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Risk of insulin resistance applying 3 different scales in 703,472 spanish workers: Associated variables

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Abstract

Objective: Insulin resistance (IR) is a highly prevalent condition that causes significant morbidity and has a multifactorial etiology. The objective of this study is to assess the risk of developing IR by applying three different criteria, and to determine how IR is associated with various sociodemographic variables, tobacco consumption, and obesity using the Body Mass Index (BMI) and the Clínica Universidad de Navarra Body Adiposity Estimator (CUN BAE) criteria.

Materials and methods: A cross-sectional descriptive study of 703,472 Spanish workers, evaluating the influence of age, sex, social class, tobacco consumption, and obesity (based on BMI and CUN BAE criteria) on the prevalence of IR by applying the Triglycerides Glucose Index (TyG index), Metabolic Score for Insulin Resistance (METS-IR), and Triglycerides/HDL-cholesterol scales.

Results: The prevalence of high IR risk varies with the different criteria applied. The variables that most increase the risk of high IR across all three criteria are obesity (both BMI and CUN BAE) and age.

Conclusion: The high IR risk profile according to all three scales is an older male from social class III, a smoker, and obese.

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Introduction

Obesity and insulin resistance are two metabolic conditions that have reached alarming prevalence in recent decades and represent a global public health issue. Obesity, characterized by an excess of body fat, affects more than a billion people worldwide and is associated with a wide range of chronic diseases, including type 2 diabetes mellitus (T2DM), cardiovascular diseases, and various types of cancer (1). Among the many complications related to obesity, insulin resistance has emerged as a central component in the pathophysiology of metabolic diseases, and its relationship with obesity has been widely documented (2).

Insulin resistance refers to a reduced capacity of peripheral tissues, such as skeletal muscle, liver, and adipose tissue, to adequately respond to insulin, a hormone crucial for regulating glucose and lipid metabolism (3). This condition leads to a series of metabolic alterations, such as compensatory hyperinsulinemia, which over time can exhaust pancreatic beta-cell function, culminating in the development of T2DM (4). Several studies have shown that obesity, particularly the increase in visceral fat, is one of the main predisposing factors for insulin resistance (5).

One of the distinctive features of obesity is the change in the behavior of adipose tissue, which shifts from being a simple energy storage to an active endocrine organ capable of secreting a series of bioactive molecules known as adipokines (6). These adipokines, which include leptin, adiponectin, resistin, and tumor necrosis factor-alpha (TNF-α), play a critical role in the regulation of energy metabolism, inflammation, and insulin sensitivity (7). Dysfunction in adipokine secretion in obese individuals contributes to a pro-inflammatory environment that exacerbates insulin resistance (8).

Among the proposed mechanisms to explain the relationship between obesity and insulin resistance, one of the most studied is the role of chronic low-grade inflammation that accompanies the obese state. In obese individuals, adipose tissue becomes infiltrated with immune cells, particularly macrophages, which secrete pro-inflammatory cytokines such as TNF-α and interleukin-6 (IL-6) (9). These cytokines interfere with insulin signaling in peripheral tissues, blocking insulin action and promoting a state of insulin resistance (10).

In fact, experimental studies have shown that inhibiting these cytokines can improve insulin sensitivity, highlighting the central role of inflammation in the pathogenesis of this condition (11).

In addition to inflammation, the accumulation of ectopic lipids in non-adipose organs, such as the liver and skeletal muscle, also contributes to the development of insulin resistance (12). This phenomenon, known as lipotoxicity, results from lipid overload in these tissues, leading to mitochondrial dysfunction, the production of toxic metabolites, and the disruption of normal insulin signaling (13). Lipotoxicity is not only a key factor in insulin resistance but is also linked to other metabolic complications, such as non-alcoholic fatty liver disease (NAFLD) (14).

