

Supplementary table 1. Baseline characteristics of individuals with vs. without glucose measurement within the NCS and the 40-y cohorts

Characteristics	NCS		40-y	
	Glucose non-missing	Glucose missing	Glucose non-missing	Glucose missing
Total, n (%)	60,695 (100)	29,295 (100)	131,551 (100)	261,010 (100)
Sex, n (%)				
Male	31,120 (51.3)	14,926 (51.0)	69,382 (52.7)	127,152 (48.7)
Female	29,575 (48.7)	14,369 (49.0)	62,169 (47.3)	133,858 (51.3)
Age, years				
Mean (SD)	40.0 (6.9)	39.6 (7.8)	41.3 (1.3)	42.6 (5.7)
Category, n (%)				
<30	6,418 (10.6)	4,173 (14.2)	43 (0.0)	752 (0.3)
30-44	37,214 (61.3)	21,284 (72.7)	131,267 (99.8)	246,105 (94.3)
45-59	17,063 (28.1)	3,709 (12.7)	175 (0.1)	974 (0.4)
≥60	0 (0)	129 (0.4)	66 (0.1)	13,179 (5.0)
Baseline year, n (%)				
1974-1979	60,308 (99.4)	35 (0.1)	0 (0)	0 (0)
1980-1984	387 (0.6)	6,221 (21.2)	0 (0)	0 (0)
1985-1989	0 (0)	23,039 (78.7)	0 (0)	86,835 (33.3)
1990-1994	0 (0)	0 (0)	6,501 (4.9)	174,124 (66.7)
1995-1999	0 (0)	0 (0)	125,050 (95.1)	51 (0)
Follow-up time, years				
Mean (SD)	31.7 (8.4)	25.2 (5.6)	15.3 (2.4)	20.7 (4.5)
Category, n (%)				
<10	2,260 (3.7)	1,118 (3.8)	4,023 (3.1)	10,916 (4.2)
10-19	4,759 (7.8)	2,248 (7.7)	127,528 (96.9)	76,884 (29.4)
20-29	8,954 (14.8)	21,362 (72.9)	0 (0)	173,210 (66.4)
≥30	44,722 (73.7)	4,567 (15.6)	0 (0)	0 (0)
Smoking status, n (%)				
Never smoker	21,339 (35.2)	10,627 (36.3)	25,134 (19.1)	93,423 (35.8)
Ex-smoker	10,888 (17.9)	6,077 (20.7)	80,438 (61.1)	61,170 (23.4)
Current smoker	28,379 (46.8)	12,586 (43.0)	24,743 (18.9)	106,365 (40.8)
Smoking intensity, pack years, n (%)				
<20	23,679 (83.4)	9,965 (79.2)	19,750 (79.8)	79,286 (74.5)
≥20	3,764 (13.3)	2,482 (19.7)	4,694 (19.0)	25,666 (24.1)
Pack years missing	936 (3.3)	139 (1.1)	299 (1.2)	1,413 (1.4)
Smoking status missing	89 (0.1)	5 (0.0)	1,236 (0.9)	52 (0.0)
Body mass index, kg/m ² ; n (%)				
Mean (SD)	24.7 (3.5)	24.6 (3.6)	25.6 (3.8)	24.9 (3.6)
Category, n (%)				
18.5-24.9	36,326 (59.9)	17,608 (60.1)	65,271 (49.6)	149,010 (57.1)
25-29.9	19,855 (32.7)	9,432 (32.2)	51,406 (39.1)	90,484 (34.7)
≥30	4,514 (7.4)	2,255 (7.7)	14,874 (11.3)	21,516 (8.2)
Systolic BP, mmHg; mean (SD)	132.9 (16.7)	130.2 (15.7)	127.4 (12.5)	131.2 (15.7)

