

SUPPLEMENTAL MATERIAL

Method used to estimate the prevalence of metabolically healthy obesity (MHO) in previously published studies based on the stringency of selection criteria

Study Selection

Studies were eligible for inclusion if they met the following criteria:

- Obesity was defined as a BMI ≥ 30 kg/m²
- Participants were all adults (age ≥ 18 years)
- Results were from a population-based cross-sectional or longitudinal study
- MHO was defined using standard metabolic syndrome criteria according to National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) (1), American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI) scientific statement (2), or harmonized position stand (Harmonized criteria) (3) guidelines and/or by using the homeostatic model assessment of insulin resistance (HOMA-IR) (4).
- MHO prevalence using metabolic syndrome criteria was defined as ≤ 2 abnormal values out of all 5 components of the metabolic syndrome (i.e., waist circumference, blood pressure, and plasma triglyceride, HDL-cholesterol and fasting blood glucose concentrations), or ≤ 1 or 0 abnormal values when waist circumference was excluded from analysis (i.e., ≤ 1 or 0 out of the remaining 4 components).
- Studies were performed in the United States, Canada or Europe.

Studies were excluded if they met the following criteria:

- Participants with known type 2 diabetes (5) were oversampled.
- When the same study cohort has been used in multiple studies, the results from the largest reported number of people with obesity were included.

Data analysis

Results from studies were grouped according to the following criteria to define MHO:

- ≤ 2 Metabolic syndrome components (n=25 studies): ≤ 2 abnormal values when using all 5 components of the metabolic syndrome or ≤ 1 abnormal values when waist circumference was excluded from the analysis;
- 0 abnormal metabolic syndrome components when waist circumference was excluded from analysis (n=12);
- HOMA-IR score below (details in Tables 2 and 4) a certain cut-off value or percentile (n=11);
- 0 abnormal metabolic syndrome components when waist circumference was excluded from analysis in combination with a low HOMA-IR score (n=3).

For each of these groups, the total number of people with obesity and the number of people with MHO was extracted from the papers; the overall MHO prevalence for each of the groups was calculated as the sum of the number of people with MHO in all studies divided by the total number of people with obesity in all studies.

Supplemental Table 1. Studies that used ≤ 2 components of the metabolic syndrome or ≤ 1 components of the metabolic syndrome excluding waist circumference to determine the prevalence of metabolically healthy obesity (MHO)

	Study name	Country	Definition of MHO	Total number of participants with obesity	Number of participants with MHO	MHO prevalence (%)
Katzmarzyk et al. 2005 (6)	Aerobics Center Longitudinal Study (ACLS)	USA	≤ 2 NECP ATP III	2,620	1,019	38.9
Meigs et al. 2006 (7)	Framingham Offspring Study	USA	≤ 2 AHA/NHLBI scientific statement	638	236	37.0
Wildman et al. 2008 (8)	NHANES 1999-2004	USA	≤ 2 AHA/NHLBI scientific statement	1,665	651	39.1
Koster et al. 2010 (9)	Health, Aging and Body Composition (Health ABC)	USA	≤ 2 AHA/NHLBI scientific statement	729	224	30.7
Shea et al. 2011 (10)	Complex Diseases in the Newfoundland population: Environment and Genetics (CODING)	Canada	≤ 2 AHA/NHLBI scientific statement	420	124	29.5
Pajunen et al. 2011 (11)	Finnish type 2 diabetes (FIN-D2D) survey	Finland	≤ 2 Harmonized criteria	703	94	13.4
Durward et al. 2012 (12)	<i>National Health and Nutrition Examination Survey (NHANES) III</i>	USA	≤ 2 AHA/NHLBI scientific statement	1,160	513	44.2
Bradshaw et al. 2013 (13)	Atherosclerosis Risk in Communities (ARIC)	USA	≤ 2 NECP ATP III	4,024	1,602	39.8
Hinnouho et al. 2013 (14)	Whitehall II	UK	≤ 1 AHA/NHLBI scientific statement excluding waist circumference	638	236	37.0

Supplemental Table 1 continued.