The relationship between obesity and insulin resistance is not limited to body fat accumulation and inflammation but also includes changes in mitochondrial function, oxidative stress, and intracellular signaling (15). Oxidative stress, in particular, is an important mediator in metabolic dysfunction, as reactive oxygen species (ROS) produced in excess during obesity damage cellular structures and alter insulin signaling (16). These processes not only affect glucose homeostasis but also contribute to vascular dysfunction and the onset of cardiovascular complications (17).

In terms of interventions, weight loss has been shown to be an effective strategy for improving insulin sensitivity in obese individuals. Modest reductions in body weight, on the order of 5-10%, can significantly improve metabolic function and reduce the risk of developing T2DM (18). Additionally, changes in adipose tissue composition, such as a reduction in visceral fat, appear to be particularly important in reversing insulin resistance (19).

Finally, emerging research has highlighted the role of the gut microbiome in regulating insulin resistance in the context of obesity. Intestinal dysbiosis, or an imbalance in the composition of the microbiota, has been associated with systemic inflammation and insulin resistance, suggesting a new potential therapeutic target in the treatment of metabolic diseases (20). Although human studies are still in their early stages, interventions that modulate the microbiota, such as supplementation with prebiotics or probiotics, could offer new avenues to combat insulin resistance in obese individuals (21).

The objective of this study is to assess the risk of developing IR by applying three different criteria, and to determine how IR is associated with various sociodemographic variables, tobacco consumption, and obesity using the Body Mass Index (BMI) and the Clínica Universidad de Navarra Body Adiposity Estimator (CUN BAE) criteria.

Materials and methods

A descriptive, cross-sectional study was performed in 707,470 spanish workers between January 2018 and December 2019. 3998 workers were previously excluded (358 were < 18 or > 69 years old, 3015 did not agree to participate and 698 lacked a variable to calculate insulin resistance scales). Leaving 703,472 workers (421,079 men y 282,393 women). Flow chart was given in Figure 1.

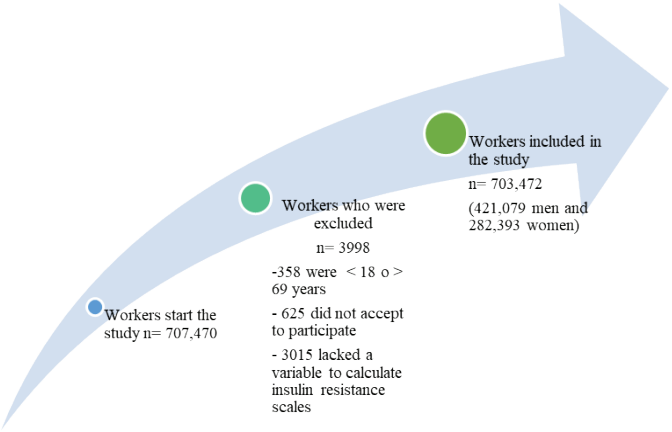

Figure 1: Flow chart of participants.

Inclusion Criteria

One of the inclusion criteria for selecting the sample was being between 18 and 69 years of age. Additional criteria included having an employment contract with one of the companies participating in the study, signing an informed consent form to participate in the research, and providing permission for the data to be used in epidemiological studies.

Determination of variables

Healthcare professionals from the various participating companies determined the anthropometric, analytical, and clinical variables required to calculate different cardiometabolic risk scales. Measurement techniques were standardized to minimize potential biases in obtaining these variables.

Measurements were taken with the participant standing upright and with their abdomen relaxed. A SECA scale was used to measure both weight and height.

Blood pressure was measured using an OMRON-M3 sphygmomanometer. After a ten-minute rest period, three readings were taken, with one-minute intervals between each reading, and the average of the three readings was calculated.

Following a fasting period of at least twelve hours, blood glucose, triglycerides, and total cholesterol were measured using various techniques, along with precipitation methods to determine HDL-cholesterol. LDL-cholesterol was calculated using the Friedewald formula, valid for triglyceride levels up to 400 mg/dL. All analytical parameters were expressed in milligrams per deciliter (mg/dL).

