Normal-weight obesity

Prof. Nicola Veronese

UNICAMILLUS

REGIONE DEL VENETO

ULSS3 SERENISSIMA

Definizione

- L'obesità a peso normale (NWO) è una condizione clinica in cui una persona ha un **indice di massa corporea (BMI) nell'intervallo normale (18,5–24,9 kg/m^2)** ma una **percentuale di grasso corporeo sufficientemente alta** da porre un rischio cardiometabolico aumentato**—simile o superiore a quello osservato nelle persone con obesità**.
- Le persone con NWO spesso sembrano avere una dimensione corporea "normale" secondo il BMI, ma presentano **un'adiposità eccessiva e una riduzione della massa magra**, il che può aumentare il rischio di resistenza all'insulina, malattie cardiovascolari e sindrome metabolica.

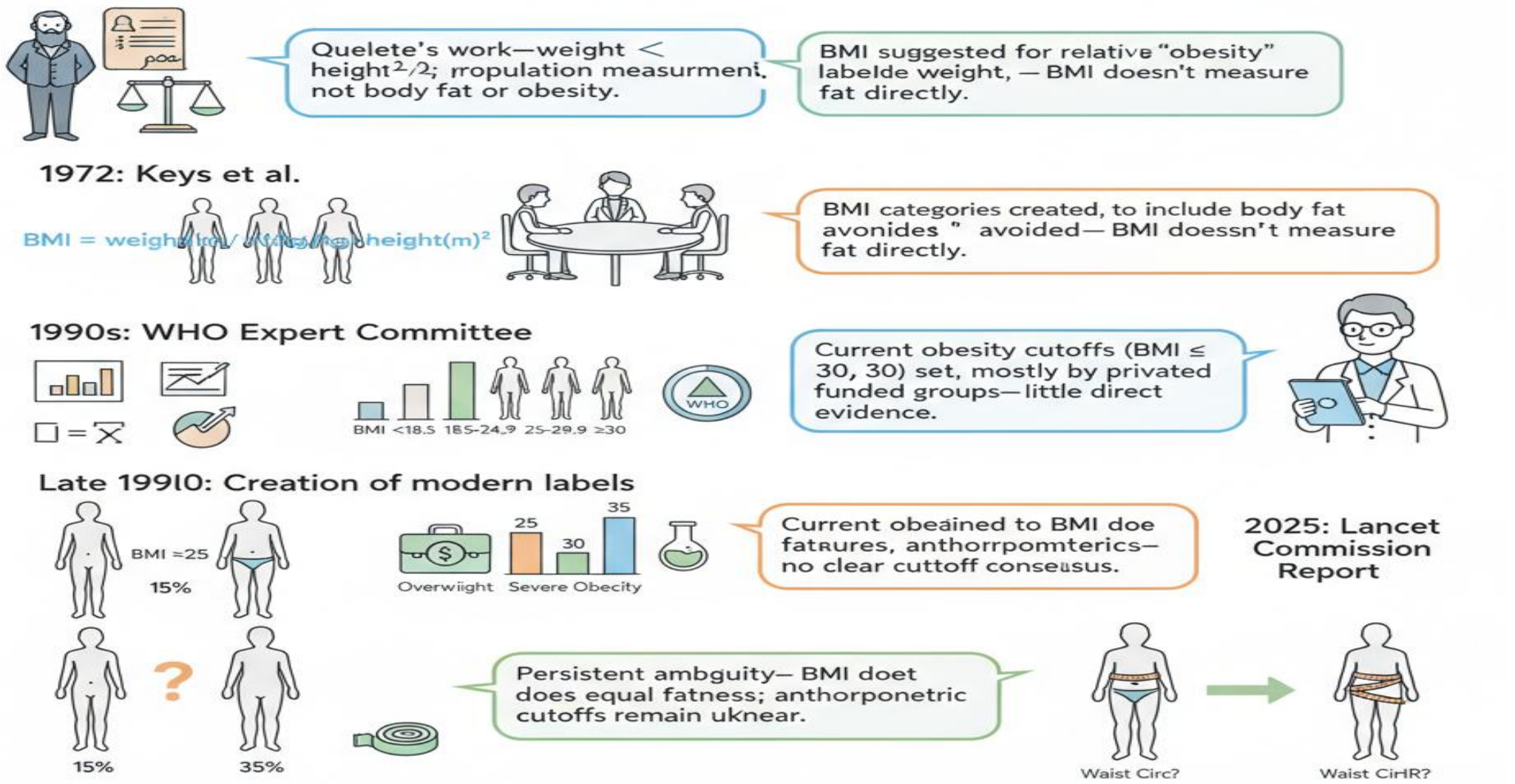
De Lorenzo, A et al., AJCN, 2006

Problemi con la definizione

- Manca un consenso riguardo ai limiti percentuali di grasso corporeo e ai metodi di misurazione della percentuale di grasso corporeo.
- La percentuale di grasso corporeo superiore al 25% e al 35% rispettivamente per uomini e donne è considerata alta dall'American Association of Clinical Endocrinology e dall'American College of Endocrinology.
- Le linee guida dell'American College of Sports Medicine descrivono una percentuale di grasso corporeo rispettivamente del 10–22% e del 20–32% per uomini e donne, come soddisfacente per la salute.
- Tuttavia, l'Organizzazione Mondiale della Sanità non ha ancora definito un valore di soglia per una percentuale elevata di grasso corporeo per definire l'obesità.

