## **Electronic Supplementary Materials**

## Are people with metabolically healthy obesity really healthy? A prospective cohort study of 381,363 UK Biobank participants

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**ESM Table 1**. Criteria for metabolically healthy

Biomarker	Criteria for Metabolically Healthy
BP	SBP <130 mmHg and DBP <80 mmHg and no antihypertensive medications
C-reactive protein (CRP)	CRP <3 mg/L
Triacylglycerols	Triacylglycerols <2.3 mmol/L
Low-density lipoprotein cholesterol (LDL-c)	LDL-c <3 mmol/L and no cholesterol lowering medications
High-density lipoprotein cholesterol (HDL-c)	HDL-c >1 mmol/L
Glycated haemoglobin	HbA <sub>1c</sub> <42 mmol/mol (6%) and no diabetes medications

**ESM Table 2**. Association between MHO and incidence outcomes

	Model 1		Model 2	
	HR (95% CI)	Р	HR (95% CI)	Р
Diabetes	,		,	
MHN	1 (Reference)		1 (Reference)	
MHO	4.79 (4.27, 5.37)	< 0.0001	4.55 (4.05, 5.10)	< 0.0001
MUN	5.67 (5.16, 6.22)	< 0.0001	5.43 (4.94, 5.96)	< 0.0001
MUO	14.79 (13.56, 16.13)	< 0.0001	13.72 (12.57, 14.98)	< 0.0001
ASCVD				
MHN	1 (Reference)		1 (Reference)	
МНО	1.22 (1.14, 1.30)	< 0.0001	1.15 (1.08, 1.23)	< 0.0001
MUN	1.68 (1.61, 1.75)	< 0.0001	1.62 (1.55, 1.69)	< 0.0001
MUO	1.90 (1.82, 1.99)	< 0.0001	1.77 (1.69, 1.85)	< 0.0001
MI				
MHN	1 (Reference)		1 (Reference)	
MHO	1.26 (1.14, 1.39)	< 0.0001	1.20 (1.09, 1.32)	0.0003
MUN	1.93 (1.82, 2.05)	< 0.0001	1.87 (1.76, 1.98)	< 0.0001
MUO	2.14 (2.00, 2.28)	< 0.0001	1.99 (1.87, 2.13)	< 0.0001
Stroke				
MHN	1 (Reference)		1 (Reference)	
MHO	1.12 (1.03, 1.22)	0.01	1.07 (0.98, 1.17)	0.12
MUN	1.32 (1.25, 1.39)	< 0.0001	1.28 (1.21, 1.36)	< 0.0001
MUO	1.48 (1.39, 1.57)	< 0.0001	1.40 (1.31, 1.49)	< 0.0001
HF				
MHN	1 (Reference)		1 (Reference)	
MHO	1.93 (1.78, 2.10)	< 0.0001	1.81 (1.67, 1.96)	< 0.0001
MUN	1.55 (1.46, 1.65)	<0.0001	1.49 (1.40, 1.58)	< 0.0001
MUO	2.93 (2.76, 3.11)	<0.0001	2.68 (2.52, 2.84)	< 0.0001
Respiratory disease				
MHN	1 (Reference)		1 (Reference)	
MHO	1.37 (1.33, 1.41)	< 0.0001	1.30 (1.26, 1.35)	<0.0001
MUN	1.32 (1.29, 1.35)	<0.0001	1.27 (1.24, 1.30)	<0.0001
MUO	1.65 (1.61, 1.68)	< 0.0001	1.53 (1.49, 1.57)	<0.0001
COPD				
MHN	1 (Reference)		1 (Reference)	
MHO	1.41 (1.31, 1.51)	<0.0001	1.18 (1.10, 1.27)	<0.0001
MUN	1.82 (1.74, 1.90)	<0.0001	1.62 (1.55, 1.70)	<0.0001
MUO Madal 1: Adjusted for ag	2.24 (2.13, 2.35)	<0.0001	1.74 (1.66, 1.83)	<0.0001

Model 1: Adjusted for age, sex, and ethnicity only.

