



## Anti-obesity drug therapy in clinical practice: Evidence of a poor prescriptive attitude



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### ABSTRACT

Obesity is a worldwide growing problem for the health care systems and its treatment is strongly recommended. Orlistat, naltrexone/bupropion, and liraglutide are approved for weight loss in Italy in patients with a Body Mass Index (BMI)  $\geq 30$  kg/m<sup>2</sup> or  $\geq 27$  kg/m<sup>2</sup> with concomitant diseases. However, the prescription of these drugs is significantly low worldwide. General practitioners (GPs) play a key role in the early diagnosis and appropriate management of obesity. The aim of the study was to investigate the management of obesity and the prescriptive attitude of anti-obesity drugs in a general practice setting.

All patients registered in lists of 8 GPs with a recorded diagnosis of obesity or BMI values  $\geq 30$  kg/m<sup>2</sup> in the period 2017–2018, were recruited. A descriptive analysis of demographic and clinical characteristic was carried out. The Spearman's correlation rank test was applied to identify correlations between BMI and all the variables of interest.

Among 1301 obese patients, only 66.1 % had been diagnosed and 29.4 % had no registered BMI value. Patients with recorded BMI, were overweight (7.8 %) or in the obesity class I (38.8 %), class II (14.1 %), and class III (7.1 %), respectively.

The obese patients (class 1–3) were older [66 (55–76) vs 49 (32–59);  $p < 0.01$ ], and had more concurrent diseases [5 (3–8) vs 4 (2–6);  $p < 0.01$ ] than patients who reached a BMI  $< 30$  Kg/m<sup>2</sup>. Moreover, most of obese were high cardiovascular risk (HCVR) patients (67.0 % vs 31.9 %;  $p < 0.01$ ). The BMI was directly related to age ( $r_s$  0.14;  $p < 0.01$ ), diabetes ( $r_s$  0.19;  $p < 0.01$ ), hypertension ( $r_s$  0.14;  $p < 0.01$ ), heart failure ( $r_s$  0.09;  $p < 0.01$ ), HCVR ( $r_s$  0.12;  $p < 0.01$ ) and number of comorbidities ( $r_s$  0.08;  $p = 0.01$ ). No prescriptions of orlistat or naltrexone/bupropion were found. Liraglutide was prescribed only in 7 patients because of the concomitant presence of diabetes.

Our results suggest a low adherence to guide line recommendations for obesity management and confirm an under-prescription of anti-obesity drugs in Italy.

### 1. Introduction

Obesity represents one of the most important and challenging health issues across the globe. Epidemiologists pointed out that, by 2025, the worldwide prevalence of obesity will reach 18 % in the male population and 21 % in the female population, with 6% of men and 9% of women presenting a body mass index (BMI) higher than 40 kg/m<sup>2</sup> [1]. The

World Obesity Federation defined obesity as a chronic disease with relapsing characteristics [2]. Indeed, the dramatic increase in obesity will also boost the prevalence of metabolic syndrome and type 2 diabetes and will cause a dramatic rise in the health-care expenditure [3,4]. Obesity also plays a key role in worsening high and very high cardiovascular risk [5]; therefore, fighting against the dramatic spread of obesity is of paramount importance.