Diastolic BP, mmHg; mean (SD)	82.2 (11.1)	79.2 (10.8)	75.4 (10.2)	79.5 (10.3)
Mid-BP, mmHg; mean (SD)	107.6 (12.6)	104.7 (12.3)	101.4 (11.6)	105.4 (12.2)
Triglycerides, mmol/L; mean (SD)	1.67 (1.09)	1.71 (1.17)	1.74 (1.2)	1.74 (1.2)
Fasting status, hours; n (%)				
<4	51,147 (84.3)	24,427 (83.4)	104,322 (79.3)	210,795 (80.8)
4-<8	8,534 (14.1)	4,287 (14.6)	21,971 (16.7)	44,402 (17.0)
≥8	1,014 (1.6)	581 (2.0)	5,258 (4.0)	5,813 (2.2)
Diabetes, n (%)				
No	60,308 (99.4)	29,078 (99.3)	129,961 (98.8)	258,524 (99.0)
Yes	337 (0.5)	205 (0.7)	1167 (0.9)	2350 (0.9)
Unknown	50 (0.1)	12 (0.0)	423 (0.3)	136 (0.1)

Abbreviations: NCS, Norwegian Counties Study; 40-y, Age 40-programme; SD, standard deviation; BP, blood pressure.

Supplementary table 2. Results from multiplicative and additive interaction tests of metabolic health status and body mass index on obesity-related cancer risk, using three different categorisations of body mass index level

Cancer type	Normal weight vs. overweight or obese			Normal weight vs. obese			Normal weight vs. overweight vs. obese ¹
	P multiplicative	P additive	RERI	P multiplicative	P additive	RERI	P multiplicative
All obesity-related cancers							
All	0.54	0.23	0.04 (-0.03,0.11)	0.66	0.31	0.07 (-0.06,0.20)	0.48
Women	0.55	0.77	-0.01 (-0.09,0.08)	0.76	0.99	0.00 (-0.15,0.15)	0.18
Men	0.21	0.04	0.13 (0.01,0.25)	0.11	0.02	0.34 (0.07,0.61)	0.25
Colon							
All	0.17	0.09	0.11 (-0.02,0.24)	0.53	0.42	0.11 (-0.16,0.38)	0.65
Women	0.44	0.40	0.08 (-0.10,0.26)	0.85	0.87	0.03 (-0.31,0.37)	0.75
Men	0.34	0.17	0.13 (-0.06,0.31)	0.36	0.18	0.30 (-0.14,0.73)	0.64
Rectal							
All	0.2	0.17	0.11 (-0.04,0.25)	0.52	0.48	0.10 (-0.18,0.39)	0.56
Women	0.71	0.73	-0.04 (-0.30,0.21)	0.26	0.30	0.24 (-0.69,0.21)	0.52
Men	0.05	0.03	0.21 (0.02,0.40)	0.06	0.04	0.39 (0.02,0.76)	0.10
Pancreatic							
All	0.55	0.65	-0.05 (-0.29,0.18)	0.58	0.74	-0.08 (-0.53,0.38)	0.71
Women	0.42	0.53	-0.13 (-0.52,0.26)	0.50	0.63	-0.17 (-0.88,0.54)	0.66
Men	0.72	0.69	0.06 (-0.24,0.35)	0.97	0.94	0.02 (-0.58,0.63)	0.97
Postmenopausal breast							
Women	0.22	0.23	-0.07 (-0.18,0.04)	0.41	0.43	-0.08 (-0.29,0.12)	0.42
Endometrial							
Women	0.07	0.01	0.38 (0.12,0.65)	0.32	0.07	0.53 (-0.04,1.10)	0.50
Ovarian							
Women	0.48	0.48	-0.09 (-0.34,0.16)	0.63	0.63	0.10 (-0.29,0.49)	0.28
Renal cell							
All	0.87	0.44	0.10 (-0.16,0.37)	0.78	0.15	0.40 (-0.14,0.95)	0.38

