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Original article

Comparative evolution of metabolic health status in obese individuals using novel and conventional anthropometric indexes: a decade-long analysis in Spanish workers

Evolución comparativa del estado de salud metabólica en individuos con obesidad mediante índices antropométricos convencionales y novedosos: un análisis de una década en trabajadores españoles

Miguel García-Samuelsson[1,2], Pedro Juan Tárraga-López[3], Ángel Arturo López-González[1,2,4,5]*, Carla Busquets-Cortés[1,2], Alberto Ramírez-Gallegos[5], Joan Obrador de Hevia[1,2], José Ignacio Ramírez-Manent[1,4,5,6]

1. University Institute of Health Sciences (IUNICS), Palma de Mallorca, Spain
2. Faculty of Dentistry, ADEMA University School, Palma de Mallorca, Spain
3. Faculty of Medicine, University of Castilla La Mancha, Albacete, Spain
4. Balearic Islands Health Research Institute Foundation, Palma de Mallorca, Spain
5. Balearic Islands Health Service, Palma de Mallorca, Spain
6. Faculty of Medicine, University of the Balearic Islands, Palma de Mallorca, Spain

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***Correspondance:** Ángel Arturo López González. a.lopez@eua.edu.es

Abstract

Introduction: the concept of metabolically healthy obesity (MHO) challenges traditional assumptions about the uniform health risks associated with obesity. However, the prevalence and longitudinal evolution of MHO remain underexplored, particularly when different anthropometric indexes are applied.

Objective: to analyze and compare the prevalence and 10-year evolution of MHO versus metabolically non-healthy obesity (MNHO) using various obesity-related indexes, including body mass index (BMI), waist-to-height ratio (WtHR), relative fat mass (RFM), and METS-VF, in a large working population.

Materials and method: we conducted a retrospective cross-sectional analysis of 68,884 Spanish workers (45,498 men and 23,386 women) from 2010 to 2020. Participants were classified as MHO or MNHO using three diagnostic criteria and evaluated across different obesity indexes. Temporal changes in prevalence were assessed for each category.

Results: men exhibited higher rates of metabolic unhealthiness across all indexes and time points. Regardless of the criteria used, MHO individuals presented significantly lower BMI, WtHR, RFM, and METS-VF values compared to MNHO counterparts ($p<0.001$). Over the decade, all obesity indexes showed an increasing trend in the proportion of metabolically non-healthy individuals. For example, among men with obesity grade I, the percentage of MNHO increased from 56.7% to 79.2% (criterion 2), and among women, from 68.1% to 88.5%.

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Conclusions: MHO prevalence is substantially influenced by the index and definition applied. Despite stable obesity rates, the metabolic health of obese individuals declined over time. These findings support the need for improved screening strategies integrating multiple indexes beyond BMI to better identify high-risk individuals.

Keywords: Metabolically healthy obesity. Obesity phenotypes. Population-based study. Relative fat mass. Body mass index. Metabolic score for visceral fat. (METS-VF)

Resumen

Introducción: el concepto de obesidad metabólicamente sana (OMS) cuestiona las suposiciones tradicionales sobre los riesgos para la salud asociados de forma uniforme con la obesidad. No obstante, la prevalencia y evolución longitudinal de la OMS siguen siendo poco exploradas, especialmente cuando se aplican diferentes índices antropométricos.

Objetivo: analizar y comparar la prevalencia y la evolución a 10 años de la obesidad metabólicamente sana (OMS) frente a la obesidad metabólicamente no sana (OMNS), utilizando diversos índices relacionados con la obesidad, incluidos el índice de masa corporal (IMC), la razón cintura-estatura (cintura/altura), la masa grasa relativa (RFM) y el puntaje metabólico de grasa visceral (METS-VF), en una amplia población trabajadora.

Materiales y método: se realizó un análisis retrospectivo de corte transversal en 68.884 trabajadores españoles (45.498 hombres y 23.386 mujeres) entre los años 2010 y 2020. Los participantes fueron clasificados como OMS u OMNS según tres criterios diagnósticos y evaluados mediante distintos índices de obesidad. Se analizaron los cambios temporales en la prevalencia de cada categoría.

Resultados: los hombres mostraron mayores tasas de alteración metabólica en todos los índices y puntos temporales. Independientemente del criterio empleado, los individuos clasificados como OMS presentaron valores significativamente inferiores de IMC, cintura/altura, RFM y METS-VF en comparación con sus pares OMNS (p<0,001). A lo largo de la década, todos los índices de obesidad evidenciaron una tendencia creciente en la proporción de personas metabólicamente no sanas. Por ejemplo, entre los hombres con obesidad de grado I, el porcentaje de OMNS aumentó del 56,7% al 79,2% (criterio 2), y entre las mujeres, del 68,1% al 88,5%.

Conclusiones: La prevalencia de OMS está considerablemente influenciada por el índice y la definición utilizados. A pesar de que las tasas de obesidad se mantuvieron estables, la salud metabólica de las personas con obesidad se deterioró con el tiempo. Estos hallazgos respaldan la necesidad de mejorar las estrategias de cribado mediante la integración de múltiples índices más allá del IMC, con el fin de identificar con mayor precisión a los individuos con alto riesgo.

