWHS	0.84	[0.80-0.89]	1.29	[1.26-1.31]
PLCO	0.85	[0.81-0.90]	1.29	[1.26-1.32]
SMC	0.85	[0.80-0.89]	1.29	[1.26-1.31]
USRT	0.85	[0.80-0.90]	1.29	[1.27-1.32]
VITAL	0.85	[0.80-0.90]	1.29	[1.26-1.32]
WHS	0.85	[0.80-0.89]	1.29	[1.27-1.32]
WLH	0.85	[0.80-0.89]	1.29	[1.26-1.31]
All studies	0.85	[0.80-0.89]	1.28	[1.26-1.31]

b)Male participants

Omitted study	BMI15-<25 kg/m <sup>2</sup>		BMI 25-<50 kg/m <sup>2</sup>	
	HR	[95% CI]	HR	[95% CI]
AARP	0.98	[0.87-1.11]	1.39	[1.33-1.45]
AHS-1	0.88	[0.79-0.97]	1.36	[1.32-1.40]
AHS	0.91	[0.82-1.01]	1.36	[1.32-1.41]
CLUE	0.91	[0.83-1.01]	1.35	[1.31-1.40]
COSM	0.88	[0.79-0.98]	1.36	[1.32-1.41]
HPFS	0.88	[0.79-0.98]	1.36	[1.32-1.41]
MCCS	0.91	[0.82-1.01]	1.37	[1.33-1.41]
PHS	0.87	[0.79-0.97]	1.35	[1.31-1.39]
PLCO	0.93	[0.84-1.03]	1.35	[1.31-1.40]
USRT	0.92	[0.83-1.01]	1.36	[1.30-1.40]
VITAL	0.90	[0.82-1.00]	1.36	[1.32-1.40]
All studies	0.90	[0.82-1.00]	1.36	[1.32-1.40]

†Summary hazard ratios calculated using weighted-least squares meta-analysis.

\*No cancer or heart disease at baseline. AHS-1 Adventist Health Study 1. AHS – Agricultural Health Study.



Table 9: Estimated hazard ratios<sup>†</sup> (and 95% CI) for death from any cause according to BMI category: by smoking status