Women	0.44	0.78	-0.06 (-0.51,0.38)	0.96	0.50	0.30 (-0.56,1.15)	0.21
Men	0.85	0.36	0.16 (-0.18,0.49)	0.73	0.19	0.47 (-0.24,1.18)	0.77
Multiple myeloma							
All	0.30	0.30	-0.17 (-0.50,0.15)	0.69	0.69	-0.10 (-0.62,0.41)	0.76
Women	0.22	0.26	-0.25 (-0.68,0.18)	0.17	0.22	-0.47 (-1.22,0.28)	0.36
Men	0.98	0.96	-0.01 (-0.45,0.43)	0.40	0.38	0.30 (-0.37,0.98)	0.69
Liver, intrahepatic bile ducts							
All	0.31	0.09	0.38 (-0.05,0.82)	0.75	0.28	0.54 (-0.44,1.53)	0.89
Gallbladder							
All	0.15	0.21	-0.34 (-0.85,0.19)	0.25	0.37	-0.46 (-1.46,0.54)	0.26
Other obesity-related							
All	0.46	0.25	0.24 (-0.17,0.66)	0.29	0.10	0.81 (-0.17,1.78)	0.48

Abbreviations: RERI, relative excess risk for interaction

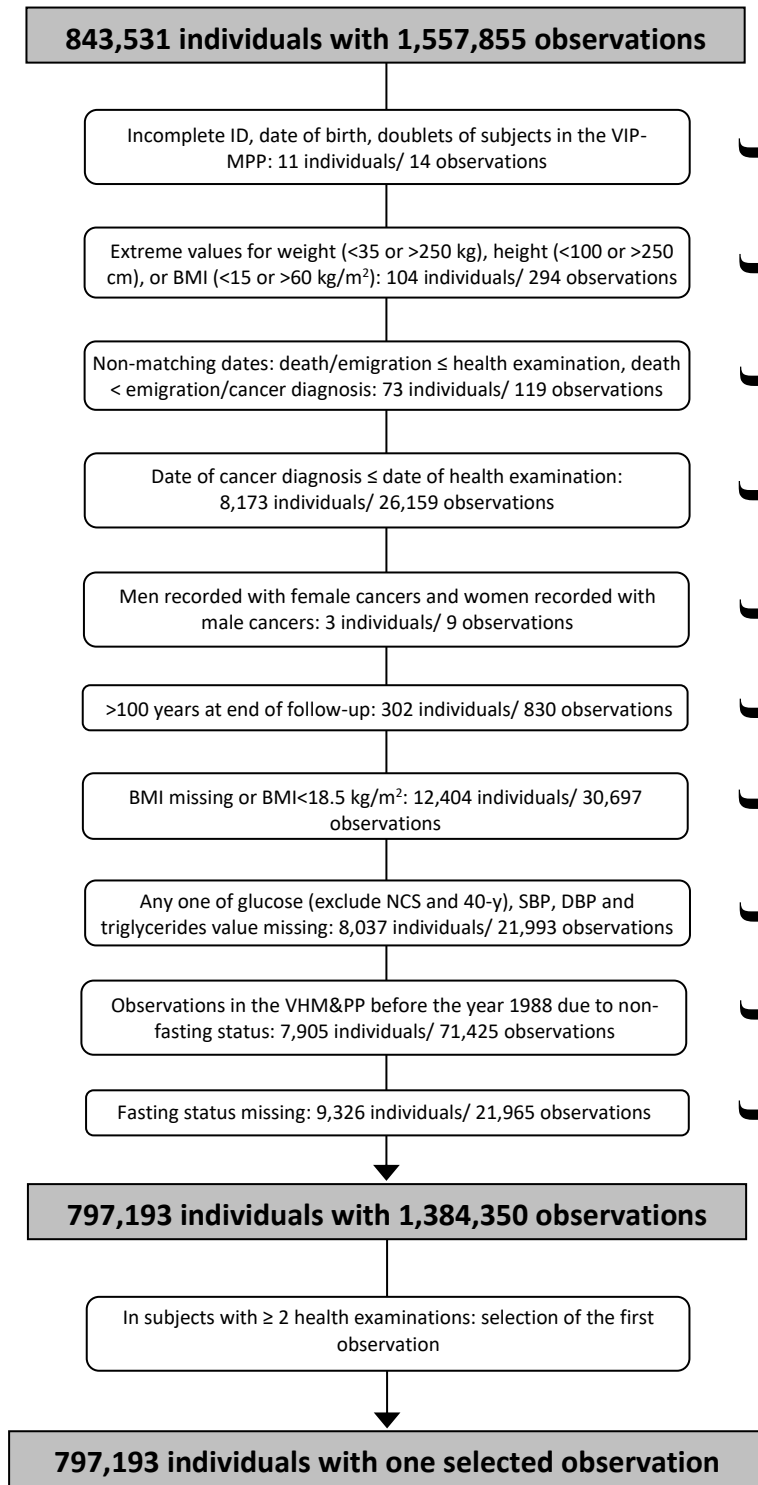
1. Only multiplicative interaction was tested. This 2 x 3 multiplicative interaction test corresponded to the BMI-health status categories analysed by Cox regression. Multiplicative interactions of metabolic health status and body mass index were tested by the Wald test of the respective product term in the Cox model using age as time scale, adjusted for sex, baseline age, and smoking status and pack-years, and stratified cohort and date of birth. Additive interactions of metabolic health status and body mass index were investigated by calculating the Relative Excess Risk for interaction as $RR_{11}-RR_{10}-RR_{01}+1$, for which the delta method was used to obtain confidence interval. RERI, Relative Excess Risk for interaction; CI, confidence interval; Metabolically healthy: middle and lowest tertile of metabolic score; Metabolically unhealthy: top tertile of metabolic score. Metabolic score composes equal weight from mid-blood pressure, glucose, and triglycerides; Normal weight: $18.5 \leq BMI < 25 \text{ kg/m}^2$; Overweight: $25 \leq BMI < 30 \text{ kg/m}^2$; Obese: $BMI \geq 30 \text{ kg/m}^2$