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The management of obesity is a complex procedure: change of the lifestyle of patients is the fundamental first step in the weight-loss programs. However, the efficacy of this intervention is very weak, producing a decrease in body weight of only 3–10 %, that is also accompanied by an high rate of weight regain [6]. The reason for the poor efficacy of healthy lifestyle choices mainly stems in the priming of complex biological and hormonal counter-regulation mechanisms sustaining the regain of weight. The main counter-regulation processes are: a decrease in the energy expenditure [7]; modification in the central nervous system regulation of satiety and hunger that reprograms periodical increases in food intake [8]; activation of molecular events that augment insulin resistance, the number of adipocyte and facilitate fat accumulation. Interestingly, it has been suggested that the counter-regulatory mechanisms are long lasting and often not reversible [9–11]. In light of the poor results obtained with the implementation of healthy lifestyle programs, the attention has been focused on the use of complementary therapeutic strategies such as bariatric surgery and pharmacotherapy that may provide a long-lasting weight loss effect. Pharmacotherapy is recommended in patients with a BMI greater than 30 kg/m<sup>2</sup> or greater than 27 kg/m<sup>2</sup> with concomitant diseases [12,13]. It must be also considered that because of the obesity epidemic, it is necessary to apply various therapies (nutritional, cognitive-behavioral, pharmacological and surgical), differently combined in each patient. Indeed, drug therapy aims not so much to increase weight loss but to reduce the risk of developing pathologies related to an increase in cardiovascular risk and to allow a greater number of obese patients to achieve and maintain their outcomes. In addition, it should be emphasized that during an anti-obesity drug therapy, patients must be actively engaged in a lifestyle change program, capable of providing the strategies and tools necessary to achieve a significant loss of weight and to keep the weight as constant as possible over time. However, while the prescription rate of drugs to treat metabolic diseases is in adherence to the accepted guidelines, weight loss drugs prescription rate to manage obesity is significantly low, at least in US [14–16].

Recent surveys showed that obesity affects more than 10 % of adults and about 30 % of adolescents in Italy [17–19]. Orlistat, liraglutide and naltrexone/bupropion are approved in Italy for the obesity treatment, but anti-obesity drug utilization and prescription data are still lacking. The aim of the study was to evaluate anti-obesity drugs prescription and obesity management in a general practice setting.

## 2. Materials and methods

### 2.1. Study design and data collection

An observational retrospective study was carried out at the Department of Clinical and Experimental Medicine of the University of Messina in collaboration with 8 general practitioners (GPs) in Sicily. All patients ( $\geq 18$  years) with a recorded diagnosis of obesity, or with at least one BMI (kg/m<sup>2</sup>)  $\geq 30$  kg/m<sup>2</sup>, were recruited during the 2017–2018 period.

Demographic and clinical characteristics including age, sex, laboratory tests, comorbidities, drugs prescriptions and their indication of use were collected in a specific database. Drugs were classified according to the Anatomical Therapeutic Chemical (ATC) classification system. Concomitant diseases were coded according to the International Classification of Diseases 9th revision (ICD 9). Obese patients were grouped into 5 obesity classes based on BMI values, according to accepted guidelines [12]:

- Normal-weight, BMI values  $< 25.0$  kg/m<sup>2</sup>;
- Overweight, BMI values between 25.0 kg/m<sup>2</sup> and 29.9 kg/m<sup>2</sup>;
- Class I obesity, BMI values between 30.0 kg/m<sup>2</sup> and 34.9 kg/m<sup>2</sup>;
- Class II obesity, BMI values between 35.0 kg/m<sup>2</sup> and 39.9 kg/m<sup>2</sup>;
- Class III obesity or extreme obesity, BMI values  $\geq 40.0$  kg/m<sup>2</sup>.

High cardiovascular risk (HCVR) patients were identified, according to the latest guidelines of European Cardiology Society [20], if at least one of the following conditions were found: familial dyslipidemia; diabetes plus complications; atherosclerosis; ischemic heart diseases; cerebrovascular disease; patients with at least one recorded value of low density lipoprotein (LDL)  $\geq 190$  mg / dL or total cholesterol  $\geq 310$  mg / dL. In addition, the number of HCVR patients who reached the LDL target (LDL  $< 70$  mg / dL) were assessed.

Patients with BMI  $> 30.0$  kg/m<sup>2</sup> or BMI  $> 27$  kg/m<sup>2</sup> with obesity-related concomitant diseases (obstructive sleep apnea, hyperlipidemia, hypertension, diabetes) were considered available to anti-obesity drugs treatment.

A patient encrypted code was used to maintain anonymity. The study has been carried out in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki). In Italy, observational retrospective studies based on clinical records do not require approval by ethics committee. However, this project has been submitted to the Ethics Committee of Messina University Hospital according to the legal requirements concerning observational studies and received the relative acknowledgment number (n°. 10,280).