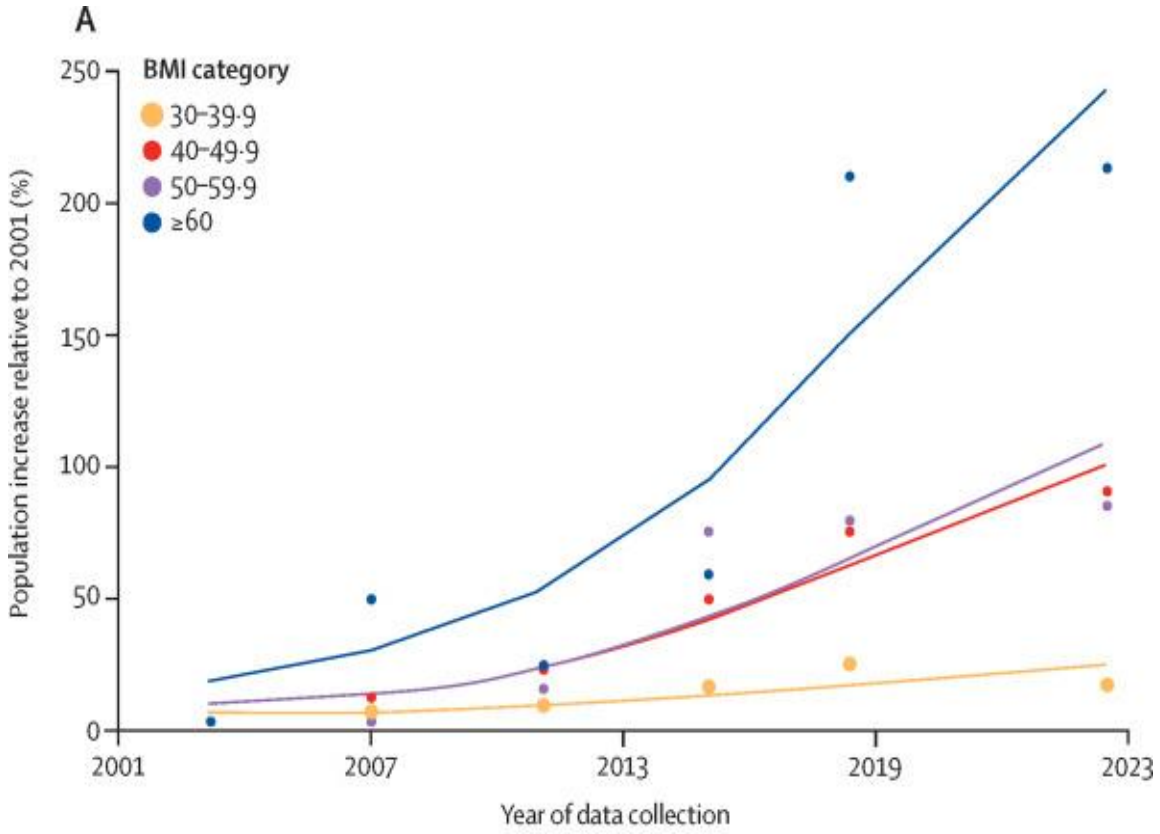
Wijayatunga et al. . Int J Obes 2021

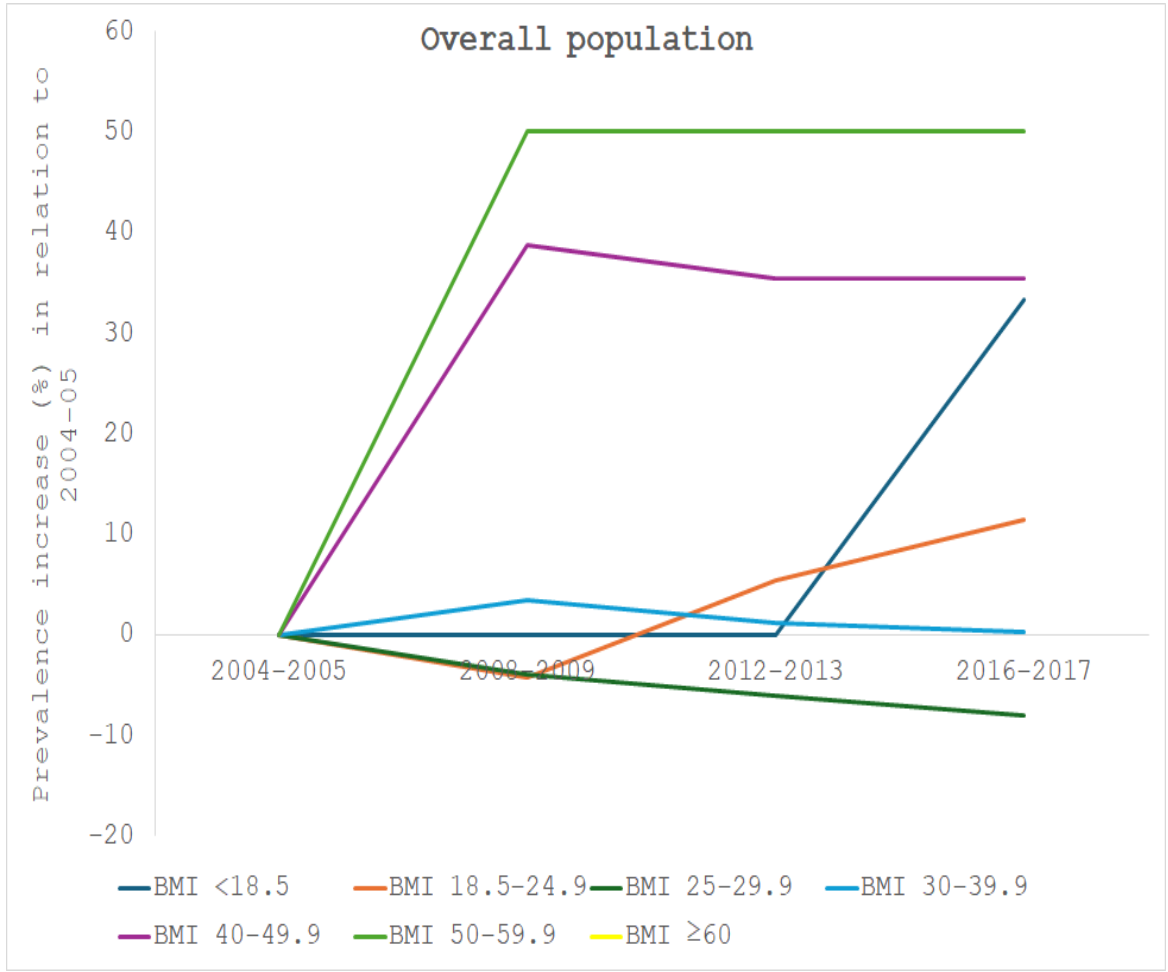
La lunga storia del BMI...



Fleagal, Jama Net Open, 2025

Il problema dell'obesità estrema...

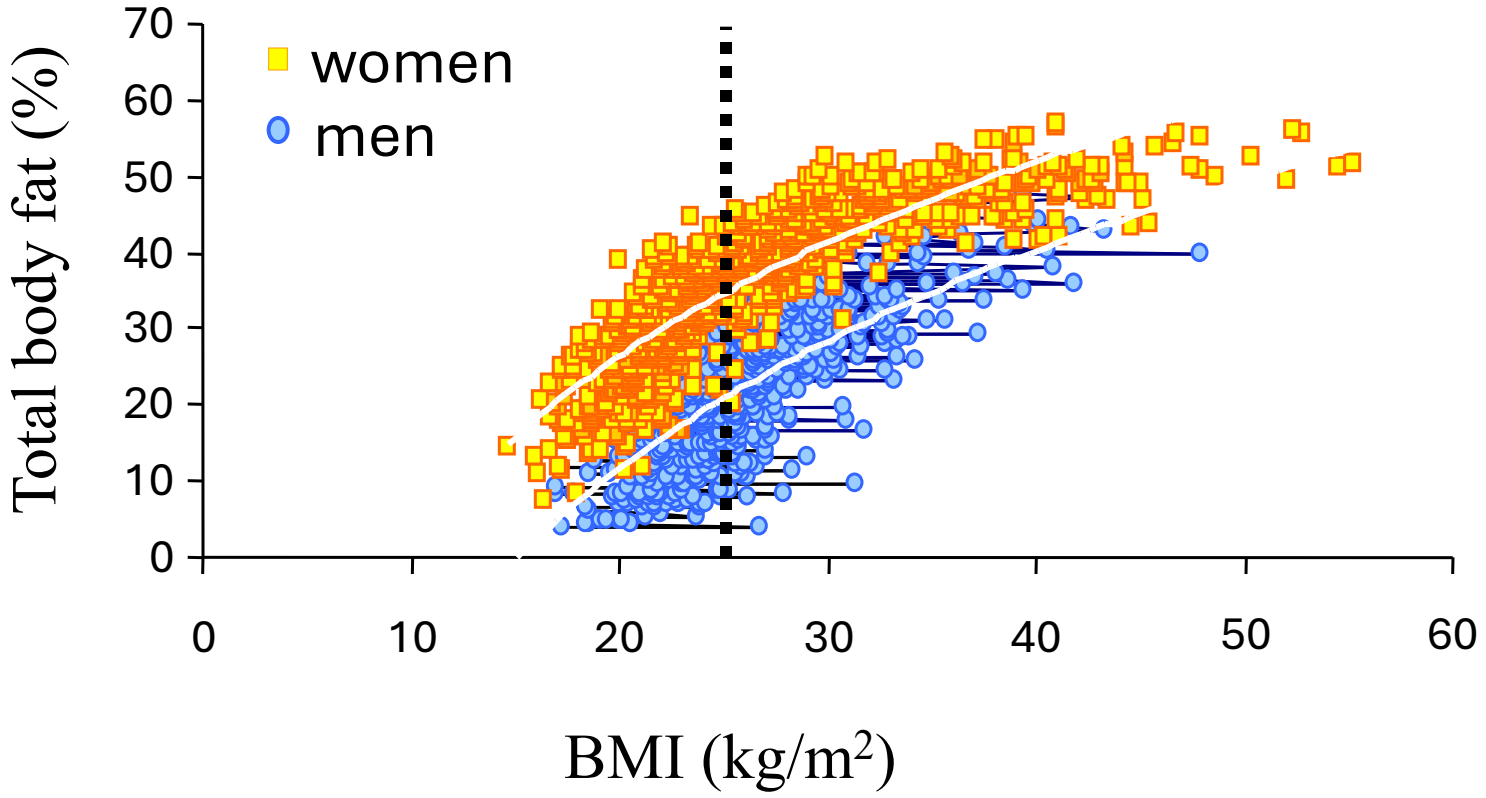




Karchmar et al., Lanc Diab End, 2025

Veronese et al., ACER, submitted

RELAZIONE TRA BMI E MASSA GRASSA



Adapted from: Gallagher et al. *Am J Clin Nutr* 2000;72:694.

