

## **TITLE PAGE**

### **Title:**

To treat or not to treat: comparison of different criteria to determine whether weight loss is recommended

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## **Abstract:**

### *Background*

Currently, excess body weight, which characterises overweight and obese individuals, is diagnosed based on the BMI ( $\geq 25$  kg/m<sup>2</sup>) in order to determine the need for preventive-therapeutic interventions. However, the importance of body adiposity as a health risk factor is becoming acknowledged. Even in normal weight subjects, a sedentary lifestyle may predispose to increased adiposity. Different criteria have been proposed for the evaluation of body adiposity: total body fat as percentage of body fat (%BF) both alone and as it is related to metabolic syndrome risk; body fat distribution as reflected by the waist circumference; and the body fat mass index (BFMI).

We hypothesised that BMI underestimates the number of subjects who need lifestyle intervention.

### *Methods*

Anthropometric measurements and body composition assessments (by BIA and DXA) were done in 63 Caucasian subjects (23 males, 40 females; 20-65 years of age; BMI 16.5-33.5 kg/m<sup>2</sup>; %BF 9.3-47.5%) They were then classified according to BMI (A), abdominal fat distribution (B), %BF by DXA (C), metabolic syndrome risk (D), and BFMI (E).

### *Results*

Using the different criteria, different percentages of the subjects would have been assessed as requiring weight loss: (A)41.3%; (B)36.5%; (C)47.6%; (D)55.3%; and (E)53.5%.

### *Conclusions*

Using adiposity as the criterion for weight loss recommendations results in a larger number of subjects being identified. A larger database of body fat, morbidity and mortality is needed to obtain population-specific reference data.

## **Background**

It is generally accepted that several important diseases are related to overweight and obesity, including metabolic syndrome and type 2 diabetes mellitus, cardiovascular diseases, some tumours, gallbladder diseases, nonalcoholic steatohepatitis, sleep apnea and osteoarthritis [1-6]. The endocrine role of adipose tissue is mainly responsible for all of these diseases [7,8]. Therefore, excess body adiposity and not excess body weight is detrimental to health. Thus, paradoxically, metabolically-obese normal-weight individuals who are not considered to be obese on the basis of height and weight are hyperinsulinemic, insulin-resistant, predisposed to type 2 diabetes mellitus, hypertriglyceridemic, and have premature coronary heart disease; they respond favourably to caloric restriction [9-11].

Health professionals should assess patients based on their body composition rather than on their weight [12]. Thus, new clinical criteria have been introduced to evaluate body adiposity, such as percentage body fat (%BF), both alone [13] and as it is related to metabolic syndrome risk [14], and waist circumference, which is a good index of abdominal adiposity [1,15]. Recently, the body fat mass index (BFMI, calculated as fat mass in Kg divided by height squared in m<sup>2</sup>), was introduced as part of nutritional assessment and has been suggested as an additional element in qualitative evaluation of BMI [16-18].

Nevertheless, currently patients are assessed for treatment based on their Body Mass Index (BMI), which is calculated as body weight (in kg) divided by the height squared (in m<sup>2</sup>) [1].

The aim of our study was to determine whether BMI underestimates the number of subjects who need a lifestyle intervention in comparison to criteria based on adiposity, such as total body fat, waist circumference, and BFMI.

## **Methods**

### *Sample*

Sixty-three Caucasian subjects (23 males and 40 females), aged 20-65 years, volunteered for the study following a public advertising campaign.

Inclusion criteria were: age between 18 and 65 years; good health status; sedentary; not on a low-calorie diet; and not on drug therapy for acute or chronic illnesses.

Subjects participated from January 2004 to January 2005 to the nutritional assessment and body composition analysis done at the Human Nutrition and Eating Disorders Research Centre, University of Pavia, in partnership with the IRCCS Fondazione Salvatore Maugeri where the diagnostic radiology examinations were done.

### *Study design*

The subjects attended the Dietology outpatient clinic early in the morning after an overnight fast. On arrival, they emptied their bladders. Anthropometric measurements were taken. Body composition was assessed by bioimpedance analysis (BIA) and then by dual-energy X-ray absorptiometry (DXA). Later in the morning the examinations were completed and the subjects were allowed to eat.