Palabras clave: Obesidad metabólicamente sana. Fenotipos de obesidad. Estudio poblacional. Masa grasa relativa. Índice de masa corporal. Puntaje metabólico de grasa visceral. (METS-VF)

Introduction

Obesity continues to represent one of the most pressing global health concerns, with over one billion individuals affected and its burden steadily increasing across all age groups and socioeconomic strata. The World Health Organization (WHO) estimates that more than 650 million adults were obese in 2022, contributing to more than 4 million deaths annually through associated conditions such as cardiovascular disease (CVD), type 2 diabetes *mellitus* (T2DM), and several types of cancer[1]. Traditionally, obesity has been defined and classified by body mass index (BMI), a simple anthropometric indicator of excess body weight relative to height. However, BMI does not distinguish between fat and lean mass or account for fat distribution, a critical determinant of metabolic health[2].

This limitation has driven increasing attention toward more nuanced classifications of obesity, most notably the concept of metabolically healthy obesity (MHO). Individuals with MHO exhibit an elevated BMI but maintain a favorable cardiometabolic profile, characterized by normal insulin sensitivity, blood pressure, lipid levels, and inflammatory markers[3]. Estimates suggest that between 10% and 30% of obese individuals may be classified as MHO, depending on the criteria used and the population studied[4]. The clinical relevance of MHO remains highly debated, with some authors viewing it as a transient or unstable state rather than a truly protective phenotype[5].

Indeed, longitudinal studies have shown that a significant proportion of MHO individuals progress to metabolically unhealthy obesity (MNHO) over time, particularly with advancing age, weight gain, or the development of central adiposity[6]. In a prospective study by Mongraw-Chaffin et al., approximately 50% of MHO adults transitioned to a metabolically unhealthy phenotype over a 10-year follow-up[7]. Moreover, large meta-analyses have demonstrated that MHO individuals remain at higher risk of cardiovascular events and all-cause mortality than their metabolically healthy normal-weight (MHNW) counterparts[8,9]. These findings suggest that while MHO

may represent a state of relative rather than absolute protection, it still confers elevated long-term health risks.

The instability and prognostic ambiguity of MHO are further complicated by the lack of a standardized definition. Different studies employ varying criteria to define MHO, including the absence of metabolic syndrome components, favorable insulin resistance markers, or specific cutoffs for lipid and glucose values[10]. This inconsistency leads to substantial heterogeneity in prevalence estimates and makes comparisons between studies difficult. Consequently, there is growing interest in refining the identification of MHO and MNHO individuals using more sensitive and physiologically relevant metrics of adiposity and fat distribution.

Alternative anthropometric indices, such as the waist-to-height ratio (WtHR), relative fat mass (RFM), and the metabolic score for visceral fat (METS-VF), have shown promising utility in capturing central adiposity and visceral fat dysfunction, which are key drivers of metabolic impairment[11-13]. WtHR has emerged as a reliable predictor of cardiometabolic risk across various populations and has been recommended as superior to BMI in clinical guidelines for cardiovascular prevention[14]. A WtHR ≥0.5 has been proposed as a universal cutoff for increased cardiometabolic risk, regardless of sex or, ethnicity[15].

Relative fat mass, an equation derived from height and waist circumference, has been shown to outperform BMI in estimating whole-body fat percentage, especially among women and older adults[16]. Unlike BMI, RFM captures the influence of central fat accumulation, which is more closely linked to insulin resistance, lipid abnormalities, and inflammation[17]. Furthermore, the METS-VF index—incorporating WtHR, age, sex, fasting glucose, triglycerides, and HDL-cholesterol—has demonstrated strong associations with visceral fat, hepatic steatosis, and metabolic risk across diverse cohorts[18,19]. Its application in occupational and epidemiological studies offers a promising avenue for improved risk stratification in clinical practice.

Despite the emergence of these novel indices, few studies have systematically compared the prevalence and evolution of MHO versus MNHO using multiple adiposity-based tools. Most investigations rely on BMI and metabolic syndrome definitions alone, neglecting more precise measures of visceral adiposity and metabolic dysfunction. Moreover, limited data are available on the temporal dynamics of metabolic health among obese individuals, particularly in large-scale, real-world cohorts. Occupational health databases, which regularly collect biometric and laboratory data over time, offer a valuable resource for addressing these gaps.

In the Spanish context, recent evidence indicates a steady increase in obesity and overweight prevalence among the working-age population, raising concerns about future burdens of cardiometabolic diseases[20]. A national occupational cohort study conducted between 2010 and 2020 identified a growing proportion of workers shifting from MHO to MNHO, with notable sex-based disparities in obesity patterns[21]. However, most prior analyses were based on BMI alone, without considering alternative indexes such as WtHR, RFM, or METS-VF. Given the evolving nature of obesity phenotypes and the heterogeneity in metabolic risk within obese individuals, a more comprehensive assessment incorporating various indexes is warranted.

The present study aims to address these knowledge gaps by analyzing the prevalence and evolution of MHO versus MNHO in a large cohort of 68,884 Spanish workers over a ten-year period. Using three different diagnostic criteria and four anthropometric/metabolic indexes (BMI, WtHR, RFM, METS-VF), we:

1. Quantify the proportion of MHO individuals across sex and index.
2. Examine temporal changes in MHO/MNHO status from 2010 to 2020.
3. Compare the discriminatory capacity of each index in capturing metabolic deterioration among obese individuals.