Gender was classified as male or female. Age was determined by subtracting the date of birth from the date of the medical examination. The highest level of education completed was recorded, with three recognized levels: primary, secondary, and university education.

To determine social class, the criteria of the Spanish Society of Epidemiology22, based on the types of jobs included in the 2011 National Classification of Occupations (CNO-11), were applied. Three social class tiers were established:

- Social Class I: This group includes university-trained professionals, artists, professional athletes, and managers.
- Social Class II: This category covers skilled self-employed individuals and intermediate-level professions.
- Social Class III: This class includes unskilled laborers.

Individuals were classified as smokers if they had smoked at least once in the past 30 days or if they had quit smoking less than a year ago.

Adherence to the Mediterranean diet was assessed using a 14-question survey, scored on a scale of 0 or 1. A score of nine or higher indicated high adherence (23,24).

Physical activity levels were determined using the International Physical Activity Questionnaire (IPAQ)(25). This self-administered questionnaire aimed to measure the amount of physical activity performed.

Different scales were calculated to evaluate the risk of insulin resistance (IR).

- Metabolic insulin resistance score (METS-IR) [26]. METS-IR = Ln [(2 glycaemia) + triglycerides] BMI)/ (Ln[HDL-c]). Values were considered high from 50 up.
- TyG index [27] = Ln [triglycerides (mg/dL) glycaemia (mg/dL)/2]. Values were considered high from 8.72 up in men and 8.67 up in women [28].
- Triglycerides/HDL-c [29]. Values were considered high from 2.4 up. This was obtained by dividing the value of triglycerides by the value of HDL cholesterol.

The overweight and obesity scales determined are:

- Body Mass Index (BMI): Calculated by dividing weight (in kilograms) by height squared (in meters). BMI is classified into the following categories: underweight (less than 18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), and obese (over 30 kg/m^2).
- Clínica Universidad de Navarra Body Adiposity Estimator (CUN BAE) (30): The formula is:

Table 1: Characteristics of the population.

	Men n=421.079	Women n=282.393	
	Mean (SD)	**Mean (SD)**	**p-value**
Age	40.8 (11.2)	39.8 (10.9)	<0.0001
Height	174.7 (7.0)	161.9 (6.5)	<0.0001
Weight	81.5 (14.9)	66.4 (14.2)	<0.0001
Systolic blood pressure	128.9 (15.5)	118.2 (15.7)	<0.0001
Diastolic blood pressure	78.4 (10.9)	73.2 (10.4)	<0.0001
Total cholesterol	192.5 (39.1)	191.0 (36.2)	<0.0001
HDL-c	50.5 (8.9)	57.2 (9.4)	<0.0001
LDL-c	117.9 (36.9)	115.9 (34.7)	<0.0001
Triglycerides	123.5 (92.2)	89.1 (47.6)	<0.0001
Glycaemia	91.1 (19.2)	87.8 (15.1)	<0.0001
	n (%)	**n (%)**	**p-value**
18-29 years	80231 (18.9)	59384 (20.8)	<0.0001
30-39 years	112646 (26.6)	81534 (28.6)	
40-49 years	126967 (30.0)	84206 (29.6)	
50-59 years	86109 (20.3)	49872 (17.5)	
60-69 years	17678 (4.2)	10069 (3.5)	
Social class I	18974 (4.5)	18391 (6.5)	<0.0001
Social class II	61597 (14.5)	68513 (24.0)	
Social class III	343060 (81.0)	198161 (69.5)	
Non smokers	279806 (66.0)	195523 (68.5)	<0.0001
Smokers	143825 (34.0)	89542 (31.5)	
Underweight BMI	4511 (1.1)	9727 (3.4)	<0.0001
Normal weight BMI	160957 (38.0)	149447 (52.4)	
Overweight BMI	174024 (41.1)	77974 27.4)	
Obesity BMI	84139 (19.8)	47917 (16.8)	
Normal weight CUN BAE	80008 (18.9)	72692 (25.5)	<0.0001
Overweight CUN BAE	123633 (29.2)	76978 (27.0)	
Obesity CUN BAE	219990 (51.9)	135395 (47.5)	