Model 2: Additionally adjusted for education level and deprivation index. MHN: metabolically healthy non-obese; MHO; metabolically healthy obese; MUN; metabolically unhealthy non-obese; MUO metabolically unhealthy obese

**ESM Table 3**. Association between MHO and mortality outcomes

2	Model 1		Model 2	
	HR (95% CI)	Р	HR (95% CI)	Р
All-cause mortality	,		,	
MHN	1 (Reference)		1 (Reference)	
MHO	1.27 (1.19, 1.36)	< 0.0001	1.21 (1.13, 1.29)	< 0.0001
MUN	1.38 (1.33, 1.44)	< 0.0001	1.34 (1.28, 1.40)	< 0.0001
MUO	1.69 (1.62, 1.77)	< 0.0001	1.57 (1.49, 1.64)	< 0.0001
ASCVD				
MHN	1 (Reference)		1 (Reference)	
MHO	1.47 (1.28, 1.68)	< 0.0001	1.36 (1.18, 1.56)	< 0.0001
MUN	1.96 (1.80, 2.14)	< 0.0001	1.87 (1.72, 2.04)	< 0.0001
MUO	2.50 (2.29, 2.74)	< 0.0001	2.23 (2.04, 2.45)	< 0.0001
MI				
MHN	1 (Reference)		1 (Reference)	
МНО	1.76 (1.34, 2.33)	< 0.0001	1.63 (1.23, 2.15)	0.0006
MUN	2.53 (2.12, 3.02)	< 0.0001	2.41 (2.02, 2.88)	< 0.0001
MUO	3.08 (2.55, 3.71)	< 0.0001	2.74 (2.27, 3.32)	< 0.0001
Stroke				
MHN	1 (Reference)		1 (Reference)	
МНО	1.13 (0.90, 1.43)	0.30	1.06 (0.84, 1.34)	0.63
MUN	1.32 (1.14, 1.53)	0.0003	1.27 (1.09, 1.47)	0.002
MUO	1.59 (1.36, 1.87)	< 0.0001	1.45 (1.23, 1.71)	< 0.0001
HF				
MHN	1 (Reference)		1 (Reference)	
МНО	2.11 (1.65, 2.70)	< 0.0001	1.92 (1.50, 2.46)	< 0.0001
MUN	2.01 (1.68, 2.40)	< 0.0001	1.90 (1.59, 2.27)	< 0.0001
MUO	3.40 (2.85, 4.05)	< 0.0001	2.97 (2.49, 3.55)	< 0.0001
Respiratory disease				
MHN	1 (Reference)		1 (Reference)	
MHO	1.40 (1.23, 1.60)	< 0.0001	1.24 (1.09, 1.42)	0.002
MUN	1.72 (1.57, 1.87)	< 0.0001	1.60 (1.46, 1.74)	< 0.0001
MUO	2.38 (2.18, 2.60)	< 0.0001	2.00 (1.83, 2.19)	< 0.0001
COPD				
MHN	1 (Reference)		1 (Reference)	
MHO	1.09 (0.83, 1.44)	0.53	0.86 (0.65, 1.13)	0.27
MUN	1.96 (1.68, 2.29)	< 0.0001	1.68 (1.44, 1.97)	< 0.0001
MUO	2.71 (2.31, 3.18)	< 0.0001	1.92 (1.63, 2.26)	< 0.0001

Model 1: Adjusted for age, sex, and ethnicity only.

Model 2: Additionally adjusted for education level and deprivation index. MHN: metabolically healthy non-obese; MHO; metabolically healthy obese; MUN; metabolically unhealthy non-obese; MUO metabolically unhealthy obese

**ESM Table 4**. Association between incident diabetes and subsequent outcomes with adjustment of baseline MHO status

	HR (95% CI)	Р
Incident ASCVD	0.68 (0.59, 0.80)	<0.0001
Incident HF	1.00 (0.86, 1.17)	0.97
All-cause mortality	0.88 (0.79, 0.99)	0.03
Fatal ASCVD	0.83 (0.66, 1.06)	0.14
Fatal HF	1.29 (0.89, 1.87)	0.18

Adjusted for age, sex ethnicity, education, deprivation, smoking, alcohol drinking, television viewing, physical activity, intake of fruit and vegetables, oily fish, red meat and processed meat, and baseline MHO status

Incident diabetes was the exposure variable coded as 1 when diabetes was recorded between the baseline assessment and the incidence of the outcome (for people who developed the outcome) or the date of censoring (for censored observations), or 0 otherwise.