BMI & MORTALITA'

Table 1. Summary Random-Effects Hazard Ratios (HRs) of All-Cause Mortality for Overweight and Obesity Relative to Normal Weight

	Self-reported or Measured Height and Weight			Height and Weight					
				Measured			Self-reported		
	No. of HRs	Summary HR (95% CI)	I^2, %	No. of HRs	Summary HR (95% CI)	I^2, %	No. of HRs	Summary HR (95% CI)	I^2, %
BMI of 25-<30									
All ages	140	0.94 (0.91-0.96)[a]	85.0	89	0.93 (0.89-0.95)[a]	75.8	51	0.96 (0.92-1.00)[a]	90.4
Mixed ages	107	0.95 (0.92-0.98)[a]	86.8	67	0.93 (0.89-0.96)[a]	79.6	40	0.98 (0.93-1.03)[a]	90.7
Age ≥65 y only	33	0.90 (0.86-0.94)[a]	51.2	22	0.90 (0.84-0.95)	31.2	11	0.90 (0.84-0.96)[a]	71.0
BMI of ≥30									
All ages	84	1.18 (1.12-1.25)[a]	86.7	56	1.13 (1.06-1.19)[a]	73.4	28	1.29 (1.18-1.41)[a]	89.7
Mixed ages	63	1.23 (1.16-1.31)[a]	87.2	41	1.16 (1.10-1.24)[a]	74.6	22	1.36 (1.25-1.48)[a]	86.1
Age ≥65 y only	21	1.03 (0.94-1.12)[a]	61.5	15	0.98 (0.86-1.12)[a]	61.1	6	1.09 (0.96-1.23)[a]	67.0
BMI of 30-<35									
All ages	53	0.95 (0.88-1.01)[a]	86.8	30	0.94 (0.86-1.03)[a]	80.5	23	0.95 (0.85-1.06)[a]	90.1
Mixed ages	42	0.96 (0.89-1.04)[a]	87.7	24	0.95 (0.86-1.06)[a]	83.2	18	0.97 (0.87-1.09)[a]	90.0
Age ≥65 y only	11	0.87 (0.72-1.05)[a]	76.3	6	0.89 (0.71-1.11)	56.2	5	0.83 (0.58-1.20)[a]	85.7
BMI of ≥35									
All ages	53	1.29 (1.18-1.41)[a]	81.7	30	1.25 (1.13-1.39)[a]	65.4	23	1.34 (1.16-1.55)[a]	88.3
Mixed ages	42	1.32 (1.19-1.45)[a]	82.8	24	1.28 (1.14-1.44)[a]	68.9	18	1.35 (1.16-1.58)[a]	89.0
Age ≥65 only	11	1.20 (0.94-1.52)[a]	70.6	6	1.10 (0.89-1.34)	25.1	5	1.29 (0.77-2.17)[a]	85.2

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).
[a] Indicates significant heterogeneity ($P < .05$).

Flegal et al., JAMA 2013

IMPLICAZIONI PER LA POPOLAZIONE GENERALE

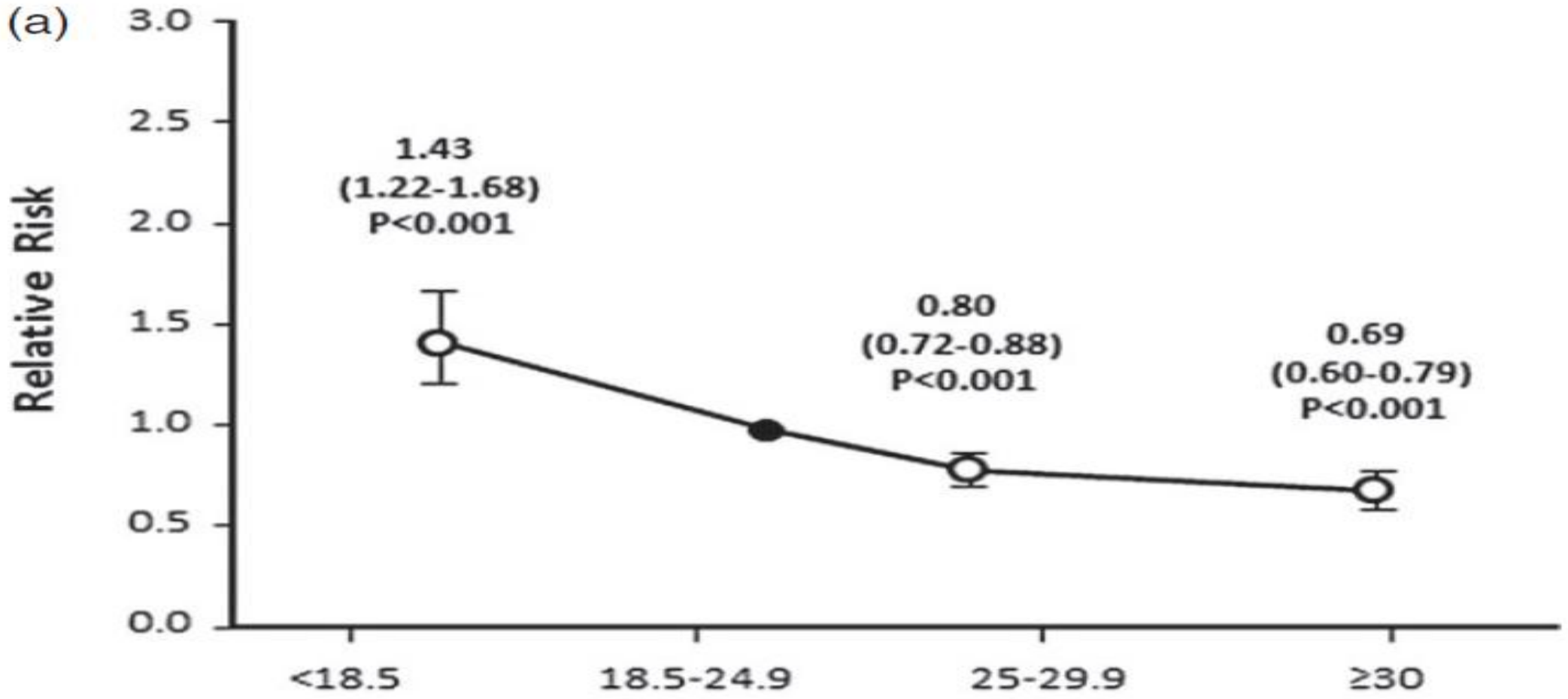
Our Absurd Fear of Fat

Campos, NY Times, 2013

In this instance, the Op-Ed was reacting to a meta-analysis, published this week in JAMA, and itself the subject of extensive media attention, indicating that mortality rates go up as obesity gets severe, but that mild obesity and overweight are actually associated with lower overall mortality than so-called “healthy” weight.

BMI & MORTALITA' IN CASA DI RIPOSO

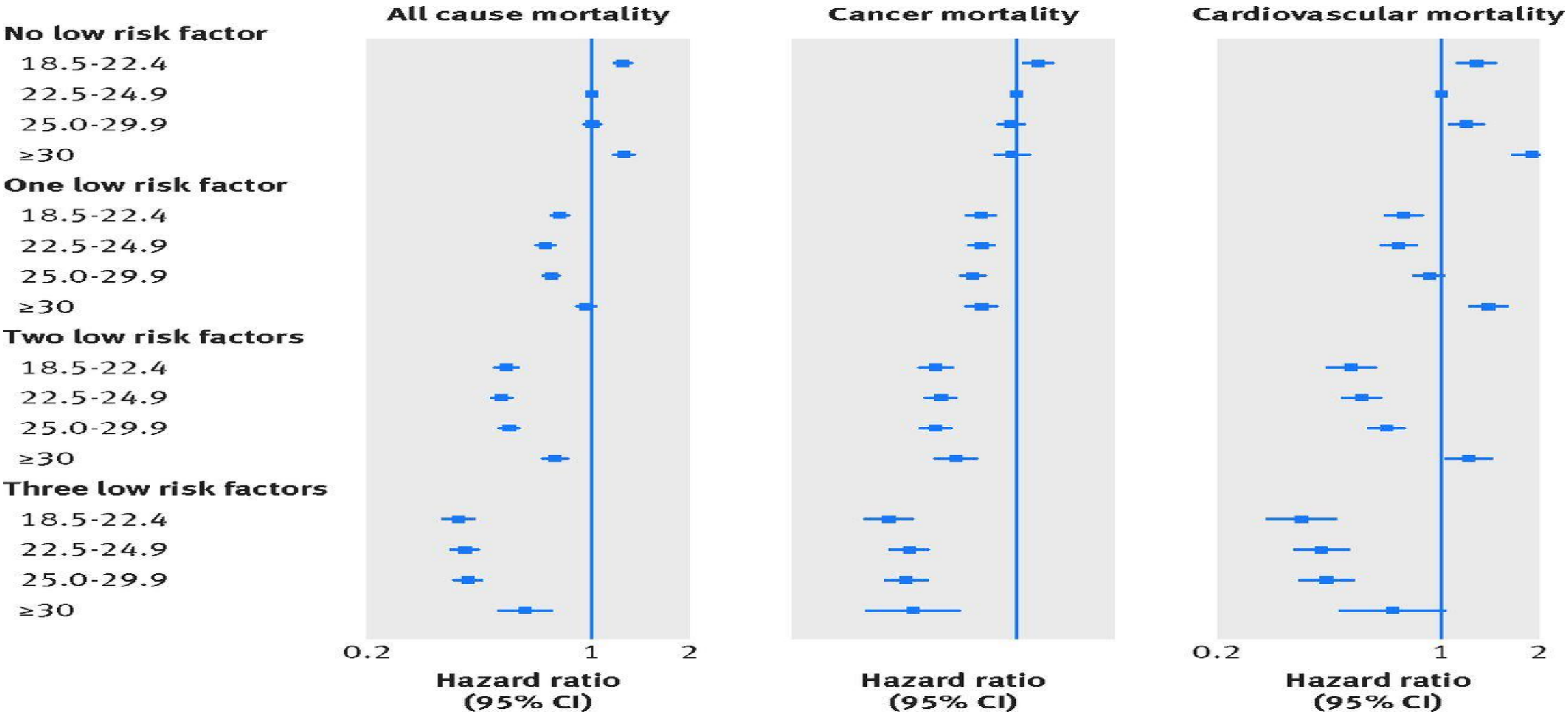
20 studi; 19,538 residenti in casa di riposo; 5,223 morti