HDL-c High density lipoprotein-cholesterol. LDL-c Low density lipoprotein-cholesterol.
BMI Body mass index. CUN BAE Clínica Universitaria de Navarra Body adiposity estimator.
SD Standard deviation

CUN BAE = −44.988 + (0.503×age) + (10.689×sex) + (3.172 × BMI) − (0.026 × BMI^2) + (0.181 × BMI×sex) − (0.02×BMI×age) − (0.005×BMI^2×sex) + (0.00021 × BMI^2×age For sex: Male = 0, Female = 1. Obesity > 25% males and > 35% females.

Ethical approval

The 2013 Helsinki Declaration50 and all other ethical guidelines governing research were followed. Participants' privacy and anonymity were always

Table 2: Mean values of different insulin resistance risk scales according sociodemographic variables and tobacco consumption by sex

		TyG index		METS-IR		TG/HDL-c	
Men	n	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
18-29 years	80231	8.2 (0.5)	<0.0001	34.9 (7.5)	<0.0001	1.8 (1.4)	<0.0001
30-39 years	112646	8.4 (0.6)		38.1 (8.0)		2.4 (1.9)	
40-49 years	126967	8.6 (0.6)		40.5 (8.5)		2.8 (2.3)	
50-59 years	86109	8.7 (0.6)		42.2 (8.5)		3.1 (2.4)	
60-69 years	17678	8.8 (0.6)		43.2 (8.3)		3.2 (2.0)	
Social class I	18974	8.4 (0.5)	<0.0001	38.5 (7.5)	<0.0001	2.4 (2.0)	<0.0001
Social class II	61597	8.5 (0.6)		38.9 (7.9)		2.5 (2.1)	
Social class III	343060	8.6 (0.6)		39.4 (8.7)		2.6 (2.2)	
Non smokers	279806	8.5 (0.6)	<0.0001	39.3 (8.5)	<0.0001	2.6 (2.1)	<0.0001
Smokers	143825	8.7 (0.6)		39.8 (8.6)		2.9 (2.2)	
Underweight BMI	4511	8.1 (0.5)	<0.0001	24.5 (1.7)	<0.0001	1.6 (1.1)	<0.0001
Normal weight BMI	160957	8.3 (0.5)		32.2 (3.1)		1.9 (1.4)	
Overweight BMI	174024	8.6 (0.6)		39.9 (3.7)		2.7 (2.1)	
Obesity BMI	84139	8.8 (0.6)		52.2 (7.1)		3.8 (2.8)	
Normal weight CUN BAE	80008	8.1 (0.5)	<0.0001	29.7 (2.7)	<0.0001	1.7 (1.2)	<0.0001
Overweight CUN BAE	123633	8.3 (0.5)		34.9 (2.7)		2.1 (1.6)	
Obesity CUN BAE	219990	8.7 (0.6)		45.1 (7.5)		3.2 (2.5)	
Women		Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
18-29 years	59384	8.0 (0.4)	<0.0001	32.4 (7.8)	<0.0001	1.4 (0.8)	<0.0001
30-39 years	81534	8.1 (0.4)		34.2 (8.3)		1.5 (0.9)	
40-49 years	84206	8.2 (0.5)		35.9 (8.4)		1.7 (1.0)	
50-59 years	49872	8.4 (0.5)		37.8 (8.4)		2.0 (1.2)	
60-69 years	10069	8.5 (0.5)		38.9 (8.2)		2.1 (1.2)	
Social class I	18391	8.1 (0.4)	<0.0001	32.7 (7.3)	<0.0001	1.5 (0.9)	<0.0001
Social class II	68513	8.1 (0.5)		33.7 (7.8)		1.6 (0.9)	
Social class III	198161	8.2 (0.5)		35.9 (8.7)		1.7 (1.0)	
Non smokers	195523	8.2 (0.5)	<0.0001	35.2 (8.5)	<0.0001	1.6 (1.0)	<0.0001
Smokers	89542	8.2 (0.5)		35.0 (8.4)		1.6 (1.0)	
Underweight BMI	9727	7.9 (0.4)	<0.0001	23.6 (1.5)	<0.0001	1.2 (0.6)	<0.0001
Normal weight BMI	149447	8.0 (0.4)		29.9 (2.9)		1.4 (0.7)	
Overweight BMI	77974	8.3 (0.5)		37.9 (3.1)		1.8 (1.1)	
Obesity BMI	47917	8.5 (0.5)		49.8 (7.0)		2.3 (1.3)	
Normal weight CUN BAE	72692	7.9 (0.4)	<0.0001	26.9 (2.2)	<0.0001	1.2 (0.6)	<0.0001
Overweight CUN BAE	76978	8.1 (0.4)		31.4 (2.2)		1.4 (0.7)	
Obesity CUN BAE	135395	8.3 (0.5)		41.7 (7.7)		2.0 (1.2)	