By leveraging a rich longitudinal dataset and adopting a multidimensional approach to obesity phenotyping, this study contributes to the understanding of how different measures of adiposity affect MHO classification and its temporal progression. The findings have important implications for clinical screening, early prevention, and personalized management of obesity-related risk in working populations.

Materials and method

Study design and population

This research comprised two complementary components:

1. A cross-sectional analysis to examine the distribution of metabolically healthy obesity (MHO) and metabolically non-healthy obesity (MNHO) phenotypes according to various anthropometric and metabolic indexes.
2. A retrospective longitudinal analysis to assess the 10-year evolution (2010–2020) of MHO/MNHO prevalence among Spanish workers.

Data were obtained from routine annual occupational health examinations performed between January 2010 and December 2020. The full cohort included 68,884 adult workers (45,498 men and 23,386 women), aged 18 to 69 years, from diverse industrial and service sectors throughout Spain. For the longitudinal component, we included only those individuals who had at least one health examination recorded in both the initial period (2010–2012) and the final period (2018–2020).

All examinations were conducted by licensed occupational physicians and nurses using standardized protocols. Written informed consent was obtained from all participants. The study complied with the principles of the Declaration of Helsinki and was approved by the relevant institutional ethics committee.

Inclusion criteria

Participants were eligible for the study if they met all the following conditions:

- A diagnosis of obesity, defined as a body mass index (BMI) ≥ 30 kg/m^2
- Age between 18 and 69 years at the time of evaluation
- Employment in one of the companies participating in the study
- Provision of informed consent to participate in the research

The participant selection and flow through the study are illustrated in **Figure 1.**

Anthropometric and clinical assessments

Anthropometric data included height, weight, and waist circumference. BMI was calculated as weight (kg) divided by height squared (m^2). Waist-to-height ratio (WtHR) was computed by dividing waist circumference (cm) by height (cm). Relative fat mass (RFM) was estimated using the sex-specific equation validated for adult populations:

- For men: RFM = 64 − (20 × height/waist circumference)
- For women: RFM = 76 − (20 × height/waist circumference)[22]

Systolic and diastolic blood pressure were measured in the seated position after a 5-minute rest using calibrated automatic sphygmomanometers. Blood samples were collected after overnight fasting and analyzed for glucose, triglycerides, HDL-cholesterol, LDL-cholesterol, and total cholesterol using standardized enzymatic techniques.

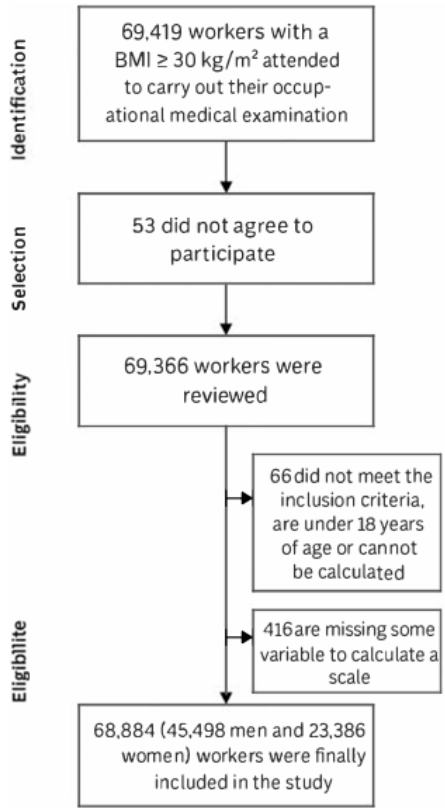

Figure 1. Flow diagram of participant.

The Metabolic Score for Visceral Fat (METS-VF) was calculated using the validated composite formula incorporating age, sex, waist-to-height ratio, glucose, triglycerides, HDL-cholesterol, and BMI, according to the following expression:

METS-VF = 4.466 + 0.011 × (METS-IR)^3 + 3.239 × (waist/height)^3 + 0.319 × sex + 0.594 × ln(age)

Where METS-IR = ln[(2 × glucose) + triglycerides] × BMI / ln(HDL-c), and sex = 1 for men and 0 for women[23]. This index has shown strong correlations with MRI-quantified visceral fat and hepatic steatosis[24].

Definition of metabolically healthy obesity (MHO)

Participants with BMI ≥30 kg/m^2 were categorized as obese. Metabolically healthy obesity (MHO) was identified using three operational definitions adapted from previous studies[25]:

- Criterion 1: Absence of metabolic syndrome (MetS) components (excluding central obesity), based on NCEP ATP III criteria.
- Criterion 2: Presence of no more than one abnormal cardiometabolic parameter (blood pressure, HDL-c, triglycerides, fasting glucose).
- Criterion 3: All cardiometabolic values within the normal range: fasting glucose <100 mg/dL, triglycerides <150 mg/dL, HDL ≥40 mg/dL (men)

or ≥50 mg/dL (women), and blood pressure <130/85 mmHg.

Individuals with ≥2 abnormal parameters were considered to have metabolically non-healthy obesity (MNHO).