Veronese, Obesity Reviews, 2015

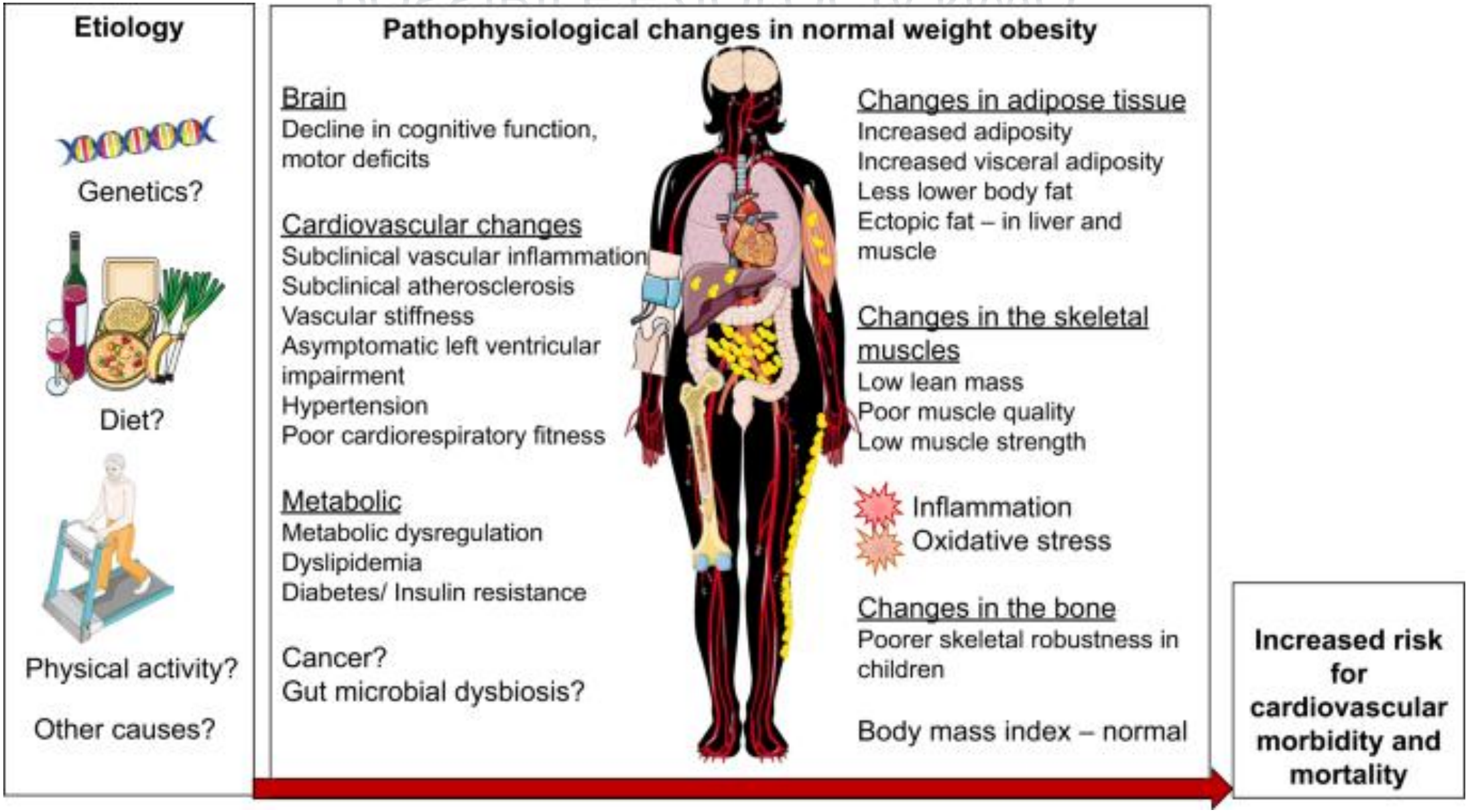
MORTALITA' PER BMI E STILE DI VITA

71,695 F+38,219 M; follow-up medio: 32 anni; NHS and HPFS



Veronese et al., BMJ, 2016

POSSIBILE EZIOLOGIA NWO



Wijayatunga et al. . Int J Obes 2021

BMI-based definition of obesity

No obesity

No excess fat mass

(eg, athletes)

Obesity

Excess fat mass

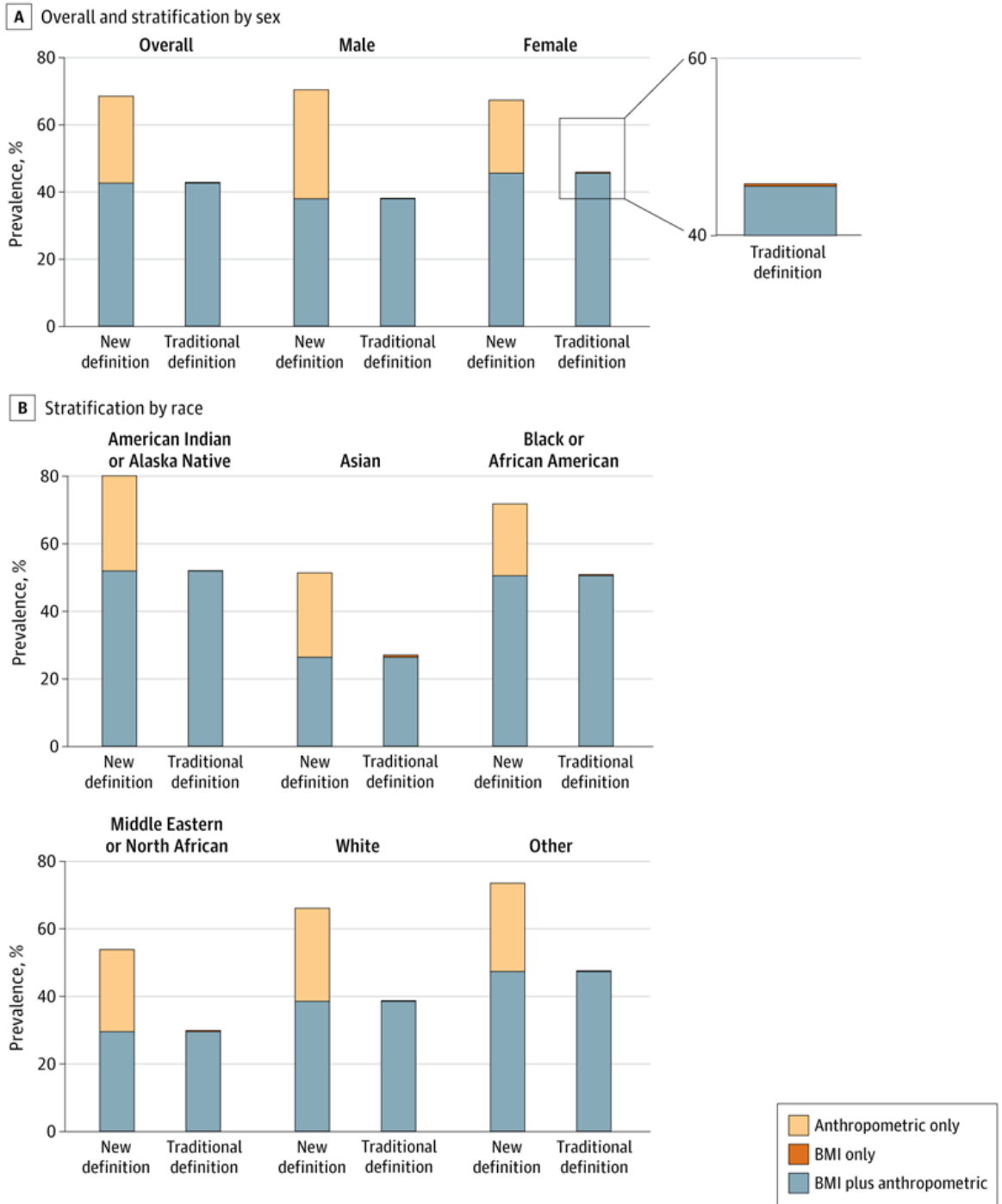
No ongoing illness

Ongoing illness

Lancet Commission, 2025

	Preclinical obesity	Clinical obesity
Excess adiposity	✓  + ✓  (BMI) (Waist circumference, etc)	✓  + ✓  (BMI) (Waist circumference, etc)
Mechanisms and pathophysiology	Alterations of cells and tissue → Alterations of organ structure	→ Alterations of organ function → End-organ damage
Clinical manifestations	Minor or absent (substantially preserved organ function)	Signs and symptoms; Limitations of daily activities; Complications
Detection and diagnosis	Anthropometrics, medical history, review of organ systems, and further diagnostic assessment as needed   	   

Lancet Commission, 2025



Nuovi cut-offs, nuove prevalenze

- In this analysis of the All of Us cohort that included 301 026 adults, **the prevalence of obesity increased by 60% when using the new definition compared with the traditional BMI-based definition**.
- This rise was driven by inclusion of individuals with anthropometric-only obesity (ie, elevated anthropometrics despite BMI below the traditional obesity threshold).