BMI Body mass index. CUN BAE Clínica Universitaria de Navarra Body adiposity estimator.

SD Standard deviation. TyG index Triglyceride Glucose index. METS-IR Metabolic score for insulin resistance. TG/HDL-c Triglyceride/ High density lipoprotein-cholesterol.

guaranteed. The study was approved by the Balearic Islands Research Ethics Committee (CEI-IB), which granted approval under reference number IB 483/20. Since all data were coded, only the lead investigator had access to participants' identities. Organic Law 3/2018, passed on December 5, 2018, ensures that study participants can always access, rectify, cancel, or object to the use of their collected data. The law also safeguards digital rights.

Statistical analysis

Student's t-test was used to analyze quantitative data and determine means and standard deviations. For categorical variables, the chi-square test was used to evaluate prevalence. Binomial logistic regression analysis was performed, and odds ratios with 95% confidence intervals were calculated. Statistical analyses were conducted using SPSS version 29.0. A p-value of less than 0.05 was considered statistically significant for this study.

Result

The 703,472 workers in the study presented the following anthropometric, clinical, analytical, sociodemographic, tobacco consumption, and overweight and obesity data as shown in Table 1. The average age of the participants was slightly over 40 years. All variables showed less favorable values in women.

Men made up 59.9% of the participants, while women accounted for 40.1%. The largest age group was between 30 and 49 years old. Most participants belonged to social class III. Smoking rates were 34.01% among men and 31.5% among women.

According to BMI criteria, 19.8% of men are obese, and 51.9% are classified as obese according to CUN BAE criteria. In women, these percentages are 16.8% and 47.5%, respectively.

The mean values of the three IR risk scales increase with age and with decreasing socio-economic status. Values are also higher among smokers. The mean values of TGA index, METS-IR and TG/HDL-c increase with increasing BMI and CUN BAE. The mean values are always lower in women. In all cases the observed differences are statistically significant as shown in table 2.

The prevalence of elevated TyG index, METS-IR and TG/HDL-c also increases with age, with smoking and with increasing BMI and CUNBAE values, while it decreases with increasing social class. All observed differences show a high statistical significance as shown in table 3.

In the multinomial logistic regression (table 4) we observed that all the variables analysed increase the probability of presenting high values of the three IR risk scales, of which the ones with the highest odds ratios are age, BMI and CUN BAE. In all cases the differences show statistical significance.

Discussion

Insulin resistance (IR) is a metabolic condition that affects millions of people worldwide, contributing to the development of diseases such as type 2 diabetes mellitus (T2DM) and cardiovascular diseases (4). Various factors, such as gender, age, social class, body mass index (BMI), and the CUNBAE index, influence insulin resistance values, highlighting the importance of analyzing these factors comprehensively to better understand their contribution to IR risk.