a) Female participants

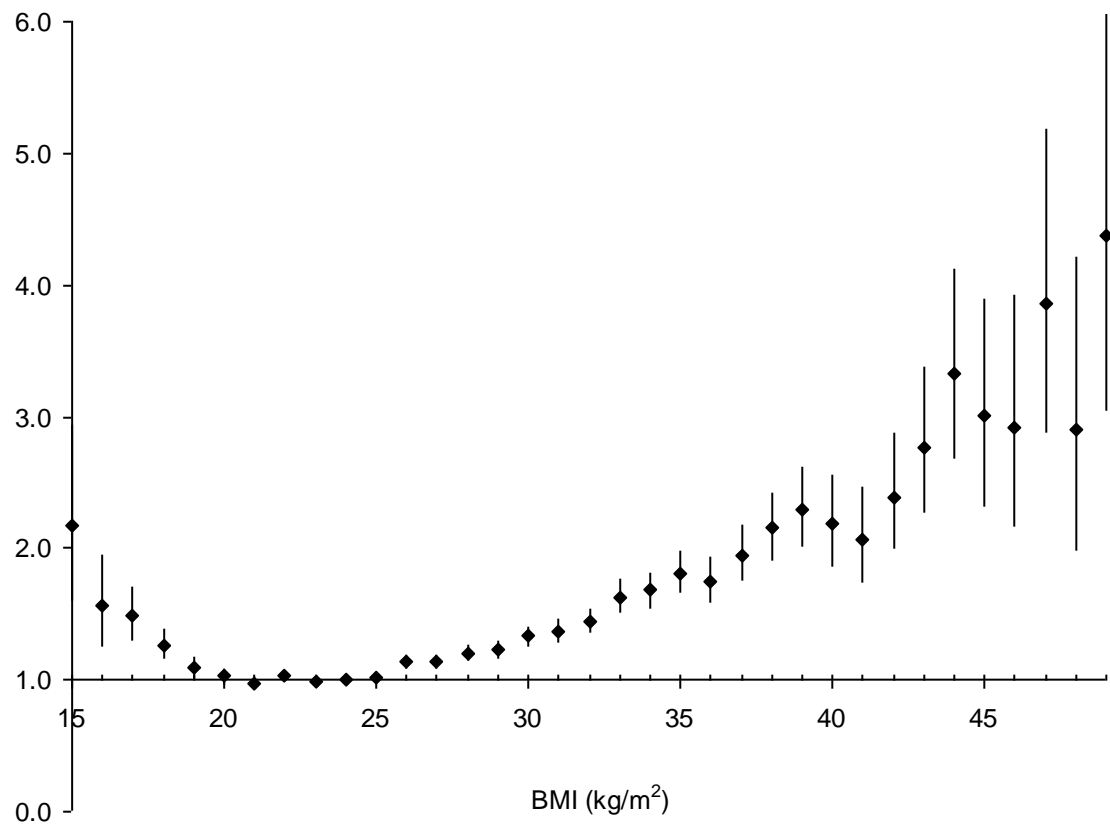
Smoking status		BMI (kg/m <sup>2</sup> )								
		15-18.4	18.5-19.9	20-22.4	22.5-24.9	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9
ASR	Never smokers	368	278	249	239	264	281	347	450	610
Adjusted HR [95% CI]		1.47 [1.33-1.62]	1.14 [1.07-1.22]	1.00 [0.96-1.04]	1.00 -	1.09 [1.05-1.14]	1.19 [1.14-1.24]	1.44 [1.38-1.50]	1.88 [1.77-2.00]	2.51 [2.30-2.73]
ASR	Former smokers (20+ yrs since quitting)	364	300	231	221	232	265	325	415	650
Adjusted HR [95% CI]		1.7 [1.39-2.07]	1.33 [1.17-1.50]	1.04 [0.97-1.13]	1.00 -	1.09 [1.00-1.18]	1.22 [1.11-1.34]	1.51 [1.39-1.66]	1.94 [1.70-2.21]	2.9 [2.45-3.43]
ASR	Former smokers (<20 yrs since quitting)	1245	841	691	601	560	766	713	911	1468
Adjusted HR [95% CI]		2.02 [1.70-2.39]	1.50 [1.32-1.71]	1.26 [1.15-1.37]	1.00 -	1.00 [0.92-1.09]	1.06 [0.96-1.17]	1.17 [1.06-1.28]	1.40 [1.23-1.60]	1.75 [1.49-2.06]
ASR	Current smokers	1086	879	741	684	680	763	870	976	952
Adjusted HR [95% CI]		1.67 [1.54-1.81]	1.27 [1.20-1.35]	1.05 [1.00-1.09]	1.00 -	1.04 [0.99-1.09]	1.11 [1.04-1.18]	1.26 [1.18-1.34]	1.56 [1.41-1.73]	1.77 [1.51-2.08]

b) Male participants

Smoking status		BMI (kg/m <sup>2</sup> )								
		15-18.4	18.5-19.9	20-22.4	22.5-24.9	25-27.4	27.5-29.9	30-34.9	35-39.9	40-49.9
ASR		638	316	325	300	327	369	437	570	882
Adjusted HR [95% CI]	Never smokers	1.37 [1.09-1.71]	1.01 [0.85-1.20]	1.00 [0.93-1.07]	1.00 -	1.06 [1.01-1.12]	1.21 [1.14-1.28]	1.44 [1.35-1.53]	2.06 [1.85-2.28]	2.93 [2.49-3.44]
ASR		547	375	301	307	300	342	381	530	962
Adjusted HR [95% CI]	Former smokers (20+ yrs since quitting)	1.86 [1.11-3.09]	1.18 [0.84-1.66]	0.98 [0.86-1.11]	1.00 -	0.97 [0.89-1.05]	1.11 [1.01-1.21]	1.27 [1.15-1.41]	1.53 [1.27-1.83]	2.58 [1.92-3.47]
ASR		1381	1356	914	742	698	725	736	919	1132
Adjusted HR [95% CI]	Former smokers (<20 yrs since quitting)	2.36 [1.87-2.99]	1.97 [1.61-2.40]	1.32 [1.19-1.46]	1.00 -	0.94 [0.88-1.01]	0.87 [0.82-0.96]	0.92 [0.84-0.99]	1.12 [0.98-1.27]	1.66 [1.34-2.06]
ASR		2235	1301	1094	956	957	915	1016	1116	1643
Adjusted HR [95% CI]	Current smokers	2.30 [1.98-2.67]	1.37 [1.22-1.54]	1.15 [1.08-1.23]	1.00 -	0.92 [0.87-0.97]	1.00 [0.93-1.06]	1.14 [1.06-1.22]	1.26 [1.11-1.44]	1.70 [1.36-2.11]

†Hazard ratios calculated with age as the underlying time scale, stratified by study and adjusted for alcohol (g/day), education, marital status and overall physical activity. ASR- age-standardized rate, standardized using the US general population.