Assessment of physical activity and Mediterranean diet adherence

Physical activity was assessed using the short version of the International Physical Activity Questionnaire (IPAQ-SF), which has been validated in European working populations[26]. The questionnaire records the frequency and duration of walking, moderate, and vigorous activity during the preceding seven days. Participants were categorized as physically active if they achieved at least 600 MET-min/week, corresponding to moderate or high activity levels[27].

Adherence to the Mediterranean diet was evaluated using the 14-item Prevention with Mediterranean Diet (PREDIMED) questionnaire**,** which has been validated as a reliable dietary screening tool among Spanish adults[28]. The questionnaire assigns 1 point per item meeting a predefined criterion (e.g., olive oil as main fat, ≥3 servings of legumes/week, ≥3 pieces of fruit/day), with total scores ranging from 0 to 14. A score ≥9 was considered indicative of good adherence[29].

Sociodemographic and lifestyle variables

Participants reported their age, sex, educational level, occupational social class, and smoking status via structured interview.

Educational level was classified as primary, secondary, or university.

Socioeconomic status was determined using the classification system proposed by the Spanish Society of Epidemiology, based on the 2011 National Classification of Occupations (CNO-11). Participants were categorized into three occupational social classes as follows[30]:

- Class I: Executives, university-educated professionals, elite athletes, and artists.
- Class II: Intermediate-level professionals and skilled self-employed workers.
- Class III: Manual laborers and low-skilled workers.

Smoking status was classified as current smoker or non-smoker.

Statistical analysis

Descriptive statistics were presented as means and standard deviations (SD) for continuous variables, and frequencies with percentages for categorical variables. Sex-stratified comparisons were made using T-tests for continuous variables and chi-square tests for categorical variables.

For the cross-sectional analysis, we compared obesity indices (BMI, WtHR, RFM, METS-VF) between MHO and MNHO groups across the three MHO criteria. For the longitudinal analysis, we calculated the percentage change in MHO and MNHO prevalence from 2010–2012 to 2018–2020 within each obesity index category. Paired comparisons were performed for individuals with repeated measures, and statistical significance was assessed using McNemar's test or Wilcoxon signed-rank test as appropriate.

All statistical analyses were conducted using IBM SPSS Statistics version 29.0 (IBM Corp., Armonk, NY, USA). A two-tailed p-value <0.05 was considered statistically significant.

Results

Table 1 provides a comprehensive characterization of the cohort, (n=68,884), highlighting significant sex-based differences across anthropometric, clinical, and behavioral variables. Men exhibited higher mean values for body weight, waist circumference, blood pressure, and serum triglycerides, while women had higher HDL-cholesterol levels and a healthier lifestyle profile, including greater adherence to the Mediterranean diet and lower smoking prevalence. Notably, despite a similar educational distribution, women were more frequently classified in higher social classes. These differences underscore the importance of sex-stratified analysis when evaluating metabolic health and obesity-related risk factors.

Table 2 compares the performance of four obesity indexes (BMI, WtHR, RFM, METS-VF) across various definitions of MHO and MNHO in both sexes. Consistently, MNHO individuals presented significantly worse anthropometric and metabolic index values than MHO counterparts, regardless of the criterion applied (all p<0.001). This trend was observed across both sexes, though absolute values differed, with women displaying higher RFM but lower METS-VF values. The data confirm the robustness of these indexes in differentiating metabolic phenotypes and support the potential utility of alternative measures (e.g., RFM, METS-VF) in clinical settings.

Table 1. Sociodemographic, anthropometric, clinical, and lifestyle characteristics of the study population by sex.

	Men n=45,498	Women n=23.386	
	Mean (SD)	Mean (SD)	p-value
Age (years)	42.9 (10.0)	42.0 (10.4)	<0.001
Height (cm)	173.2 (7.1)	160.0 (6.7)	<0.001
Weight (kg)	99.7 (12.4)	87.5 (12.3)	<0.001
Waist (cm)	96.7 (8.9)	83.3 (8.8)	<0.001
Hip (cm)	108.6 (7.9)	109.5 (9.3)	<0.001
Systolic BP (mmHg)	131.8 (16.2)	124.0 (15.9)	<0.001
Systolic BP (mmHg)	81.0 (10.7)	76.9 (11.0)	<0.001
Total cholesterol (mg/dL)	204.1 (38.8)	200.3 (37.4)	<0.001
HDL-cholesterol (mg/dL)	48.3 (7.0)	51.2 (7.1)	<0.001
LDL-cholesterol (mg/dL)	124.5 (37.5)	127.1 (37.0)	<0.001
Triglycerides (mg/dL)	158.6 (108.4)	110.5 (55.8)	<0.001
Glucose (mg/dL)	92.3 (14.0)	89.0 (13.4)	<0.001
	%	%	p-value
< 30 years	10.0	13.5	<0.001
30-39 years	28.3	28.2	
40-49 years	34.5	32.3	
50-59 years	22.6	21.9	
60-69 years	4.6	4.3	
Elementary school	63.7	64.9	<0.001
High school	32.3	30.6	
University	4.0	4.5	
Social class I	4.6	4.2	<0.001
Social class II	15.7	21.4	
Social class III	79.7	74.4	
No physical activity	96.5	95.3	<0.001
Yes physical activity	3.5	4.7	
No Mediterranean diet	91.8	85.1	<0.001
Yes Mediterranean diet	8.2	14.9	
Non-smokers	68.3	74.0	<0.001
Smokers	31.7	26.0	

Notes: BP, blood pressure. HDL, high density lipoprotein. LDL, low density lipoprotein.
SD, standard deviation

Table 2. Mean values of obesity indexes according to different MHO/MNHO definitions in men and women.