Gender has been shown to be a key factor in determining IR values. Recent studies indicate that women, especially after menopause, have a significantly higher risk of developing IR compared to men, largely due to the hormonal changes that occur during this stage of life (31). Before menopause, estrogen plays a protective role in regulating glucose metabolism, promoting greater insulin sensitivity, and limiting the accumulation of visceral fat, which is directly related to IR (32). However, after menopause, the decline in estrogen levels promotes the redistribution of fat toward the visceral area, increasing the risk of IR in older women (33).

In men, IR is also strongly associated with the accumulation of visceral fat, but hormonal differences between the sexes create variations in fat distribution, which can influence the results of insulin resistance scales. Despite these differences, it has been shown that both men and women experience an increase in IR with fat accumulation, emphasizing the importance of accurately evaluating adiposity to determine IR risk in both sexes (34).

Age is another determinant factor in the development of IR. As people age, changes in body composition occur, such as loss of muscle mass and increased adiposity, especially in the visceral area. These metabolic changes contribute to the development of IR, even in individuals with a normal BMI (35). Furthermore, aging is associated with increased oxidative stress and chronic low-grade inflammation, known as "inflammaging,"

which exacerbates metabolic dysfunction and raises the risk of IR (36).

In this context, both BMI and the CUNBAE index can lose accuracy in older populations, as they do not adequately account for fat redistribution and muscle loss that occur with age (37). Studies have shown that traditional BMI-based scales underestimate the risk of IR in older adults, highlighting the need to use

Table 3: Prevalence of high values of different insulin resistance risk scales according sociodemographic variables and tobacco consumption by sex

		TyG index high		METS-IR high		TG/HDL-c high	
Men	n	%	p-value	%	p-value	%	p-value
18-29 years	80231	10.7	<0.0001	3.1	<0.0001	6.4	<0.0001
30-39 years	112646	21.8		5.4		13.3	
40-49 years	126967	31.6		8.3		18.7	
50-59 years	86109	38.6		10.6		21.9	
60-69 years	17678	43.1		11.4		23.6	
Social class I	18974	23.6	<0.0001	5.7	<0.0001	15.7	<0.0001
Social class II	61597	25.1		6.5		16.4	
Social class III	343060	27.5		7.4		15.7	
Non smokers	279806	26.5	<0.0001	7.3	<0.0001	15.9	<0.0001
Smokers	143825	27.9		6.9		15.7	
Underweight BMI	4511	7.1	<0.0001	0.1	<0.0001	5.6	<0.0001
Normal weight BMI	160957	13.2		0.7		10.7	
Overweight BMI	174024	30.0		1.1		26.5	
Obesity BMI	84139	48.1		55.6		50.2	
Normal weight CUN BAE	80008	8.2	<0.0001	1.1	<0.0001	6.7	<0.0001
Overweight CUN BAE	123633	17.1		3.2		14.2	
Obesity CUN BAE	219990	39.3		22.5		37.6	
Women	n	%	p-value	%	p-value	%	p-value
18-29 years	59384	6.4	<0.0001	2.6	<0.0001	6.6	<0.0001
30-39 years	81534	8.5		3.8		9.0	
40-49 years	84206	12.8		4.7		12.4	
50-59 years	49872	22.8		5.6		18.6	
60-69 years	10069	28.8		6.1		21.6	
Social class I	18391	8.2	<0.0001	2.5	<0.0001	9.2	<0.0001
Social class II	68513	11.1		3.0		10.5	
Social class III	198161	13.5		4.8		12.3	
Non smokers	195523	12.5	<0.0001	4.2	<0.0001	11.4	<0.0001
Smokers	89542	12.9		4.3		12.1	
Underweight BMI	9727	3.6	<0.0001	0	<0.0001	5.8	<0.0001
Normal weight BMI	149447	6.2		0.2		8.8	
Overweight BMI	77974	16.0		0.5		21.8	
Obesity BMI	47917	28.8		39.0		41.8	
Normal weight CUN BAE	72692	3.8	<0.0001	0.5	<0.0001	6.0	<0.0001
Overweight CUN BAE	76978	6.8		2.4		9.7	
Obesity CUN BAE	135395	20.6		13.7		28.7	

BMI Body mass index. CUN BAE Clínica Universitaria de Navarra Body adiposity estimator.