In addition, the IMS, IQVIA database was used to analyze the consumption of drugs currently approved by the European Medicines Agency (EMA) for the treatment of obesity (orlistat, liraglutide, naltrexone/bupropion) from 01/09/2016 to 31/08/2018 in Italy and in Sicily.

### 2.2. Statistical analysis

A descriptive analysis was carried out to assess demographic and clinical characteristics of patients, stratified by obesity classes.

Absolute and relative frequencies with 95 % Confidence Interval (95 % CI) were evaluated for the categorical variables, while medians with interquartile range (Q1-Q3) were calculated for continuous variables. Drug consumption in Italy and in Sicily was evaluated as defined daily dose (DDD) per 1,000,000 inhabitants per die together with 95 % Confidence Interval. The Kolmogorov–Smirnov test for normality was performed to evaluate normal distribution. Since some of the numerical variables were not normally distributed, a non-parametric approach was used. The Mann–Whitney *U* test for independent sample was applied for continuous variables and two-tailed Pearson chi-squared test for categorical variables. The Spearman's correlation rank test was applied to identify associations between BMI and all the variables of interest. A *p* value  $< 0.05$  was considered statistically significant. Statistical analysis was performed with SPSS version 23.0 (IBM Corp., SPSS Statistics).

## 3. Results

A total of 1301 (10.6 %) patients were included in the study, within a population of 12,388 people registered in the lists of 8 GPs.

Patients with a diagnosis of obesity were 860 (66.1 %), while in 441 (33.9 %) at least one value of BMI  $\geq 30.0$  kg/m<sup>2</sup> was recorded during the two-year study period, without any related diagnosis of obesity. Patients were classified as follows: normal-weight 36 (2.8 %) patients, overweight 102 (7.8 %), class I obesity 505 (38.8 %), class II obesity 183 (14.1 %), class III obesity 93 (7.1 %). BMI value was not available on file in 382 (29.4 %) patients diagnosed with obesity in the 2 years of study. Smoking status or alcohol consumption were never recorded for most of the obese patients (68.6 % and 67.4 %, respectively).

The percentage of male obese patients (45.8 % vs 29.0 %; *p*  $< 0.01$ ) was higher than patients with a BMI  $< 30$  Kg/m<sup>2</sup>. Obese patients (class1–3) were older [66 (55–76) vs 49 (32–59); *p*  $< 0.01$ ], had more concurrent diseases [5 (3–8) vs 4 (2–6); *p*  $< 0.01$ ], and were more affected by hypertension (77.1 % vs 44.2 %; *p*  $< 0.01$ ), dyslipidemia (61.2 % vs 42.0 %; *p*  $< 0.01$ ), arthritis (51.7 % vs 40.6 %; *p* = 0.02), diabetes (46.7 % vs 12.3 %; *p*  $< 0.01$ ), cerebrovascular