### *Anthropometric measurements*

Body weight with the subjects wearing minimal clothing was measured to the nearest 0.1 kg using a scale balance equipped with a stadiometer (Lohman TG 1998). Body height was measured to the nearest 0.5 cm with the subjects standing without shoes. The BMI was calculated as the weight (kg) divided by the height squared ( $m^2$ ).

The subjects were then divided into 4 subclasses according to WHO BMI cut-offs [1] :

A) BMI: “underweight” :  $BMI < 18.5 \text{ kg/m}^2$

“normal weight”:  $BMI = 18.5 - 24.9 \text{ kg/m}^2$

“overweight” :  $BMI = 25 - 29.9 \text{ kg/m}^2$

“obese” : BMI  $\geq$  30 kg/m<sup>2</sup>

Waist circumference was measured to the nearest 0.1 cm with a measuring tape at the midpoint between the lower border of the ribs and the upper border of the pelvis.

The subjects were then divided into 3 subclasses according to gender-specific waist circumference values related to the risk of metabolic complications [1] :

- B) abdominal adiposity: “not increased” : < 80 cm females, < 94 cm males  
“increased” : 80-87.9 cm females, 94-101.9 cm males  
“substantially increased” :  $\geq$  88 cm females,  $\geq$  102 cm males

#### *Body composition assessment*

To reduce methodological biases when classifying subjects according to criteria based on adiposity, we used the same method that was reported by the reference study: DXA for total body fat [13] ; BIA for metabolic syndrome risk [14] and BFMI calculations [16] .

DXA was performed using a Norland RX-26 scanner; total body fat was reported by the device itself. BIA was performed using a Human Im Scan device (Dietosystem, Milan, Italy); total body fat was calculated using Deurenberg’s formula [19].

Subjects were then classified according to different criteria [see Appendix section]:

- C) Total body fat: subjects were classified in accordance with %BF cut-offs corresponding to the BMI cut-offs, as calculated by Gallagher for the Caucasian subgroup of the population that participated in her study [13]
- D) Metabolic syndrome risk: subjects were classified based on %BF cut-offs that had the same risk for developing metabolic syndrome as the corresponding BMI cut-offs, as calculated by Zhu in the Caucasian subgroup of the American population that participated in NHANES III [14]

E) Body fat mass index: subjects were classified according to the BFMI cut-offs corresponding to BMI cut-offs calculated by Kyle based on a wide sample of Caucasian subjects living in Switzerland [16]

#### *Statistical analysis*

Differences between the genders in anthropometric measurements and body fat indexes were tested using unpaired t-tests or  $\chi^2$ - tests. Significance was defined as  $P < 0.05$ . The agreement between BMI classes and abdominal adiposity, total body fat, metabolic syndrome risk, and Body Fat Mass Index classes was evaluated using Kendall's Tau-b test. All analyses were carried out with the statistical software program SPSS, version 13.0.

#### *Statement of Ethics*

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. The study protocol was approved by the Ethics Committee of the University of Pavia, and all subjects provided their written informed consent prior to participation.

## Results

A sample of 63 Caucasian subjects (23 men and 40 women; mean age  $38.7 \pm 13.7$  y; mean BMI  $24.1 \pm 4.0$  kg/m<sup>2</sup>; mean %BF  $29.9 \pm 10.6$  %) was recruited.

According to the classification based on BMI, 6.3% of subjects were underweight, 52.4% were normal weight, 30.2% were overweight and 11.1% were obese. Total body fat alone was low in 3.2% of subjects, normal in 49.2%, increased in 19.0% and high in 28.6%. Metabolic syndrome risk related to total body fat was low in 7.1% of subjects, normal in 37.5%, increased in 21.4% and high in 33.9%. Abdominal fat content was not increased in 63.5% of subjects, increased in 11.1% and substantially increased in 25.4%. BFMI was low in 3.6% of subjects, normal in 42.9%, increased in 32.1% and high in 21.4%.

Figure 1 shows the percentages of subjects for whom weight loss treatment would be recommended and strongly recommended according to each criterion.