TyG index Triglyceride Glucose index. METS-IR Metabolic score for insulin resistance. TG/HDL-c Triglyceride/ High density lipoprotein-cholesterol.

alternative indices like CUNBAE, which offer a more precise assessment of adiposity and its relationship to insulin resistance (38).

Social class is another key factor influencing IR values. BMI is a widely used tool to assess adiposity and predict the risk of IR, but it has significant limitations. BMI does not distinguish between fat mass and lean mass, nor does it provide information about fat distribution, which are key factors in the development of IR (42).

Table 4: Multinomial logistic regression analysis results

	TyG index high		METS-IR high		TG/HDL-c high	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Female	1		1		1	
Male	2.49 (2.45-2.52)	<0.0001	1.74 (1.70-1.78)	<0.0001	1.47 (1.45-1.50)	<0.0001
18-29 years	1		1		1	
30-39 years	1.26 (1.23-1.30)	<0.0001	1.14 (1.09-1.20)	<0.0001	1.25 (1.20-1.29)	<0.0001
40-49 years	1.91 (1.86-1.96)	<0.0001	1.51 (1.44-1.58)	<0.0001	1.80 (1.74-1.86)	<0.0001
50-59 years	3.13 (3.05-3.22)	<0.0001	2.28 (2.18-2.39)	<0.0001	2.82 (2.73-2.92)	<0.0001
60-69 years	6.37 (6.17-6.57)	<0.0001	3.83 (3.64-4.04)	<0.0001	5.30 (5.10-5.51)	<0.0001
Social class I	1		1		1	
Social class II	1.22 (1.20-1.24)	<0.0001	1.48 (1.44-1.53)	<0.0001	1.19 (1.17-1.21)	<0.0001
Social class III	1.40 (1.36-1.45)	<0.0001	1.83 (1.74-1.93)	<0.0001	1.40 (1.35-1.45)	<0.0001
Non smokers	1		1		1	
Smokers	1.11 (1.10-1.13)	<0.0001	1.03 (1.00-1.07)	<0.0001	1.07 (1.05-1.08)	<0.0001
Underweight BMI	1		1		1	
Normal weight BMI	1.85 (1.62-1.99)	<0.0001	1.62 (1.50-1.74)	<0.0001	1.73 (1.56-1.91)	<0.0001
Overweight BMI	3.97 (3.07-4.88)	<0.0001	4.89 (3.90-5.89)	<0.0001	5.66 (4.90-7.42)	<0.0001
Obesity BMI	7.33 (6.12-8.53)	<0.0001	18.13 (16.20-20.07	<0.0001	9.56 (8.10-10.97)	<0.0001
Normal weight CUN BAE	1		1		1	
Overweight CUN BAE	2.14 (1.89-2.40)	<0.0001	2.85 (2.40-3.30)	<0.0001	2,14 (1.77-2.52)	<0.0001
Obesity CUN BAE	5.44 (4.50-6.89)	<0.0001	13.50 (11.98-15.03)	<0.0001	5.80 (7.95-6.66)	<0.0001

BMI Body mass index. CUN BAE Clínica Universitaria de Navarra Body adiposity estimator.

TyG index Triglyceride Glucose index. METS-IR Metabolic score for insulin resistance. TG/HDL-c Triglyceride/ High density lipoprotein-cholesterol. OR Odss ratio. CI Confidence interval

Individuals from lower social classes have a higher prevalence of IR due to lifestyle-related factors such as limited access to healthy food, lower levels of physical activity, and a higher consumption of ultra-processed foods (39). These behaviors are strongly influenced by the socioeconomic environment, making social class an important determinant of metabolic health.