**Table 1**  
Characteristics of obese patients stratified by BMI classes.

BMI (kg/m <sup>2</sup> )	Obesity						Total
	Normal weight <sup>1</sup> ( < 25.0)	Overweight 25.0–29.9)	Class I (30.0–34.9)	Class II (35.0–39.9)	Class III (≥ 40.0)	Not available BMI <sup>2</sup>	
Number of patients	36(%)	102 (%)	505 (%)	183 (%)	93 (%)	382 (%)	1301 (%)
Age [median–Q <sub>1</sub> –Q <sub>3</sub> ]	38 (30–52)	52 (36–63)	67 (57–78)	59 (47–73)	61 (51–73)	49 (35–61)	59 (45–71)
Sex (M)	4 (11,1)	36 (35,3)	251 (49,7)	76 (41,5)	31 (33,3)	119 (31,2)	517 (39,7)
Number of comorbidities [median–Q <sub>1</sub> –Q <sub>3</sub> ]	4 (3–5)	4 (2–7)	5 (3–8)	5 (3–7)	6 (4–8)	4 (2–7)	5 (3–7)
HCVr	7 (19,4)	37 (36,3)	348 (68,9)	114 (62,3)	61 (65,6)	141 (36,9)	708 (54,4)
Comorbidities, n (%)							
Hypertension	6 (16,7)	55 (53,9)	398 (78,8)	130 (71,0)	74 (79,6)	179 (46,9)	842 (64,7)
Dyslipidaemia	9 (25,0)	49 (48,0)	325 (64,4)	103 (56,3)	50 (53,8)	125 (32,7)	661 (50,8)
Arthritis and arthrosis	12 (33,3)	44 (43,1)	267 (52,9)	90 (49,2)	47 (50,5)	146 (38,2)	606 (46,6)
Chronic pulmonary diseases	20 (55,6)	41 (40,2)	223 (44,2)	91 (49,7)	49 (52,7)	171 (44,8)	595 (45,7)
Psychiatric disease	20 (55,6)	51 (50,0)	192 (38,0)	75 (41,0)	38 (40,9)	179 (46,9)	555 (42,7)
Diabetes Mellitus	1 (2,8)	16 (15,7)	227 (45,0)	83 (45,4)	55 (59,1)	77 (20,2)	459 (35,3)
Osteoporosis	5 (13,9)	32 (31,4)	167 (33,1)	52 (28,4)	23 (24,7)	83 (21,7)	362 (27,8)
Cerebrovascular disease	3 (8,3)	22 (21,6)	172 (34,1)	40 (21,9)	17 (18,3)	67 (17,5)	321 (24,7)
Atherosclerosis	1 (2,8)	7 (6,9)	99 (19,6)	27 (14,8)	19 (20,4)	37 (9,7)	190 (14,6)
Ischemic heart disease	2 (5,6)	8 (7,8)	95 (18,8)	28 (15,3)	21 (22,6)	26 (6,8)	180 (13,8)
CKD	0 (0,0)	5 (4,9)	82 (16,2)	22 (12,0)	11 (11,8)	20 (5,2)	140 (10,8)
Gout and metabolism disorders	1 (2,8)	9 (8,8)	58 (11,5)	12 (6,6)	10 (10,8)	21 (5,5)	111 (8,5)
Malignant neoplasm	1 (2,8)	3 (2,9)	47 (9,3)	18 (9,8)	7 (7,5)	25 (6,5)	101 (7,8)
Heart failure	1 (2,8)	0 (0,0)	41 (8,1)	14 (7,7)	9 (9,7)	8 (2,1)	73 (5,6)
Periodontitis	1 (2,8)	2 (2,0)	5 (1,0)	5 (2,7)	–	2 (0,5)	15 (1,2)

BMI, body mass index; Q<sub>1</sub>, first quartile; Q<sub>3</sub>, third quartile; HCVr; high cardiovascular risk; CKD, chronic kidney disease.

<sup>1</sup> Patients with a reported diagnosis of obesity and the last BMI value under 25.

<sup>2</sup> Patients with a reported diagnosis of obesity and without any BMI value reported during the study period.

diseases (29.3 % vs 18.1 %;  $p = 0.01$ ), atherosclerosis (18.6 % vs 5.8 %;  $p < 0.01$ ), ischemic heart diseases (18.4 % vs 7.2 %;  $p < 0.01$ ), chronic kidney diseases (14.7 % vs 3.6 %;  $p < 0.01$ ), heart failure (8.2 % vs 0.7 %;  $p < 0.01$ ) than patients who have reached a BMI < 30 Kg/m<sup>2</sup>. Moreover, more than half of obese were high cardiovascular risk patients (67.0 % vs 31.9 %;  $p < 0.01$ ).

The clinical and demographic characteristics of patients, stratified by BMI classes, are shown in Table 1. Diagnosis of periodontitis was recorded only in 15 (1.2 %) patients.

Among high cardiovascular risk patients (54.4 %), at least 68.1 % of them did not reach the LDL target (LDL < 70 mg / dL) (Table 2).

BMI was directly related to age ( $r_s$  0.14;  $p < 0.01$ ), diabetes ( $r_s$  0.19;  $p < 0.01$ ), hypertension ( $r_s$  0.14;  $p < 0.01$ ), heart failure ( $r_s$  0.09;  $p < 0.01$ ), HCVr ( $r_s$  0.12;  $p < 0.01$ ) and number of comorbidities ( $r_s$  0.08;  $p = 0.01$ ).