Table 1 illustrates the percentages of agreement within the BMI classes and the other criteria classes. The most relevant disagreement was in the underweight and overweight classes. Underweight subjects had a normal abdominal fat content, but most of them (75%) had a total body fat and a metabolic syndrome risk corresponding to the normal weight class; however, this misclassification does not have important clinical consequences, since treatment would not be recommended for any of these patients based on any of the criteria. In the normal weight class, treatment was recommended in 9.1% of subjects based on abdominal fat content, 21.3% based on total body fat (strongly recommended in 6.1% of subjects), and 36.7% based on metabolic syndrome risk (strongly recommended in 16.7% of subjects). In the overweight class, there was a large disagreement between the BMI and the adiposity indexes: more than 50% of subjects would be strongly recommended for treatment based on the total body fat criteria and the metabolic syndrome risk criteria; slightly less than 50% of subjects would be strongly recommended for treatment based on the abdominal fat content

criteria. In obese subjects, there was good agreement between the criteria. Comparing the BMI and BFMI classes, 75% of the BMI underweight subjects had a “normal fat status” on BFMI; this was not clinically important. However, in the normal weight class 30% of subjects were “overfat status”, and in the overweight class 6.7% of subjects had a “normal fat status”, while 40% had a “severe overfat status”; there was good agreement between criteria in the obese class.

The agreement level between BMI classes, total body fat classes and metabolic syndrome risk classes was moderate (tau-b Kendall=0.672,  $p<0.001$  and tau-b Kendall=0.563,  $p<0.001$  respectively); the agreement level between BMI classes and abdominal fat content classes was quite good (tau-b Kendall=0.704,  $p<0.001$ ); the best agreement was between the BMI classes and the BFMI classes (tau-b Kendall=0.722,  $p<0.001$ ).

## Discussion

Obesity is a metabolic disorder that is characterised by excess body fat, which is an important risk factor for disease, due not only to its role as volume-filling organ, but primarily due to the endocrine role of adipose tissue [7,8,20].

Though the BMI is easy to calculate and can be easily used in population studies, it does not discriminate between fat mass and fat-free mass, and it does not reflect fat mass distribution in the body [21,25]. In our study, the BMI identified a lower percentage of subjects that required treatment (41.3% overall, 11.1% with a strong recommendation) than %BF alone (47.6% overall, 28.6% with a strong recommendation) and particularly compared to %BF related to metabolic syndrome risk (55.3% overall, 33.9% with a strong recommendation). The BFMI, which is an index that specifically focuses on amount of body fat compared to total body weight, identified a percentage of subjects (53.5%) similar to that identified by the metabolic syndrome risk. Waist circumference, though it did not identify a higher number of subjects for whom weight loss would be recommended, including those who need preventive intervention (36.5% vs. BMI, 41.3%), did identify a larger number of subjects at high risk, for whom treatment would be strongly recommended (25.4% vs. BMI, 11.1%).

Thus, our data confirm that indirect estimates of body composition are useful for groups but are unreliable in individuals [26]. Furthermore, our data also emphasize the importance of discriminating between lean mass and fat mass, and to relate them to body height, in order to obtain a better nutritional assessment.

The use of BMI alone to evaluate overweight and obese individuals leads to undesirable misclassification. Of note, our study sample consisted of people with a sedentary lifestyle, which may predispose to increased adiposity even before an increase in body weight becomes evident; this implies that normal weight subjects can have excessive adiposity.

Thus, there is a need to replace BMI or to supplement it with alternate diagnostic criteria, in particular those that focus on body adiposity, both alone and with reference to its distribution. If confirmed by data from a larger study, our results highlight the need to investigate the clinical consequences of excess body fat in normal weight subjects.

Several studies focused on the relationship existing between BMI and morbidity and mortality [2,3,27]. Unfortunately, to date, there have been few studies that have focused on the relationship between %BF and morbidity and mortality; besides, these studies were restricted to particular ethnic groups [14,16,28-31]. Thus, exact %BF cut-offs have not yet been determined to use clinically to evaluate an individual's health.