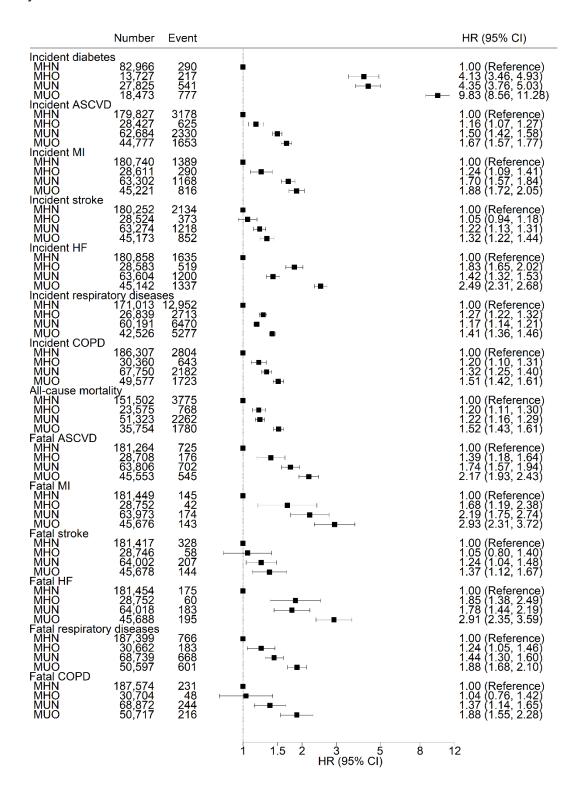
**ESM Figure 1**. Association between MHO and health outcomes with non-obesity as reference group

	Number	Event	HR (95%	CI)
Incident diabet	es			
Non-obesity	110,791	831	1.00 (Refe	erence)
MHO	13,727	217	<b></b> 2.06 (1.77	
MUO	18,473	777	<b>⊢■</b> → 4.77 (4.32	
Incident ASCV			(	., 0.20,
Non-obesity	242,511	5508	1.00 (Refe	erence)
МНО	28,427	625	1.00 (0.92	
MUO	44,777	1653	1.41 (1.34	
Incident MI	,	1000		,,,
Non-obesity	244,042	2557	■ 1.00 (Refe	erence)
MHO	28,611	290	1.00 (0.89	
MUO	45.221	816	1.50 (1.38	
Incident stroke	- ,	010	1.50 (1.50	, 1.00)
	243,526	3352	■ 1.00 (Refe	oronoo)
Non-obesity		373		
MHO	28,524 45,173	852	0.98 (0.88	
MUO	45,175	032	1.23 (1.14	1, 1.33)
Incident HF	244 462	2025	1.00 /Dof	~~~~
Non-obesity	244,462	2835	1.00 (Refe	
MHO	28,583	519	1.60 (1.45	
MUO	45,142	1337	± <b>■</b> + 2.16 (2.02	2, 2.31)
Incident respira			4.00 (D-f)	
Non-obesity	231,204		1.00 (Refe	
MHO	26,839	2713	1.20 (1.16	
MUO	42,526	5277	<b>1.33</b> (1.29	), 1.38)
Incident COPD				
Non-obesity	254,057	4986	1.00 (Refe	
MHO	30,360	643	1.08 (0.99	
MUO	49,577	1723	1.34 (1.27	<sup>'</sup> , 1.42)
All-cause morta				
Non-obesity	202,825	6037	■ 1.00 (Refe	
MHO	23,575	768	<b>1.12</b> (1.04	
MUO	35,754	1780	1.41 (1.33	3, 1.49)
Fatal ASCVD				
Non-obesity	245,070	1427	■ 1.00 (Refe	
MHO	28,708	176	<b>⊢</b> ■ 1.09 (0.93	
MUO	45,553	545	<b>⊢■</b> → 1.69 (1.52	2, 1.87)
Fatal MI				
Non-obesity	245,422	319	■ 1.00 (Refe	
MHO	28,752	42	<b>□</b> ■ 1.18 (0.85	
MUO	45,676	143	<b>□■</b> 2.02 (1.65	5, 2.48)
Fatal stroke				
Non-obesity	245,419	535	■ 1.00 (Refe	
МНО	28,746	58	□ □ □ 0.97 (0.74	
MUO	45,678	144	<b>□■</b> 1.26 (1.04	i, 1.52)
Fatal HF				
Non-obesity	245,472	358	■ 1.00 (Refe	
MHO	28,752	60	<del> 1.44</del> (1.09	), 1.89)
MUO	45,688	195	<b></b> 2.23 (1.86	3, 2.67)
Fatal respirator	y diseases			
Non-obesity	256,138	1434	■ 1.00 (Refe	erence)
МНО	30,662	183	<b></b> 1.06 (0.91	ı, 1.24)
MUO	50,597	601	⊢ <b>■</b> → 1.60 (1.45	5, 1.76)
Fatal COPD			·	
Non-obesity	256,446	475	1.00 (Refe	erence)
MHO	30,704	48	0.89 (0.66	
MUO	50,717	216	<b>⊢■</b> 1.61 (1.36	
	,			. ,
			1 1.5 2 3 5 8 12	
			HR (95% CI)	