Fourman et al., Jama Netw Open, 2025

Original Investigation | Global Health

Cardiometabolic Outcomes Among Adults With Abdominal Obesity and Normal Body Mass Index

Kedir Y. Ahmed, MPH, PhD[1,2]; Setognal B. Aychiluhm, MPH[1,3]; Subash Thapa, PhD[1] ; et al

» Author Affiliations | Article Information

RELATED ARTICLES FIGURES SUPPLEMENTAL CONTENT

Key Points

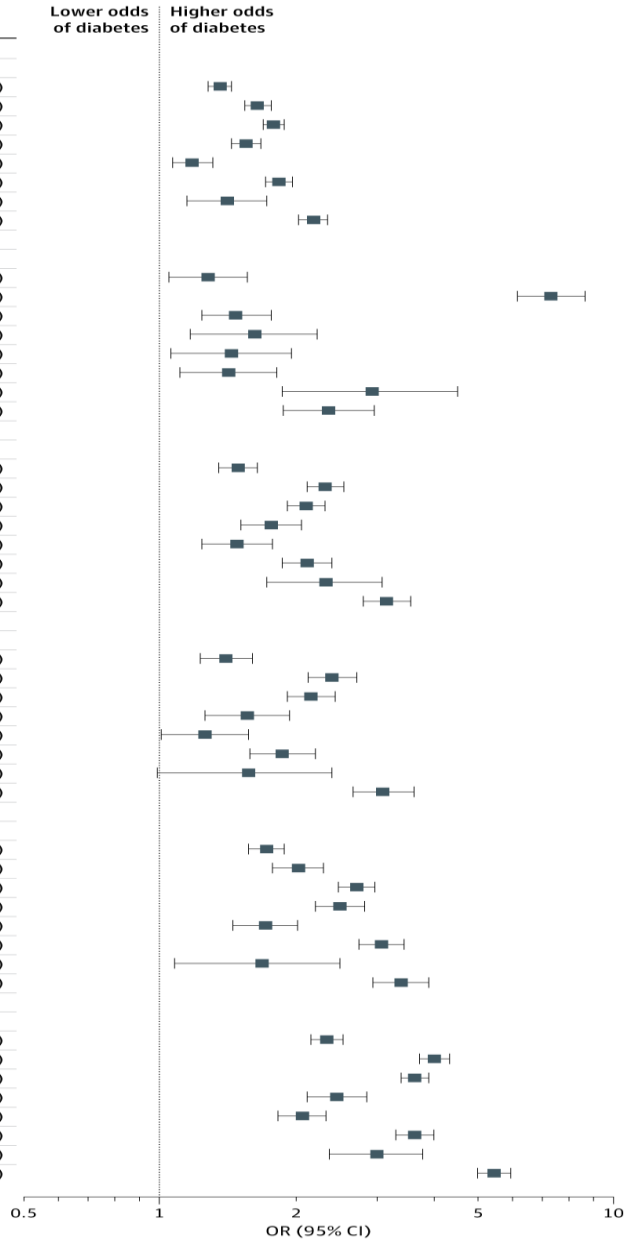
Question What is the estimated global prevalence of normal-weight abdominal obesity, and is it associated with cardiometabolic outcomes?

Findings In this cross-sectional study of 471 228 participants, the prevalence of normal-weight abdominal obesity was 21.7%, with the highest in Eastern Mediterranean and lowest in the Western Pacific regions. Normal-weight abdominal obesity was consistently associated with hypertension, diabetes, high total cholesterol, and elevated triglycerides globally.

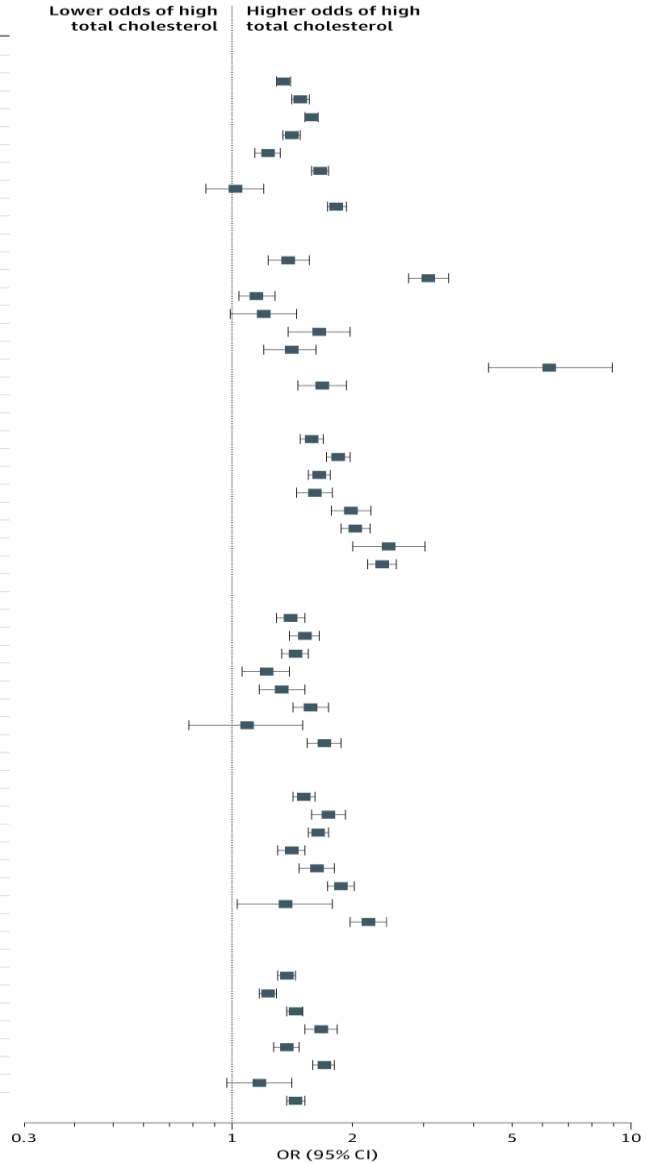
Meaning These findings suggest that public health initiatives, such as the promotion of regular physical exercise and a healthy diet, should target not only individuals with overweight or obesity but also those with a normal weight and abdominal obesity.

Evidenze dell'importanza della NWO

WHO region	OR (95% CI)
Africa	
Pattern of obesity	
Overweight	1.36 (1.28-1.44)
Obesity	1.64 (1.54-1.76)
High WC	1.78 (1.69-1.88)
High WC with normal BMI	1.55 (1.44-1.67)
Low WC with overweight	1.18 (1.07-1.31)
High WC with overweight	1.83 (1.71-1.96)
Low WC with obesity	1.41 (1.15-1.72)
High WC with obesity	2.18 (2.02-2.34)
Americas	
Pattern of obesity	
Overweight	1.28 (1.05-1.56)
Obesity	7.22 (6.10-8.58)
High WC	1.47 (1.24-1.76)
High WC with normal BMI	1.62 (1.17-2.22)
Low WC with overweight	1.44 (1.06-1.95)
High WC with overweight	1.42 (1.11-1.81)
Low WC with obesity	2.93 (1.86-4.51)
High WC with obesity	2.35 (1.87-2.96)
Eastern Mediterranean	
Pattern of obesity	
Overweight	1.49 (1.35-1.64)
Obesity	2.31 (2.11-2.54)
High WC	2.10 (1.91-2.31)
High WC with normal BMI	1.76 (1.51-2.05)
Low WC with overweight	1.48 (1.24-1.77)
High WC with overweight	2.11 (1.86-2.39)
Low WC with obesity	2.32 (1.72-3.08)
High WC with obesity	3.15 (2.80-3.56)
Europe	
Pattern of obesity	
Overweight	1.40 (1.23-1.60)
Obesity	2.39 (2.12-2.71)
High WC	2.15 (1.91-2.43)
High WC with normal BMI	1.56 (1.26-1.93)
Low WC with overweight	1.25 (1.01-1.57)
High WC with overweight	1.86 (1.58-2.20)
Low WC with obesity	1.57 (0.99-2.39)
High WC with obesity	3.09 (2.66-3.62)
Southeast Asia	
Pattern of obesity	
Overweight	1.72 (1.57-1.88)
Obesity	2.02 (1.77-2.29)
High WC	2.71 (2.47-2.97)
High WC with normal BMI	2.49 (2.20-2.82)
Low WC with overweight	1.71 (1.45-2.01)
High WC with overweight	3.07 (2.74-3.44)
Low WC with obesity	1.68 (1.08-2.49)
High WC with obesity	3.39 (2.94-3.90)
Western Pacific	
Pattern of obesity	
Overweight	2.33 (2.15-2.53)
Obesity	4.01 (3.72-4.33)
High WC	3.63 (3.39-3.90)
High WC with normal BMI	2.45 (2.11-2.85)
Low WC with overweight	2.06 (1.82-2.32)
High WC with overweight	3.63 (3.30-4.00)
Low WC with obesity	3.00 (2.36-3.78)
High WC with obesity	5.42 (4.99-5.90)