Men	MHO n=8764	MNHO n=36734		MHO 1 n=24264	MNNO 1 n=21234		MHO n=34660	MNHO n=10838	
	Mean (SD)	Mean (SD)	p-value	Mean (SD)	Mean (SD)	p-value	Mean (SD)	Mean (SD)	p-value
BMI	32.4 (2.5)	33.4 (3.3)	<0.001	32.7 (2.7)	33.7 (3.5)	<0.001	32.9 (2.9)	34.1 (3.8)	<0.001
WtHR	0.54 (0.03)	0.57 (0.05)	<0.001	0.54 (0.03)	0.59 (0.06)	<0.001	0.55 (0.04)	0.61 (0.05)	<0.001
RFM	26.5 (2.2)	28.3 (3.2)	<0.001	26.7 (2.3)	29.4 (3.2)	<0.001	27.1 (2.6)	30.8 (2.8)	<0.001
METS-VF	6.8 (0.3)	7.1 (0.3)	<0.001	6.8 (0.3)	7.2 (0.3)	<0.001	6.9 (0.3)	7.3 (0.3)	<0.001
Women	**n=6146**	**n=17240**		**n=14448**	**n=8938**		**n=19976**	**n=3410**	
	Mean (SD)	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**
BMI	32.9 (2.7)	34.5 (4.1)	<0.001	33.4 (3.1)	35.3 (4.6)	<0.001	33.9 (3.6)	35.7 (4.8)	<0.001
WtHR	0.50 (0.03)	0.53 (0.05)	<0.001	0.51 (0.03)	0.55 (0.06)	<0.001	0.51 (0.04)	0.58 (0.06)	<0.001
RFM	35.9 (2.6)	37.7 (3.7)	<0.001	36.2 (2.8)	38.9 (4.0)	<0.001	36.6 (3.0)	40.9 (4.0)	<0.001
METS-VF	6.1 (0.4)	6.4 (0.4)	<0.001	6.2 (0.4)	6.6 (0.4)	<0.001	6.3 (0.4)	6.8 (0.4)	<0.001

Notes: MHO, metabolically healthy obesity. MNHO, metabolically non-healthy obesity. BMI, body mass index. WtHR, waist to height ratio. RFM, relative fat mass. METS-VF, metabolic score for visceral fat. SD, standard deviation.

Table 3. Prevalence of MHO across obesity classifications by sex and MHO criteria.

	Men				Women			
		MHO 0	MHO 1	MHO 2		MHO 0	MHO 1	MHO 2
	n	%	%	%	n	%	%	%
BMI obesity I	35,724	21.3	56.5	79.2	16,160	30,4	68.1	88.5
BMI obesity II	7,838	12.1	44.2	67.7	5,146	20.8	53.0	81.3
BMI obesity III	1,936	11.2	32.2	55.4	2,080	7.7	34.6	71.5
WtHR normal	4,888	28.2	72.5	95.3	9,152	32.7	73.5	94.4
WtHR high	40,610	18.2	51.0	73.9	14,234	22.1	54.2	79.6
RFM non obesity	1,792	25,4	71.4	95.1	3,216	34.4	75.1	95.0
RFM obesity	43,706	19.0	52.6	75.4	20,170	25.0	59.7	83.9
METS-VF normal	30,828	25.8	68.0	90.0	22,626	27.2	63.6	87.3
METS-VF high	14,670	5.5	22.5	47.2	760	6.2	6.3	28.4

Notes: MHO, metabolically healthy obesity. BMI, body mass index. WtHR, waist to height ratio. RFM, relative fat mass. METS-VF, metabolic score for visceral fat.

billustrates the distribution of MHO according to obesity severity and classification (BMI, WtHR, RFM, METS-VF) under three criteria. The data reveal a clear inverse relationship between obesity severity and the probability of being classified as MHO. For example, MHO prevalence dropped from 56.5% to 32.2% (men) and from 68.1% to 34.6% (women) when moving from grade I to grade III obesity (BMI). Moreover, alternative measures like RFM and METS-VF yielded higher proportions of MHO among those categorized as non-obese. These findings highlight the limitations of BMI alone in capturing metabolic health and the added value of complementary indexes.

Table 4 presents a comprehensive multivariable logistic regression analysis examining the associations between sociodemographic, lifestyle, and anthropometric factors with the likelihood of presenting metabolically non-healthy obesity (MNHO), using three distinct criteria (A, B, and C). Across all definitions, male sex, older age, lower educational attainment, lower occupational class, physical inactivity, poor adherence to the Mediterranean diet, smoking cessation (non-smoker status), and increasing obesity severity were independently associated with higher odds of MNHO.

Consistently, male participants exhibited a significantly elevated risk of MNHO compared to females, with odds ratios (ORs) ranging from 1.13 to 1.24 depending on the criterion. Age demonstrated a clear dose–response relationship, with individuals aged 60–69 years having nearly a fourfold increased risk of MNHO (OR 3.87; 95% CI: 3.40–4.35) under criterion A. This age-related trend supports prior longitudinal evidence indicating that metabolic health tends to deteriorate with aging, even in the absence of substantial weight gain.