	Study name	Country	Definition of MHO	Total number of participants with obesity	Number of participants with MHO	MHO prevalence (%)
	Martinez-Larrad et al. 2014 (15)	Spain	≤2 Harmonized criteria	1,059	423	39.9
	van Vliet-Ostaptchouk et al. 2014 (16) ^a	Estonia	≤1 NECP ATP III excluding waist circumference	2,053	1,035	50.4
	National FINRISK study (DILGOM)	Finland	≤1 NECP ATP III excluding waist circumference	946	268	28.3
	Health2000	Finland	≤1 NECP ATP III excluding waist circumference	1,342	402	30.0
	Cooperative Health Research in the Region of Augsburg (KORA)	Germany	≤1 NECP ATP III excluding waist circumference	786	341	43.4
	Collaborative Health Research in South Tyrol Study (CHRIS)	Italy	≤1 NECP ATP III excluding waist circumference	130	78	60.0
	Microisolates in South Tyrol Study (MICROS)	Italy	≤1 NECP ATP III excluding waist circumference	157	90	57.3
	Lifelines Cohort study	Netherlands	≤1 NECP ATP III excluding waist circumference	9,934	5,464	55.0
	Prevention of Renal and Vascular End stage Disease study (PREVEND)	Netherlands	≤1 NECP ATP III excluding waist circumference	1,137	456	40.1

Supplemental Table 1 continued.

	Study name	Country	Definition of MHO	Total number of participants with obesity	Number of participants with MHO	MHO prevalence (%)
van Vliet-Ostaptchouk et al. 2014 cont'd (16) ^a	Nord-Trøndelag health study (HUNT2 survey)	Norway	≤1 NECP ATP III excluding waist circumference	9,922	4,016	40.5
	National Child Development Study (NCDS)	UK	≤1 NECP ATP III excluding waist circumference	1,669	887	53.1
Kimokoti et al. 2015 (17)	Reasons for Geographic And Racial Differences in Stroke (REGARDS)	USA	≤2 Harmonized criteria	1,267	607	47.9
Phillips et al. 2015 (18)	Cork and Kerry Diabetes and Heart Disease Study (Phase II)	Ireland	≤2 NECP ATP III	581	196	33.7
Goday et al. 2016 (19)	Ibermutuamur Cardiovascular Risk Assessment (ICARIA) study	Spain	≤2 AHA/NHLBI scientific statement	70,052	38,600	55.1
Kanagasabai et al. 2017 (20)	NHANES 2005-2008	USA	≤2 Harmonized criteria	1,777	484	27.2
Mongraw-Chaffin et al. 2018 (21)	Multi-Ethnic Study of Atherosclerosis (MESA)	USA	≤2 Harmonized criteria	2,254	1,051	46.6
Total				117,663	59,097	50.2

^a Prevalence was taken from Table 4.

Supplemental Table 2. Studies that used the HOMA-IR score to determine the prevalence of metabolically healthy obesity (MHO)

	Study name	Country	Definition of MHO^a	Total number of participants with obesity	Number of participants with MHO	MHO prevalence (%)
Meigs et al. 2006 (7)	Framingham Offspring Study	USA	HOMA-IR \leq 75 th percentile among all subjects	638	283	44.3
Arnlov et al. 2011 (22)	Uppsala Longitudinal Study of Adult Men (ULSAM)	Sweden	HOMA-IR \leq 75 th percentile (\leq 3.43) among all subjects	69	21	30.4
Calori et al. 2011 (23)	Cremona Study	Italy	HOMA-IR < 2.5	380	43	11.3
Shea et al. 2011 (10)	Complex Diseases in the Newfoundland population: Environment and Genetics (CODING)	Canada	HOMA-IR \leq 25 th percentile (\leq 1.27) among all subjects	420	33	7.8
Durward et al. 2012 (12)	<i>National Health and Nutrition Examination Survey (NHANES) III</i>	USA	HOMA-IR < 2.5	1,160	228	19.7
Ogorodnikova et al. 2012 (24)	Atherosclerosis Risk in Communities (ARIC) and Cardiovascular Health Studies (CHS)	USA	HOMA-IR <25 th sex-specific percentile (<2.61 in men and <2.46 in women) among non-diabetic people with obesity	4,323	882	20.4
Hinnouho et al. 2013 (14)	Whitehall II	UK	HOMA-IR \leq 75 th sex-specific percentile (\leq 1.70 in men and \leq 1.52 in women) among all subjects	638	260	40.8
Soriguer et al. 2013 (25)	Pizarra study	Spain	HOMA-IR \leq 90 th percentile among all subjects	217	123	56.7

Supplemental Table 2 continued.