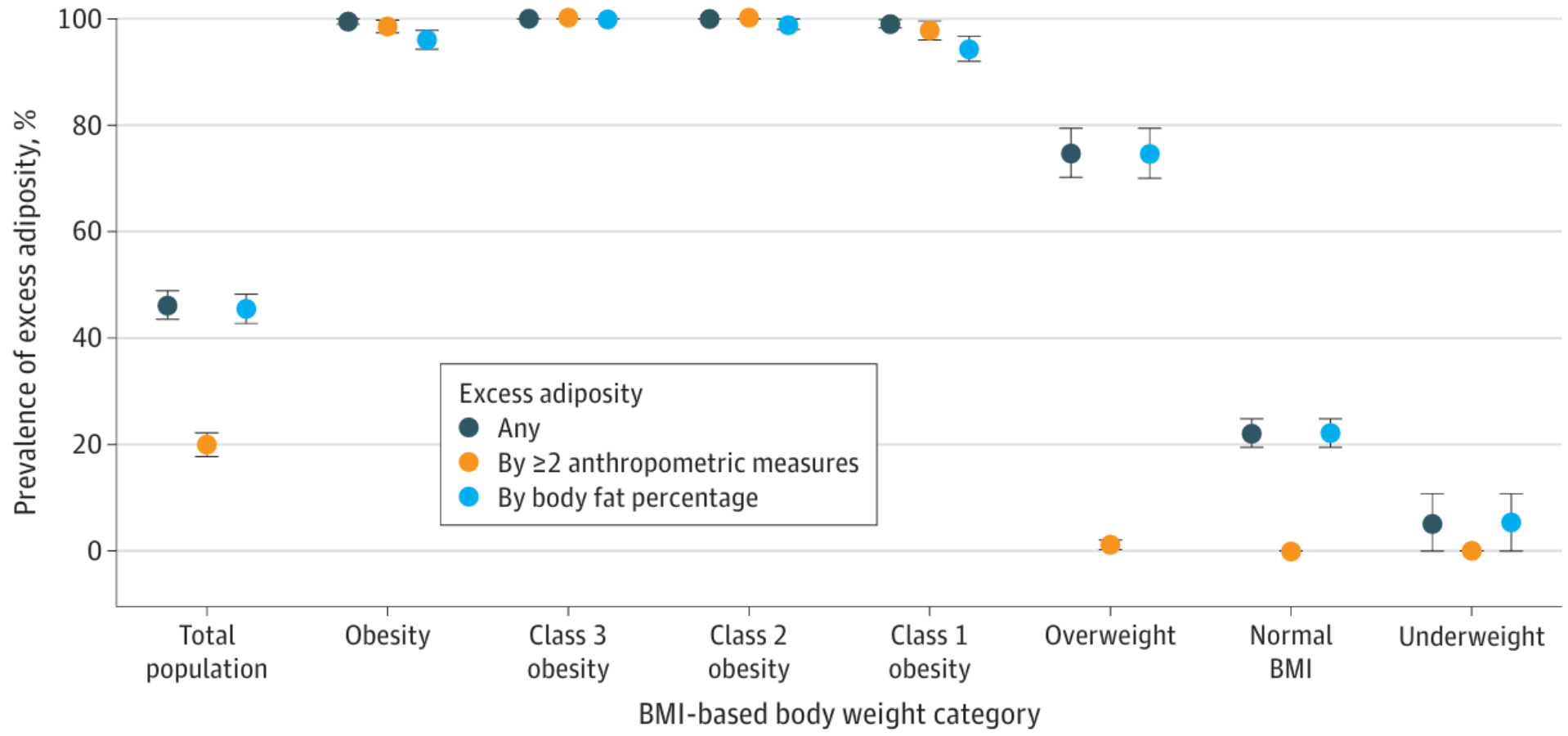
WHO region	OR (95% CI)
Africa	
Pattern of obesity	
Overweight	1.34 (1.29-1.40)
Obesity	1.48 (1.41-1.56)
High WC	1.58 (1.52-1.64)
High WC with normal BMI	1.41 (1.34-1.48)
Low WC with overweight	1.23 (1.14-1.32)
High WC with overweight	1.66 (1.58-1.74)
Low WC with obesity	1.02 (0.86-1.20)
High WC with obesity	1.82 (1.73-1.93)
Americas	
Pattern of obesity	
Overweight	1.38 (1.23-1.56)
Obesity	3.09 (2.76-3.47)
High WC	1.15 (1.04-1.28)
High WC with normal BMI	1.20 (0.99-1.45)
Low WC with overweight	1.65 (1.38-1.97)
High WC with overweight	1.41 (1.20-1.62)
Low WC with obesity	6.19 (4.37-8.89)
High WC with obesity	1.68 (1.46-1.93)
Eastern Mediterranean	
Pattern of obesity	
Overweight	1.58 (1.48-1.69)
Obesity	1.84 (1.72-1.97)
High WC	1.65 (1.55-1.76)
High WC with normal BMI	1.61 (1.45-1.78)
Low WC with overweight	1.98 (1.77-2.22)
High WC with overweight	2.03 (1.87-2.21)
Low WC with obesity	2.46 (2.00-3.03)
High WC with obesity	2.37 (2.18-2.57)
Europe	
Pattern of obesity	
Overweight	1.40 (1.29-1.52)
Obesity	1.52 (1.39-1.65)
High WC	1.44 (1.33-1.55)
High WC with normal BMI	1.22 (1.06-1.39)
Low WC with overweight	1.33 (1.17-1.52)
High WC with overweight	1.57 (1.42-1.74)
Low WC with obesity	1.09 (0.78-1.50)
High WC with obesity	1.70 (1.54-1.87)
Southeast Asia	
Pattern of obesity	
Overweight	1.51 (1.42-1.61)
Obesity	1.74 (1.58-1.92)
High WC	1.64 (1.55-1.74)
High WC with normal BMI	1.41 (1.30-1.52)
Low WC with overweight	1.63 (1.47-1.80)
High WC with overweight	1.87 (1.73-2.02)
Low WC with obesity	1.36 (1.03-1.78)
High WC with obesity	2.19 (1.97-2.43)
Western Pacific	
Pattern of obesity	
Overweight	1.37 (1.30-1.44)
Obesity	1.23 (1.17-1.29)
High WC	1.44 (1.37-1.50)
High WC with normal BMI	1.67 (1.52-1.83)
Low WC with overweight	1.37 (1.27-1.47)
High WC with overweight	1.70 (1.59-1.80)
Low WC with obesity	1.17 (0.97-1.41)
High WC with obesity	1.44 (1.37-1.52)