Adjusted for age, sex ethnicity, education, deprivation, smoking, alcohol drinking, television viewing, physical activity, and intake of fruit and vegetables, oily fish, red meat and processed meat

HR shown in logarithmic scale.

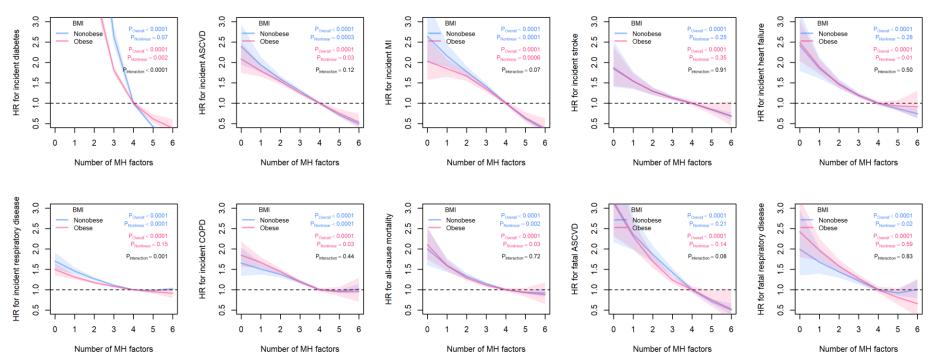
**ESM Figure 2**. Association between MHO and health outcomes in a 5-year landmark analysis



Participants who had corresponding events in the first five years of follow-up were excluded. Adjusted for age, sex ethnicity, education, deprivation, smoking, alcohol drinking, television viewing, physical activity, and intake of fruit and vegetables, oily fish, red meat and processed meat

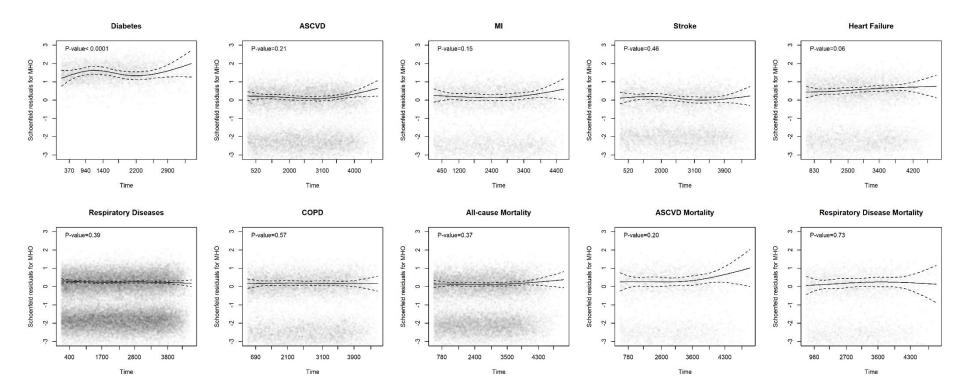
HR shown in logarithmic scale.

**ESM Figure 3**. Interaction of obesity and metabolic health with health outcomes



Main effects of obesity were not shown. Adjusted for each other and for age, sex ethnicity, education, deprivation, smoking, alcohol drinking, television viewing, physical activity, and intake of fruit and vegetables, oily fish, red meat and processed meat.

ESM Figure 4. Schoenfeld residuals for MHO



**ESM Figure 5**. Transition of metabolic health and obesity status