Patients that could be eligible for the treatment with anti-obesity drugs were 830 (63.8 %); among them 781 had a BMI ≥ 30.0 kg/m<sup>2</sup> and 49 had a BMI between 27.0 kg/m<sup>2</sup> and 29.9 kg/m<sup>2</sup> with at least one of the following comorbidities: hypertension, diabetes, sleep apnea, dyslipidemia.

No prescription of orlistat or naltrexone/bupropion was recorded. Liraglutide (n = 7), metformin (n = 278), dulaglutide (n = 12) and gliflozin (n = 7) were prescribed because of the concomitant presence of diabetes. Cholesterol-lowering drugs were prescribed only in 174

(45.1 %) of HCVr patients out of LDL target, and in 47 (62.7 %) patients in LDL target.

The overall consumption of anti-obesity drugs was 157.0 (153.8–160.2) DDD/1,000,000 inhabitants/die in Italy. In Sicily, it was 137.3 (127.0–155.5) DDD/1,000,000 inhabitants/die, significantly lower than 158.8 (155.5–162.2) DDD/1,000,000 inhabitants/die of other Italian regions ( $p = 0.0002$ ). The most used weight lowering drug was orlistat followed by liraglutide and naltrexone/bupropion. The use of Orlistat in Sicily was significantly lower than in the other Italian regions while no differences were observed concerning the liraglutide or naltrexone/bupropion consumption (Fig. 1).

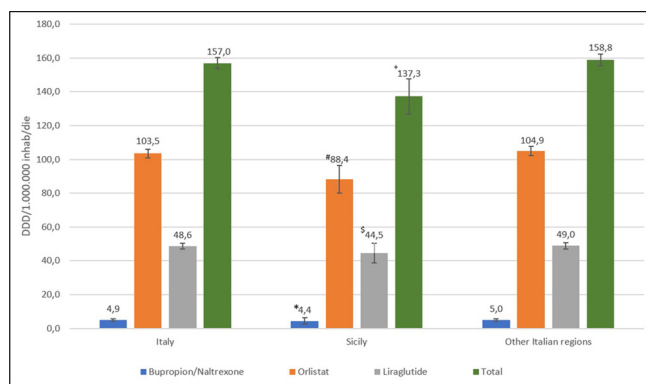
#### 4. Discussion

The management of obesity is theoretically easy to accomplish, but practically hard to implement in obese patients. Interventions such as weight loss diets and/or programs that increase physical activity, produce a not durable reduction in weight loss, with an high probability of weight regain [21]. On the other hand, the use of bariatric surgery has been proven to efficiently cause a dramatic loss of body weight and to ameliorate insulin resistance, especially within the obese population with concomitant diseases, such as type 2 diabetes and metabolic syndrome [22,23]. However, the invasiveness of the surgical procedures makes this therapeutic intervention at a considerable high risk;

**Table 2**  
LDL target (< 70 mg/dL) in high-cardiovascular risk obese patients, stratified by BMI classes.

	BMI (kg/m <sup>2</sup> )	LDL < 70 mg/dL	LDL ≥ 70 mg/dL	Missing values	Total
Number of patients, n (%)		75 (132%)	386 (681%)	106 (187%)	567
Normal-weight	< 25.0	0 (0,0%)	4 (571%)	3 (429%)	7
Overweight	25–29,9	5 (135%)	23 (622%)	9 (243%)	37
Obesity	≥ 30.0	70 (134%)	359 (686%)	94 (180%)	523
Class I	30.0–34.9	48 (138%)	238 (684%)		348
Class II	35.0–39.9	13 (114%)	76 (667%)		114
Class III	≥ 40.0	9 (148%)	45 (738%)		61

BMI, body mass index; LDL, low density lipoprotein.



**Fig. 1.** Consumption of obesity drugs in Italy, Sicily and other Italian Regions (DDD/1,000,000 inhabitants/die with relative 95 % confidence interval).