Ahmed, Jama Netw Open, 2025

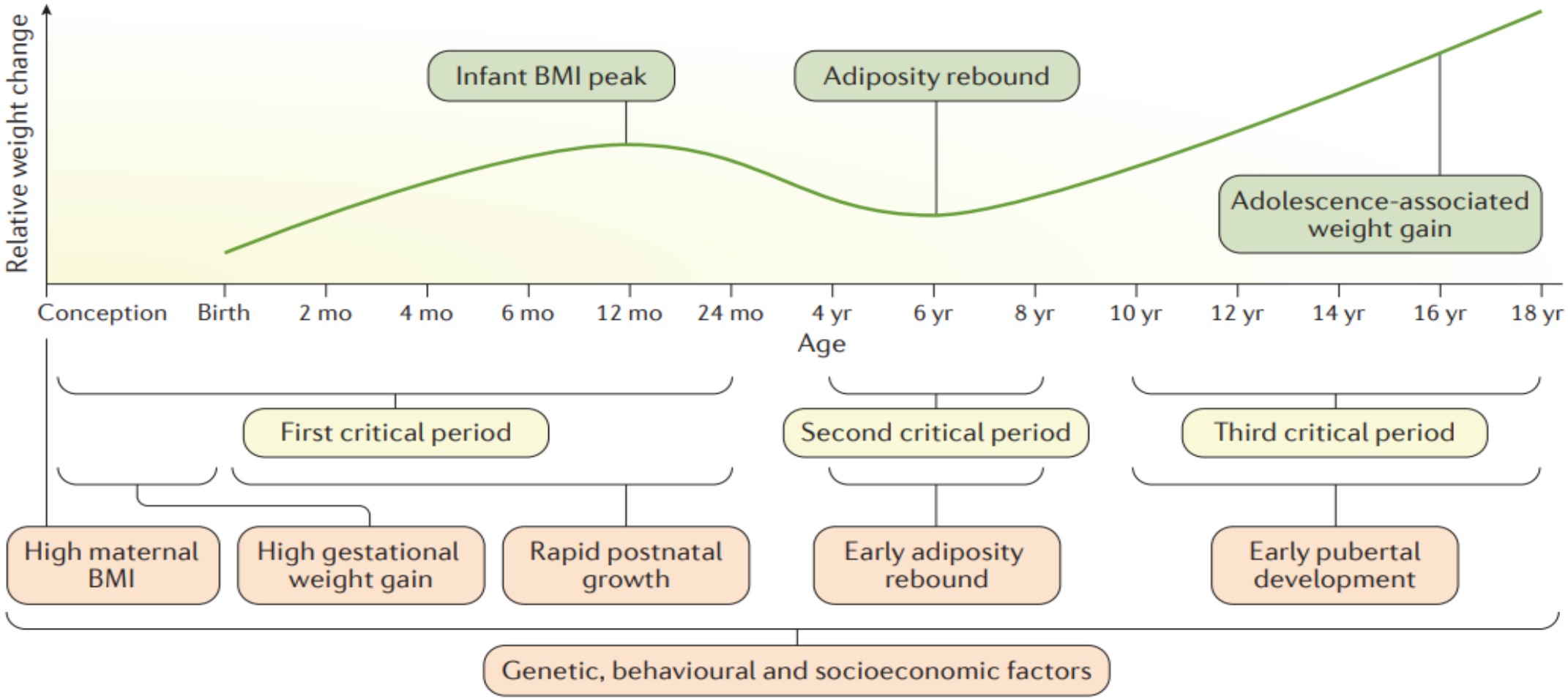
NWO nei bambini e negli adolescenti

Figure. Prevalence of Excess Adiposity by Body Mass Index (BMI) Category Among US Children and Adolescents



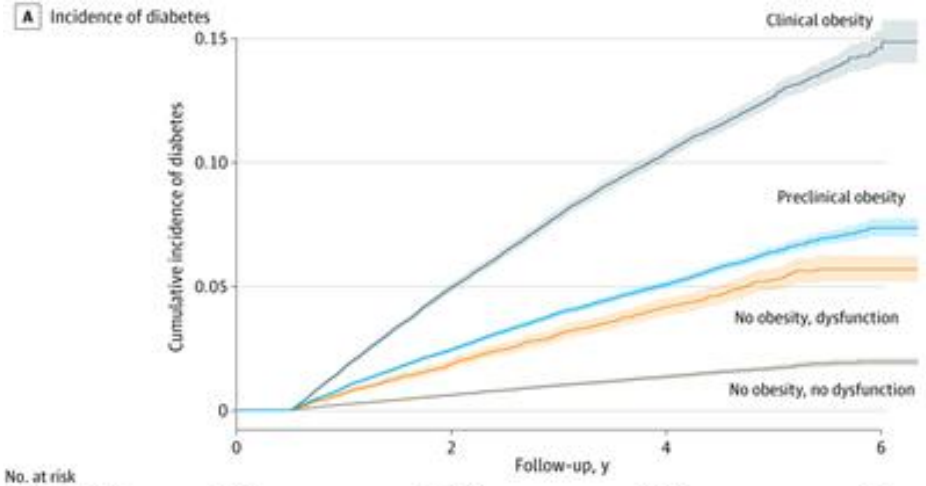
Chetty et al., JAMA Ped, 2025

BMI nella fase della crescita

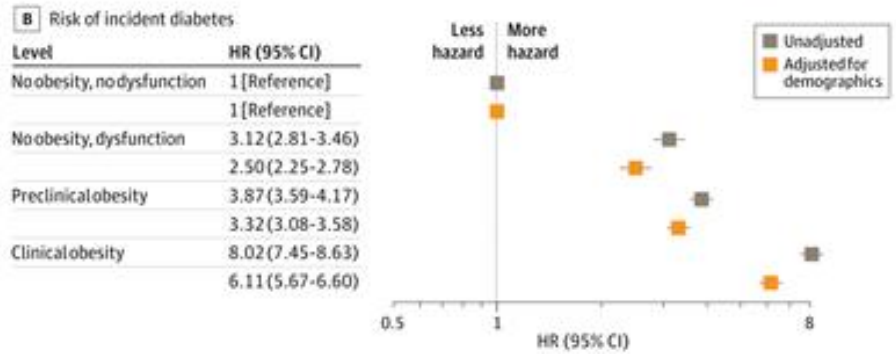


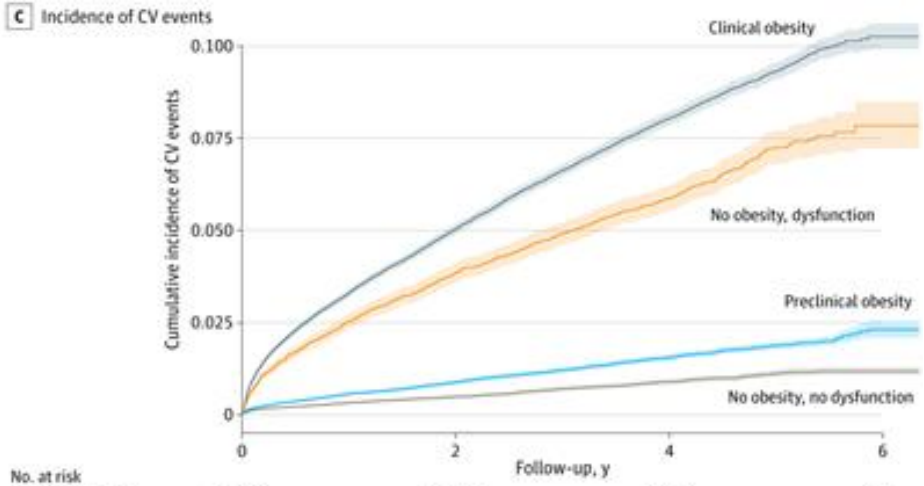
González-Muniesa et al., Nat Reviews, 2017

Conseguenze NWO, USA

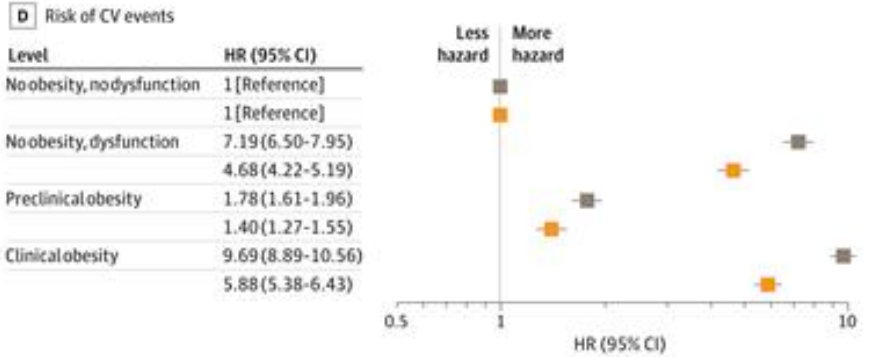


No. at risk				
Clinical obesity	68239	41732	25501	333
No obesity, dysfunction	20232	13018	8378	133
No obesity, no dysfunction	68525	52377	38569	992
Preclinical obesity	88636	65692	46901	794
No. of events				
Clinical obesity	0	2571	4652	5144
No obesity, dysfunction	0	291	559	629
No obesity, no dysfunction	0	352	708	821
Preclinical obesity	0	1821	3466	3952