Studies conducted in Europe have demonstrated a clear correlation between social class and the prevalence of metabolic diseases, including IR. People from lower social classes are at greater risk of developing obesity and, consequently, IR, due to limitations in accessing resources that promote a healthy lifestyle (40). Therefore, public health policies should focus on reducing social disparities to decrease the incidence of IR in the most vulnerable populations (41).

Despite its utility at a population level, BMI may not be sufficient to identify individuals at risk of IR, particularly in people with sarcopenic obesity, where visceral fat accumulation and muscle loss are major determinants of metabolic dysfunction (43).

Research has shown that BMI underestimates the risk of IR in individuals with normal BMI but high levels of visceral fat. In these cases, individuals may have normal BMI values but present an elevated metabolic risk, justifying the need to incorporate other indices that more accurately reflect fat distribution, such as the CUNBAE index (44).

The CUNBAE index has emerged as a promising tool to improve the assessment of IR risk. Unlike BMI, CUNBAE takes into account total adiposity and fat distribution,

making it a better predictor of IR, especially in populations with a high prevalence of visceral obesity (45). Recent studies have demonstrated that CUNBAE has a stronger correlation with IR, measured through the HOMA-IR index, compared to BMI (46).

CUNBAE is also particularly useful in populations with atypical body compositions, such as older adults and postmenopausal women, where BMI may not adequately reflect metabolic risk due to age- and gender-related changes in body composition (47). In these cases, CUNBAE provides a more accurate estimate of total and visceral fat, allowing for a more effective evaluation of IR risk.

Clinical implications and future directions

The findings linking gender, age, social class, BMI, and the CUNBAE index to insulin resistance values have important clinical implications. Integrating these variables into the assessment of IR risk can improve diagnostic accuracy and allow for more personalized preventive interventions. Given that BMI has significant limitations in predicting IR risk, especially in populations with atypical body compositions, the use of the CUNBAE index can provide a more comprehensive evaluation of adiposity and its relationship to metabolic dysfunction.

Furthermore, public health interventions that address social inequalities and promote healthy lifestyles are essential to reducing the prevalence of IR in vulnerable populations. Promoting physical activity, access to healthy foods, and reducing the consumption of ultra-processed foods should be priorities in the prevention programs for metabolic diseases, especially in lower social class individuals (48).

Among the strengths of the study, we highlight the large sample size (over 700,000 workers), the diversity of sociodemographic variables and healthy habits considered, and the wide range of insulin resistance scales analyzed.

As limitations, we highlight that insulin resistance is not measured using objective methods but rather through risk scales, as the large sample size would make such determination prohibitively expensive. Another limitation is that the study was conducted on a working population (18-69 years old), so the results cannot be extrapolated to the general population.

Conclusions

The study of the influence of gender, age, social class, BMI, and the CUNBAE index on IR values highlights the complexity of the pathophysiology of this condition. Using more precise assessment tools, such as CUNBAE, along with a comprehensive approach that considers sociodemographic factors, is essential to improve the prevention and treatment of insulin resistance.

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Ethical approval: The 2013 Helsinki Declaration50 and all other ethical guidelines governing research were followed. Participants' privacy and anonymity were always guaranteed. The study was approved by the Balearic Islands Research Ethics Committee (CEI-IB), which granted approval under reference number IB 483/20. Since all data were coded, only the lead investigator had access to participants' identities. Organic Law 3/2018, passed on December 5, 2018, ensures that study participants can always access, rectify, cancel, or object to the use of their collected data. The law also safeguards digital rights.

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Contributions

Research concept and design: AC, JLM, ASC, GV

Data analysis and interpretation: AC, JLM, NM, ML, AALG

Collection and/or assembly of data: AC, JLM, NM, ML, AALG, ASC, GV

Writing the article: AC, JLM, NM, ML, AALG, ASC, GV

Critical revision of the article: AC, JLM, NM, ML, AALG, ASC, GV

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