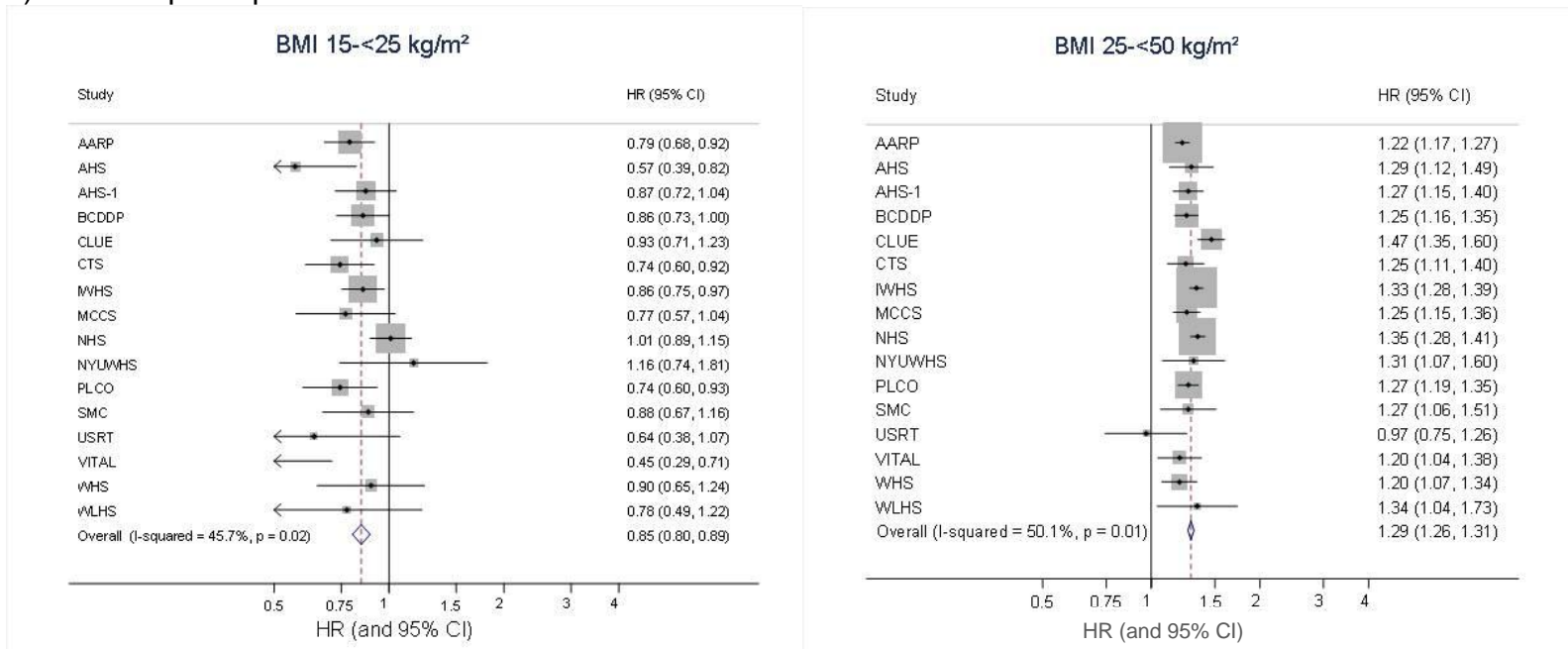
Figure 1: Estimated hazard ratios<sup>†</sup> (and 95% CI) for death from any cause according to BMI category (single units with BMI=24kg/m<sup>2</sup> as the reference category) in healthy\* never-smokers