Since %BF has important clinical consequences, and the costs to treat and the drop-out rate among "overfat subjects" are high, it is important to establish exact and unambiguous guidelines. In particular, %BF cut-offs should be defined that can be used in addition to BMI and waist circumference values already published in flow-charts for the diagnosis and treatment of subjects.

## **Conclusion**

The use of BMI alone to identify overweight and obese individuals may lead to an undesirable misclassification compared to an assessment based on body composition. Population-specific data on the relationship between body composition, morbidity, and mortality are needed to improve the diagnosis and treatment of at-risk individuals.

### **Competing interest**

The authors declare that they have no competing interest.

### **Authors' contribution**

OC: conception and design of the study; generation, collection and assembly of data; interpretation of data; drafting of the manuscript

SV: analysis and interpretation of data

GP: conception and design of the study; generation, collection and assembly of data

CT: conception and design of the study

AT: conception and design of the study; generation, collection and assembly of data; drafting of the manuscript

All authors read and approved the final manuscript.

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## Appendices

*Appendix 1:* Body fat cut-offs proposed by Gallagher et al. for Caucasians [13]:

Age and BMI	Body fat percentage (%)		
	Men	Women	
20-39 y	18.5 kg/m <sup>2</sup>	8	21
	25 kg/m <sup>2</sup>	21	33
	30 kg/m <sup>2</sup>	26	39
40-59 y	18.5 kg/m <sup>2</sup>	11	23
	25 kg/m <sup>2</sup>	23	35
	30 kg/m <sup>2</sup>	29	41
60-79 y	18.5 kg/m <sup>2</sup>	13	25
	25 kg/m <sup>2</sup>	25	38
	30 kg/m <sup>2</sup>	31	43

*Appendix 2:* Thresholds of percentage body fat ranges proposed by Zhu et al. for Caucasians [14]:

BMI (kg/m <sup>2</sup> )	Body Fat percentage (%)	
	Men	Women
18.5	11.0	22.5
25.0	21.2	30.8
30.0	29.1	37.2

*Appendix 3:* Body Fat Mass Index cut-offs proposed by Kyle et al. for healthy Caucasian adults [16]:

BMI (kg/m <sup>2</sup> )	BFMI (kg/m <sup>2</sup> )	
	Men	Women
18.5	1.8	3.9
25.0	5.2	8.2
30.0	8.3	11.8

## Figure legends

*Figure 1: Recommendation to weight loss treatment according to each criterion.*

Percentage of subjects for whom weight loss was recommended, including those for whom it was strongly recommended, based on the different criteria: BMI (Body Mass Index), WC (waist circumference, as an index of abdominal fat content), %BF (total body fat, as percentage body fat), MS (Metabolic Syndrome risk: percentage body fat related to the risk to develop Metabolic Syndrome), BFMI (Body Fat Mass Index)

Table 1: Percentage of agreement within Body Mass Index classes for all adiposity indexes investigated. The grey areas represent the main diagonal of the agreement matrix.

	Classes	<i>Body Mass Index</i>			
		Weight loss not recommended		Weight loss recommended	Weight loss strongly recommended
		underweight	normal weight	overweight	obese
Weight loss not recommended	low				
	<i>total body fat</i>	25.0	3.0	-	-
	<i>Metabolic Syndrome risk</i>	25.0	10.0	-	-
	<i>Body Fat Mass Index</i>	25.0	3.3	-	-
	normal				
	<i>total body fat</i>	75.0	75.8	15.8	-
	<i>Metabolic Syndrome risk</i>	75.0	53.3	6.7	14.3
Weight loss recommended	<i>abdominal fat content</i>	100.0	90.9	31.6	-
	<i>Body Fat Mass Index</i>	75.0	66.7	6.7	-
	increased				
	<i>total body fat</i>	-	15.2	31.6	14.3
	<i>Metabolic Syndrome risk</i>	-	20.0	40.0	-
Weight loss strongly recommended	<i>abdominal fat content</i>	-	9.1	21.1	-
	<i>Body Fat Mass Index</i>	-	30.0	53.3	14.3
	high				
	<i>total body fat</i>	-	6.1	52.6	85.7
	<i>Metabolic Syndrome risk</i>	-	16.7	53.3	85.7
Weight loss strongly recommended	<i>abdominal fat content</i>	-	-	47.4	100.0
	<i>Body Fat Mass Index</i>	-	-	40.0	85.7