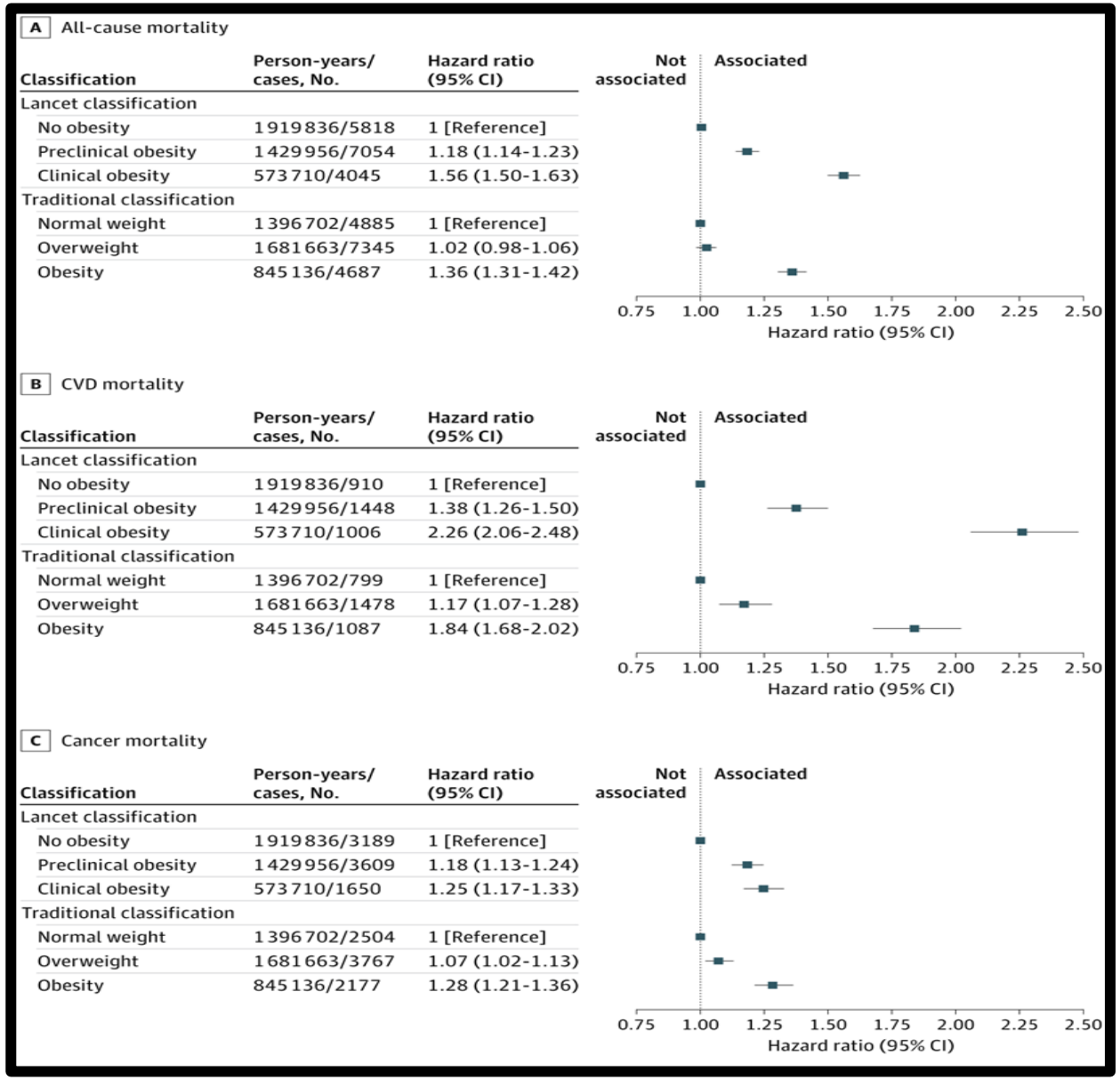
No. at risk				
Clinical obesity	108650	68407	44253	567
No obesity, dysfunction	24085	15397	10039	156
No obesity, no dysfunction	70580	54091	39960	1005
Preclinical obesity	97711	73827	53924	892
No. of events				
Clinical obesity	0	4705	6627	7112
No obesity, dysfunction	0	794	1081	1185
No obesity, no dysfunction	0	288	490	556
Preclinical obesity	0	739	1204	1348



Fourman et al., Jama Netw Open, 2025

Conseguenze della NWO, UKBB

- We categorized participants using the Lancet classification of no obesity (no excess body fat), preclinical obesity (excess body fat; no organ dysfunction), and clinical obesity (excess body fat; with organ dysfunction); and the traditional BMI-based classification of normal weight (BMI, 18.5 to <25), overweight (BMI, 25 to <30), and obesity (BMI, ≥30).
- 290 664 participants, 36% had preclinical obesity and 15% had clinical obesity.



A All-cause mortality

Classification	Person-years/ cases, No.	Hazard ratio (95% CI)
Lancet classification		
No obesity	1 919 836/5818	1 [Reference]
Preclinical obesity	1 429 956/7054	1.18 (1.14-1.23)
Clinical obesity	573 710/4045	1.56 (1.50-1.63)
Traditional classification		
Normal weight	1 396 702/4885	1 [Reference]
Overweight	1 681 663/7345	1.02 (0.98-1.06)
Obesity	845 136/4687	1.36 (1.31-1.42)

B CVD mortality

Classification	Person-years/ cases, No.	Hazard ratio (95% CI)
Lancet classification		
No obesity	1 919 836/910	1 [Reference]
Preclinical obesity	1 429 956/1448	1.38 (1.26-1.50)
Clinical obesity	573 710/1006	2.26 (2.06-2.48)
Traditional classification		
Normal weight	1 396 702/799	1 [Reference]
Overweight	1 681 663/1478	1.17 (1.07-1.28)
Obesity	845 136/1087	1.84 (1.68-2.02)

C Cancer mortality

Classification	Person-years/ cases, No.	Hazard ratio (95% CI)
Lancet classification		
No obesity	1 919 836/3189	1 [Reference]
Preclinical obesity	1 429 956/3609	1.18 (1.13-1.24)
Clinical obesity	573 710/1650	1.25 (1.17-1.33)
Traditional classification		
Normal weight	1 396 702/2504	1 [Reference]
Overweight	1 681 663/3767	1.07 (1.02-1.13)
Obesity	845 136/2177	1.28 (1.21-1.36)

Stein et al., JAMA Int Med, 2025

Editorial: andare oltre il BMI

Inoue et al., JAMA Int Med, 2025

Trattare la NWO

	Baseline diet	Weight-loss intervention	*P*
Total energy (kcal)	2,068 ± 138	1,525 ± 98	<0.001
Carbohydrate (g)	223 ± 20	169 ± 13	0.002
Protein (g)	97 ± 8	81 ± 8	0.066
Fat (g)	83 ± 7	55 ± 4	<0.001

Data are mean ± SEM for $n = 11$.

Weight loss decreased total fat mass by ~9%, VAT and SAT volumes by ~11% and ~17%, respectively, and intrahepatic fat by ~50% (all $P < 0.05$). Fasting plasma insulin, triglyceride, and total low- and high-density lipoprotein cholesterol concentrations were also reduced ($P < 0.05$). Insulin sensitivity indexes (M-value and M/I ratio) increased by 21% to 26% (both $P < 0.05$); β-cell responsivity and postprandial insulin secretion rate did not change, but insulin clearance rate increased by 16% ($P < 0.05$).

	Baseline	After weight loss	*P*
Weight (kg)	64.2 ± 3.0	61.1 ± 2.8	<0.001
BMI (kg/m^2)	22.7 ± 0.4	21.6 ± 0.4	<0.001
Body fat (%)	32.8 ± 1.8	31.7 ± 2.0	0.023
Fat mass (kg)	20.9 ± 1.2	18.9 ± 1.2	<0.001
Fat-free mass (kg)	43.2 ± 2.4	41.4 ± 2.5	<0.001
VAT (cc)	2,565 ± 230	2,309 ± 224	<0.001
SAT (cc)	1,496 ± 177	1,240 ± 150	0.001
Deep SAT (cc)	1,250 ± 168	1,094 ± 152	0.003
Superficial SAT (cc)	1,315 ± 87	1,215 ± 89	0.001
IHTG (%)	3.4 (1.9-9.2)	1.7 (1.0-4.2)	0.041
IMCL (AU)	10.7 (4.9-14.4)	9.9 (4.0-13.0)	0.534
RMR (kcal)	1,821 ± 85	1,695 ± 92	0.020
Systolic BP (mmHg)	120 ± 3	115 ± 4	0.100
Diastolic BP (mmHg)	81 ± 3	77 ± 3	0.023
Heart rate (bpm)	75 ± 3	74 ± 3	0.616

Choi et al., Obesity, 2015

Conclusioni

- Il BMI non è sufficiente per identificare il rischio cardiometabolico: la **Normal-Weight Obesity (NWO)** rivela limiti importanti dell'approccio tradizionale.
- L'eccesso di adiposità con peso normale è associato a rischio aumentato di: resistenza insulinica, eventi cardiovascolari, mortalità e ridotta qualità della vita.
- La **prevalenza della NWO è in aumento**, soprattutto con i nuovi cut-off basati su composizione corporea.
- Il riconoscimento precoce è fondamentale, soprattutto in età evolutiva, dove **il BMI può essere fuorviante**.
- **La gestione della NWO** è possibile.
- Serve un cambio di paradigma: andare oltre il BMI e adottare misure di composizione corporea nella pratica clinica e nei programmi di salute pubblica.