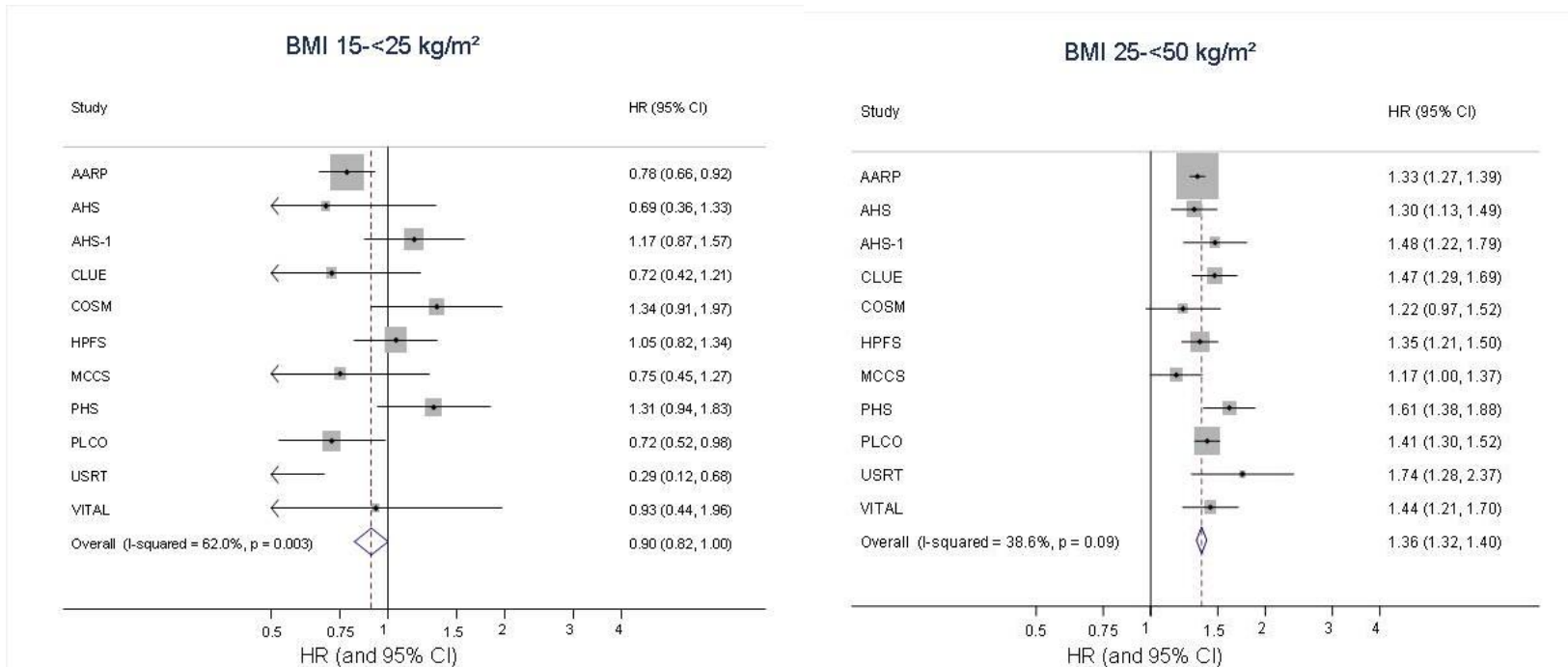
<sup>†</sup>Hazard ratios calculated with age as the underlying time scale, stratified by study and adjusted for gender, alcohol (g/day), education, marital status and overall physical activity. \*No cancer or heart disease at baseline.

Figure 2: Forest plot examining heterogeneity across cohorts by gender: estimated HR<sup>†</sup> for death from any cause per 5 unit increase in BMI in healthy never-smokers\*

a) Female participants



b) Male participants



†Hazard ratios calculated with age as the underlying time scale, adjusted for alcohol (g/day), education, marital status and overall physical activity. \*No cancer or heart disease at baseline. AHS-1 Adventist Health Study 1. AHS – Agricultural Health Study.

All female subjects BMI 15-<25 I-squared=81% and p<0.001, BMI 25-<50 I-squared=81% p<0.001.

Healthy never-smoker females 5+ years follow-up BMI 15-<25 I-squared=40% p=0.05, BMI 25-<50 I-squared=24% p=0.18.

All male subjects BMI 15-<25 I-squared=87% and p<0.001, BMI 25-<50 I-squared=90% p<0.001.

Healthy never-smoker males 5+ years follow-up BMI 15-<25 I-squared=53% p=0.02, BMI 25-<50 I-squared=25% p=0.20.