Sociodemographic variables revealed strong gradients: individuals with only elementary education had markedly higher odds of MNHO than their university-educated counterparts (e.g., OR 2.76 under criterion A), and those in social class III exhibited similarly elevated risks. These findings suggest that educational attainment and occupational status may act as proxies for health literacy, access to care, or cumulative exposure to environmental and behavioral risk factors.

Lifestyle variables demonstrated some of the most substantial associations. Physical inactivity emerged as a major determinant, with ORs as high as 5.45 under criterion C—highlighting the critical role of regular physical activity in preserving metabolic health among individuals with obesity. Similarly, poor adherence to the Mediterranean diet was significantly associated with MNHO, with ORs between 1.97 and 2.68, reaffirming the protective effects of healthy dietary patterns on cardiometabolic profiles.

Interestingly, being a non-smoker was associated with increased odds of MNHO, particularly under the strictest definition (criterion C: OR 1.73; 95% CI: 1.66–1.81). While this counterintuitive association may reflect reverse causation—where individuals quit smoking due to deteriorating health—it also underscores the complexity of lifestyle interactions in metabolic phenotyping.

Table 4. Multivariable logistic regression analysis of factors associated with metabolically non-healthy obesity (MNHO) according to three diagnostic criteria.

	MNHO (A) OR (95% CI)	MNHO (B) OR (95% CI)	MNHO (C) OR (95% CI)
Female	1	1	1
Male	1.13 (1.08-1.18)	1.24 (1.18-1.30)	1.19 (1.14-1.25)
< 30 years	1	1	1
30-39 years	1.37 (1.30-1.44)	1.10 (1.07-1.14)	1.15 (1.10-1.21)
40-49 years	1.56 (1.45-1.67)	1.21 (1.16-1.27)	1.32 (1.21-1.43)
50-59 years	2.52 (2.21-2.83)	1.48 (1.39-1.58)	1.59 (1.40-1.79)
60-69 years	3.87 (3.40-4.35)	1.99 (1.81-2.18)	2.02 (1.75-2.28)
University	1	1	1
High school	1.25 (1.19-1.32)	1.18 (1.14-1.23)	1.18 (1.14-1.23)
Elementary school	2.76 (2.30-3.22)	1.69 (1.49-1.90)	1.62 (1.48-1.77)
Social class I	1	1	1
Social class II	1.28 (1.21-1.35)	1.25 (1.19-1.31)	1.25 (1.19-1.32)
Social class III	1.67 (1.45-1.89)	1.88 (1.69-2.08)	1.71 (1.54-1.88)
Yes physical activity	1	1	1
No physical activity	3.30 (2.80-3.81)	3.48 (2.98-3.99)	5.45 (4.60-6.31)
Yes Mediterranean diet	1	1	1
No Mediterranean diet	2.22 (1.98-2.46)	1.97 (1.80-2.15)	2.68 (2.30-3.05)
Smokers	1	1	1
Non-smokers	1.13 (1.09-1.17)	1.28 (1.23-1.33)	1.73 (1.66-1.81)
Obesity I (BMI)	1	1	1
Obesity II (BMI)	1.63 (1.45-1.81)	1.44 (1.35-1.54)	1.29 (1.21-1.38)
Obesity III (BMI)	2.52 (2.25-2.79)	1.79 (1.65-1.93)	1.65 (1.44-1.87)
WtHR normal	1	1	1
WtHR high	1.29 (1.22-1.36)	1.61 (1.53-1.69)	3.04 (2.76-2.33)
RFM normal	1	1	1
RFM high	1.58 (1.39-1.78)	1.82 (1.60-2.05)	1.79 (1.55-2.04)
METS-VF normal	1	1	1
METS-VF high	4.07 (3.76-4.37)	5.88 (5.60-6.17)	9.57 (9.07-10.08)

Notes: MNHO, metabolically non-healthy obesity. BMI, body mass index. WtHR, waist to height ratio. RFM, relative fat mass. METS-VF, metabolic score for visceral fat. OR, odds ratio.

Anthropometric indicators were strong predictors across all models. Higher BMI categories conferred progressively increased risk, but notably, indexes of central adiposity (WtHR, RFM, and especially METS-VF) demonstrated stronger associations with MNHO. METS-VF, in particular, showed a striking gradient, with individuals in the high METS-VF category having nearly tenfold increased odds of MNHO under criterion C (OR 9.57; 95% CI: 9.07–10.08). This finding validates the clinical utility of METS-VF as a superior marker of visceral adiposity and metabolic dysfunction, outperforming conventional measures like BMI.

In summary, **Table 4** underscores the multifactorial nature of metabolic unhealthiness in obesity. The findings highlight the value of incorporating behavioral and sociodemographic factors alongside refined anthropometric indexes—particularly METS-VF—into risk stratification strategies. These insights support the development of targeted interventions focusing on lifestyle modification, education, and central adiposity reduction to prevent the transition to metabolically non-healthy obesity.