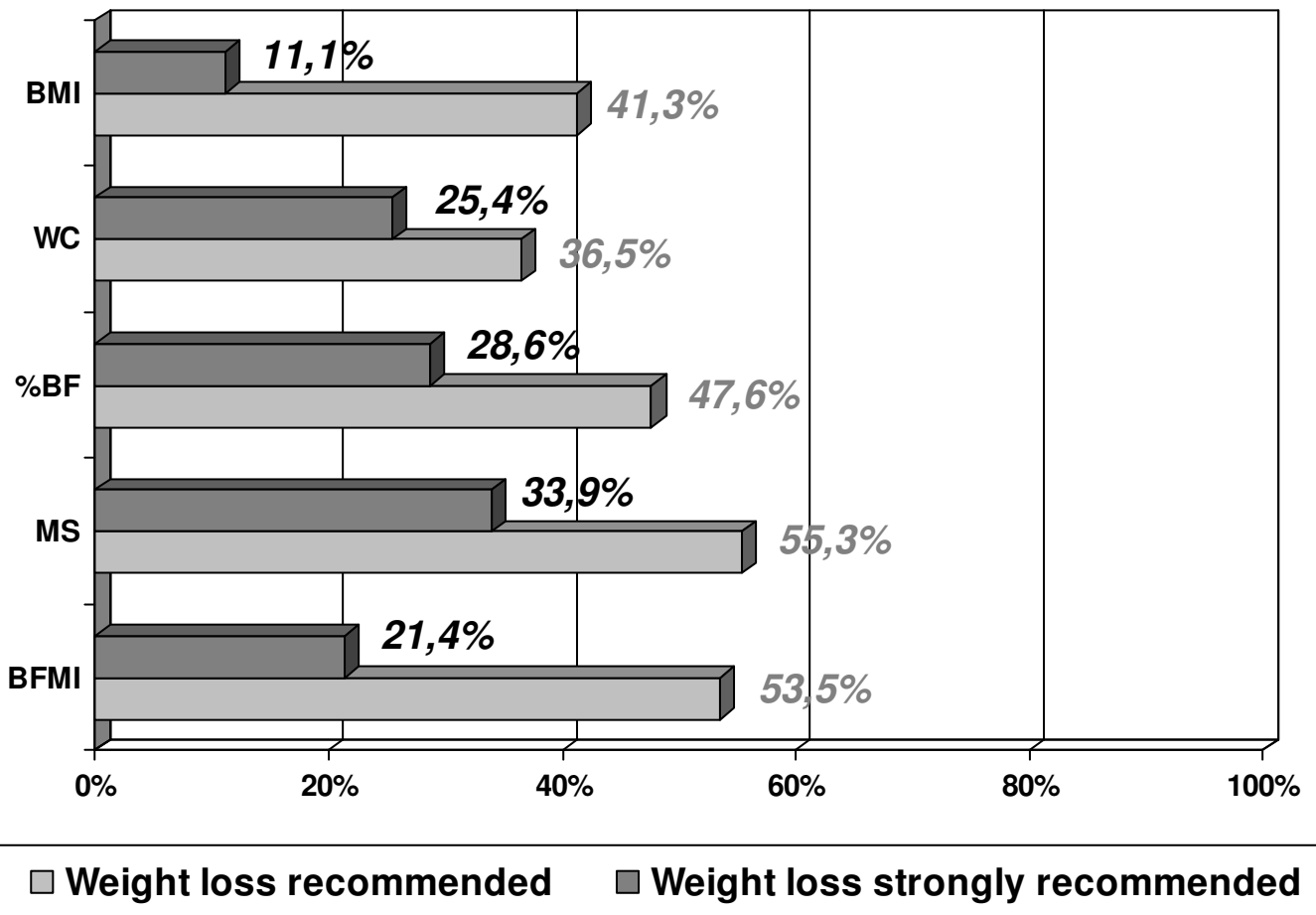


Figure 1