	Study name	Country	Definition of MHO	Total number of participants with obesity	Number of participants with MHO	MHO prevalence (%)
Arner et al. 2015 (26)	Genome wide association (GWA) study	Sweden, France and Germany	HOMA-IR < 2.21	1,969	404	20.5
Kimokoti et al. 2015 (17)	Reasons for Geographic And Racial Differences in Stroke (REGARDS)	USA	HOMA-IR ≤75 th percentile among all subjects	1,267	261	20.6
Phillips et al. 2015 (18)	Cork and Kerry Diabetes and Heart Disease Study (Phase II)	Ireland	HOMA-IR ≤75 th percentile among all subjects	581	218	37.5
Total				11,662	2,756	23.6

^a For studies that defined MHO as below a certain HOMA-IR score percentile, the corresponding HOMA-IR score(s), if available, is provided in parenthesis.

Supplemental Table 3. Studies that used 0 components of the metabolic syndrome excluding waist circumference to determine the prevalence of metabolically healthy obesity (MHO)

	Study name	Country	Definition of MHO	Total number of participants with obesity	Number of participants with MHO	MHO prevalence (%)
van Vliet-Ostapchouk et al. 2014 (16) ^a	Estonian Genome Project of University of Tartu (EGCUT)	Estonia	0 NECP ATP III excluding waist circumference	2,053	242	11.8
	National FINRISK study (DILGOM)	Finland	0 NECP ATP III excluding waist circumference	946	46	4.9
	Health2000	Finland	0 NECP ATP III excluding waist circumference	1,342	76	5.7
	Cooperative Health Research in the Region of Augsburg (KORA)	Germany	0 NECP ATP III excluding waist circumference	786	98	12.5
	Collaborative Health Research in South Tyrol Study (CHRIS)	Italy	0 NECP ATP III excluding waist circumference	130	38	29.2
	Microisolates in South Tyrol Study (MICROS)	Italy	0 NECP ATP III excluding waist circumference	157	18	11.5
	Lifelines Cohort study	Netherlands	0 NECP ATP III excluding waist circumference	9,934	1,808	18.2
	Prevention of Renal and Vascular End stage Disease study (PREVEND)	Netherlands	0 NECP ATP III excluding waist circumference	1,137	120	10.6
	Nord-Trøndelag health study (HUNT2 survey)	Norway	0 NECP ATP III excluding waist circumference	9,922	755	7.6

Supplemental Table 3 continued.

	Study name	Country	Definition of MHO	Total number of participants with obesity	Number of participants with MHO	MHO prevalence (%)
van Vliet-Ostaptchouk et al. 2014 cont'd (16) ^a	National Child Development Study (NCDS)	UK	0 NECP ATP III excluding waist circumference	1,669	305	18.3
Al-khalidi et al. 2019 (27)	<i>National Health and Nutrition Examination Survey (NHANES) III</i>	USA	0 Harmonized criteria excluding waist circumference	2,931	367	12.5
Kouviri et al. 2019 (28)	ATTICA study	Greece	0 AHA/NHLBI scientific statement excluding waist circumference	532	107	20.1
Total				31,539	3,980	12.6

^a Prevalence was taken from Table 4.

Supplemental Table 4. Studies that used 0 metabolic syndrome criteria excluding waist circumference in combination with a low HOMA-IR score to determine the prevalence of metabolically healthy obesity (MHO)

	Study name	Country	Definition of MHO	Total number of participants with obesity	Number of participants with MHO	MHO prevalence (%)
Kuk et al. 2009 (29)	<i>National Health and Nutrition Examination Survey (NHANES) III</i>	USA	0 AHA/NHLBI ATP III excluding waist circumference and HOMA-IR < 2.5	1,302	78	6.0
Soriguer et al. 2013 (25)	Pizarra study	Spain	0 NECP ATP III excluding waist circumference and HOMA-IR ≤90 th percentile among all subjects	217	23	10.6
Green et al. 2014 (30)	Framingham Heart Study Offspring (1998-2001) and Third Generation (2002-2005) cohorts	USA	0 AHA/NHLBI ATP III excluding waist circumference and HOMA-IR ≤75 th percentile among all subjects	1,285	90	7.0
Total				2,804	191	6.8

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