Table 5 provides a longitudinal perspective, revealing a significant decline in the prevalence of MHO over the 10-year period across all indexes and definitions. This decline was particularly pronounced in individuals with severe obesity and those classified using non-BMI indexes. For instance, among men with grade II obesity (criterion 2), MHO prevalence decreased by 37.2%, while among women with high WtHR, the decrease reached 59.3%. The consistency of these findings across multiple definitions underscores a worrying trend: While the degree of obesity may remain stable, metabolic health appears to be worsening. These results call for renewed public health strategies focusing on metabolic rather than purely anthropometric risk assessment.

Discussion

Our comprehensive analysis-featuring both cross-sectional and retrospective components-revealed key insights into metabolically healthy obesity (MHO) among a large Spanish worker cohort. First, MHO prevalence demonstrated significant variation depending on the anthropometric index (BMI, WtHR, RFM, METS-VF) and definition used. Second, individuals classified as MHO consistently showed more favorable metabolic profiles than their MNHO counterparts across all indices. Third, a marked rise in MNHO prevalence was observed between 2010 and 2020, despite stable overall obesity rates, suggesting a decline in metabolic health status.

Interpretation of findings

The wide variation in MHO prevalence aligns with existing meta-research demonstrating disparity due to inconsistent definitions. One meta-analysis reported prevalence estimates ranging from 2% to 44% depending on diagnostic criteria and population sampled[31]. Our findings reinforce this, particularly highlighting that central adiposity-based indices like WtHR, RFM, and the comprehensive MER-curated METS-VF detect individuals with metabolic disturbances overlooked by BMI alone. This trend is supported by recent studies that underscore central fat as a more accurate predictor of metabolic risk than BMI, alone[32,33].

The longitudinal deterioration of metabolic health observed in our cohort mirrors global trends. For example, Mongraw-Chaffin et al. reported a 50% transition from MHO to unhealthy status over 10 years, with those showing greater central adiposity at baseline more likely to convert[34]. Similarly, Drid et al. found that individuals with higher WtHR had an accelerated progression to metabolic syndrome[35]. Our results thus contribute to a growing consensus that MHO is often a temporary state, heavily influenced by central adiposity accumulation and visceral fat activity.

Strengths

1. Large, well-characterized cohort with mixed design

Our study's inclusion of 68,884 individuals with repeat measurements across two time periods strengthens both external validity and temporal inference. The mixed cross-sectional and retrospective approach aligns with methodological recommendations for robust MHO research[36].

2. Use of multiple complementary adiposity indices

Beyond BMI, we included WtHR, RFM, and METS-VF. Recent evaluation suggests that METS-VF correlates more strongly with MRI-quantified visceral adiposity and metabolic syndrome than BMI or WC alone[37]. This multidimensional approach enhances risk stratification and clinical relevance.

3. Real-world occupational health data

Data collection via mandated workplace health assessments reduces selection bias and ensures standardized procedures. Occupational epidemiology frameworks endorse such well-documented routine settings for longitudinal metabolic research[38].

4. Sex-stratified analyses

By analyzing men and women separately, we highlighted gender differences in obesity-related metabolic risk. Consistent with prior studies, women exhibited lower visceral fat and slower progression to MNHO[39], yet still experienced metabolic declines—supporting calls for gender-tailored interventions[40].

Limitations

1. Lack of direct imaging references

Although METS-VF correlates well with MRI, the absence of imaging data limits direct confirmation of visceral fat estimates. A recent systematic review notes that while surrogate indices are useful, imaging provides superior diagnostic accuracy[41].

Table 5. Temporal trends (2010–2020) in the prevalence of MHO by obesity indexes and criteria in men and women.

Men		MHO 0 pre	MHO 0 post		MHO 1 pre	MHO 1 post		MHO 2 pre	MHO 2 post	
	n	%	%	Difference	%	%	Difference	%	%	Difference
BMI Obesity I	20,317	21.4	16.8	21.3	56.7	40.3	28.9	79.2	54.4	31.3
BMI Obesity II	4,496	12.0	8.3	31.2	43.9	27.6	37.2	67.3	39.6	41.2
BMI Obesity III	1,086	9.8	5.9	39.8	33.3	19.3	41.9	56.9	28.6	49.8
WtHR normal	16,998	28.2	23.9	15.8	72.8	55.8	23.3	95.3	64.0	32.8
WtHR high	8,911	18.3	12.3	32.8	51.2	31.3	38.9	73.8	39.2	46.9
RFM non obesity	996	24.3	20.3	18.6	70.5	55.1	21.8	94.9	70.9	25.3
RFM obesity	24,903	19.2	13.5	29.6	52.8	33.8	35.9	75.4	45.8	39.2
METS-VF normal	17,635	25.9	21.3	17.8	68.1	51.2	24.8	90.0	61.4	31.8
METS-VF high	8,264	5.3	3.6	31.2	22.5	12.9	42.8	46.6	22.2	52.3
Women	**n**	**%**	**%**	**Difference**	**%**	**%**	**Difference**	**%**	**%**	**Difference**
BMI Obesity I	9,156	30.3	24.7	18.6	68.1	52.5	22.9	88.5	64.6	27.8
BMI Obesity II	2,911	20.9	15.6	25.3	53.4	36.7	31.3	81.5	52.2	35.9
BMI Obesity III	1,221	7.7	5.1	33.7	33.8	20.3	39.8	71.7	42.1	41.3
WtHR normal	12,440	32.8	25.3	22.8	73.9	55.6	24.8	94.4	64.4	31.8
WtHR high	848	21.9	13.4	38.9	54.0	30.9	42.7	79.8	32.5	59.3
RFM non obesity	1,823	33.0	29.0	12.2	75.2	60.7	19.3	94.8	71.8	24.3
RFM obesity	11,465	25.1	18.7	25.6	59.6	41.5	30.3	84.0	51.9	38.2
METS-VF normal	12,853	27.0	21.9	18.9	63.6	47.8	24.8	87.3	60.8	30.3
METS-VF high	435	2.5	1.5	41.6	5.7	3.3	42.9	29.2	12.1	58.5