Supplementary table 3. Hazard ratios and absolute risks (95% confidence interval) of all obesity-related cancer for combinations of BMI and metabolic health status before and after multiple imputations

Participants	Hazard ratio ¹						Absolute risk ⁴	
	Normal weight ²		Overweight ²		Obese ²		MHNW	MUO
	Metabolically healthy ³	Metabolically unhealthy ³	Metabolically healthy ³	Metabolically unhealthy ³	Metabolically healthy ³	Metabolically unhealthy ³		
Before MI (n=516,393)								
Women	Reference	1.13 (1.07-1.20)	1.14 (1.07-1.21)	1.16 (1.09-1.22)	1.34 (1.21-1.49)	1.45 (1.36-1.54)	11.1% (10.7%-11.5%)	15.2% (14.4%-16.0%)
Men	Reference	1.16 (1.07-1.26)	1.15 (1.08-1.23)	1.35 (1.26-1.44)	1.29 (1.12-1.49)	1.69 (1.54-1.85)	5.9% (5.6%-6.1%)	8.7% (8.0%-9.5%)
After MI (n=797,193)								
Women	Reference	1.09 (1.03-1.14)	1.14 (1.08-1.20)	1.15 (1.10-1.21)	1.34 (1.22-1.47)	1.43 (1.35-1.51)	10.7% (10.3%-11.0%)	14.4% (13.7%-15.1%)
Men	Reference	1.17 (1.08-1.27)	1.17 (1.10-1.25)	1.38 (1.29-1.48)	1.40 (1.21-1.63)	1.91 (1.74-2.09)	4.5% (4.2%-4.7%)	7.0% (6.4%-7.6%)

Abbreviations: MI, multiple imputations; MHNW, metabolically healthy normal weight; MUO, metabolically unhealthy obesity.

- Hazard ratios were calculated by use of Cox regression using age as time scale, adjusted for sex, baseline age, and smoking status and pack-years, and stratified by cohort and date of birth.
- Normal weight: $18.5 \leq \text{BMI} < 25 \text{ kg/m}^2$; Overweight: $25 \leq \text{BMI} < 30 \text{ kg/m}^2$; Obese: $\text{BMI} \geq 30 \text{ kg/m}^2$
- Metabolically healthy: middle and lowest tertile of metabolic score; Metabolically unhealthy: top tertile of metabolic score. Metabolic score composes equal weight from mid-blood pressure, glucose, and triglycerides.
- Absolute risks at age 80 years were calculated using age as time metric and death as competing event.



Supplementary figure 1. Flowchart of exclusions and selections of individuals and observations in the study.

↪ denotes exclusions.