Notes: MHO, metabolically healthy obesity. BMI, body mass index. WtHR, waist to height ratio. RFM, relative fat mass. METS-VF, metabolic score for visceral fat. PRE=year2010, POST=year2020. The formula for calculating the difference is [POST−PRE/PRE] as a percentage.

2. Lifestyle data assessed only once per participant

Physical activity and Mediterranean diet adherence were captured at a single time point via IPAQ-SF and PREDIMED questionnaires. As prior cohort analyses indicate, changes in lifestyle behaviors significantly impact metabolic outcomes, and single measurements may not reflect long-term habits[42].

3. Potential residual confounding

Despite adjustments for basic lifestyle and demographic factors, our analyses could not address genetic predispositions or environmental exposures (e.g. air pollution, workplace stress), which are known modifiers of metabolic health[43].

4. Healthy-worker survivor effect

Including only those with measurements in both periods may skew results toward healthier individuals remaining in the workforce. This bias is well-documented in occupational cohort designs and may underestimate metabolic deterioration[44].

5. Non-assessment of medication usage

We did not account for lipid-lowering, antihypertensive, or glucose-regulating medications, which could impact classification of metabolic health status. Other studies have found adjusting for medication can significantly alter MHO categorization[45].

Clinical and public health implications

Our findings have direct implications for clinical practice and public health strategies:

1. Expand routine obesity assessment beyond BMI**:** Incorporate central adiposity indices like WtHR and METS-VF in workplace screenings or primary care to detect at-risk individuals timely.
2. Early intervention based on central adiposity**:** Tailored lifestyle interventions focused on reducing visceral fat—through structured exercise programs and Mediterranean-style diets—have demonstrated efficacy in reversing metabolic deterioration[46].
3. Gender-sensitive approaches**:** While women initially may appear metabolically healthier, they also experience progressive decline, underscoring the need for sustained prevention strategies across sexes[40].

Future investigations should:

- Include repeated longitudinal measures of lifestyle behaviors to capture behavior-related metabolic transitions.
- Incorporate imaging modalities (MRI, CT, DXA) in clinical cohorts to validate surrogate indices and refine MHO definitions.
- Conduct randomized trials to determine whether targeting central adiposity can delay or prevent the transition from MHO to MNHO.
- Explore interactions with genetic, occupational, and environmental factors to create predictive algorithms for metabolic health deterioration.

Conclusions

This study of over 68,000 Spanish workers reveals that MHO prevalence varies substantially based on the adiposity index and definition used, with central adiposity markers (WtHR, RFM, METS-VF) identifying higher-risk individuals than BMI alone. Our longitudinal analysis demonstrates a significant increase in MNHO prevalence over a decade, signaling a concerning decline in metabolic health even when obesity rates remain stable. These findings highlight the inadequacies of BMI-centric screening and emphasize the need for comprehensive anthropometric and metabolic assessment. Integrating central adiposity measures into routine health evaluations could enable earlier identification of at-risk individuals, guide prevention efforts, and support targeted workplace interventions to mitigate metabolic deterioration.

Data availability statement

Due to ethical and privacy considerations, the dataset is not publicly available. Data are stored in a secure database managed by ADEMA University School. The institution's Data Protection Officer is Ángel Arturo López González.

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Conflicts of Interest

The authors declare no conflicts of interest.

Ethics approval

This study was conducted in strict accordance with national and international ethical standards governing research involving human participants, including the Declaration of Helsinki. All necessary measures were implemented to ensure participant anonymity and the confidentiality of personal data. Ethical approval was granted by the Ethics and

Research Committee of the Balearic Islands (Comité de Ética de la Investigación de las Islas Baleares), under approval reference IB 4383/20, dated 26th November 2020. Participation was entirely voluntary, and all individuals were thoroughly informed of the study's purpose and procedures prior to providing signed informed consent. To ensure confidentiality, participants were assigned unique identification codes accessible only to the project coordinator. No personally identifiable information will be published or disclosed. Participants were fully informed of their rights under current regulations, including access to their data and the right to request its modification, deletion, or restriction. The study complied fully with Organic Law 3/2018 of 5th December, on the Protection of Personal Data and Guarantee of Digital Rights.

Written informed consent was obtained from all individuals participating in the study.

Author contributions

MGS: Conceptualization, investigation, and original manuscript writing.

PJTL: Validation, statistical analysis.

ÁALG: Methodology, manuscript review.

JOdH: Data collection and curation.

CBC: Methodology, original manuscript writing.

ARG: Validation, data collection, and curation.

JIRM: Conceptualization, manuscript review.

All authors have read and agreed to the published version of the manuscript.

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