Comparison between Sicily vs Other Italian Regions.

Bupropion/Naltrexone \*p-value = 0.5617;

Orlistat #p-value = 0.0005;

Liraglutide \$p-value = 0.1744;

Total weight lowering drugs +p-value = 0.0002.

moreover, it is a very expensive procedure that cannot be reverted. Therefore, bariatric surgery is intended only for patients with extreme obesity, also presenting concomitant diseases such as diabetes and cardiovascular diseases [24].

For obese patients who are not eligible for surgery and who did not adhere to the lifestyle changes (weight loss diets and physical exercise), anti-obesity drugs represent the only rationale therapeutic intervention.

The available and approved pharmacotherapy causes 5–15 % of reduction in body weight [25]. The body weight lowering medicines accomplish their effect by reducing fat absorption (orlistat), suppressing appetite and/or reducing food craving (naltrexone/bupropion) or inducing satiety (liraglutide). These drugs cause a significant reduction in body weight, even if they have side effects that may dampen their use [12,25]. The European Medicines Agency (EMA) requires for the approval of a medicine for obesity treatment, that “efficacy” has to be clearly shown by phase 3 study lasting 1 year in a population of several thousands of patients. To get the authorization for this specific therapeutic indication, the drug must cause a placebo-subtracted decrease in body weight of at least 5% at 1 year or, alternatively, it must be proven that at least 35 % of patients administered with the medicine lost at least 5% of their baseline body weight.

In agreement with the accepted guidelines, pharmacotherapy should be suggested to patients with a BMI  $\geq 30$  kg/m<sup>2</sup> or with a BMI  $\geq 27$  kg/m<sup>2</sup> with obesity-related comorbidities such as obstructive sleep apnea, hyperlipidemia, or hypertension [13,26,27]. These recommendations have been also confirmed by the UK National Institute for Health and Care Excellence guidelines that additionally stated that the drug treatment should be primed by the manifested failure of all the lifestyle intervention to reach the target body weight [28]. However, despite the clear message brought by international guidelines, the prescription of anti-obesity medicines is limited among physicians. Indeed, data on utilization and prescription of anti-obesity drugs are still lacking in Italy. In this study, a preliminary analysis on the pharmaceutical sales of approved pharmacotherapies in Italy was carried out, using IQVIA [29], a database that integrates data science, technology and human health, thus offering to the stakeholders advanced analytics information to help health-care system. The data are useful for statistical or research activities in the field of pharmaco-economics and pharmaco-utilization. Indeed, the Italian Medicines Agency (AIFA) uses those data for the annual report of the “observatory on medicines” (OsMed). As far as drug sale is concerned, the database gives information on the “sell-in” and the “sell-out”, representing either the data flow relative to the purchase and or the outgoing sale of pharmacies in the Italian country, therefore allowing the monitoring of

drugs reimbursed by the National Health System or purchased directly by citizens.

The analyzed data suggested that in the time frame September 2016–August 2018, the consumption of anti-obesity drugs was 157 DDD and 137 DDD per 1,000,000 inhabitants per die in Italy and in the Sicily region, respectively. Since in Italy 10/12 % of people are obese, the use of anti-obesity drugs is less than that expected, although this approach is in agreement with the approach followed in other countries [14,30,31].

As a consequence, a retrospective study was carried out to investigate the anti-obesity prescribing attitude in the context of the “real-world” of the general practice. We found that 830 out of 12,388 patients had a diagnosis of obesity and most of them were eligible for a pharmacotherapy having either a BMI of  $\geq 30$  kg/m<sup>2</sup> or a BMI  $\geq 27$  kg/m<sup>2</sup> with obesity-related comorbidities. Most of the comorbidities were significantly higher in obese than in normal weight patients. In addition, BMI value directly correlates with hypertension, diabetes, heart failure, number of comorbidities, and high risk of cardiovascular diseases. Moreover, the concomitant presence of periodontitis was evaluated. In fact, recent evidence has suggested a close link between the two pathological conditions, mainly explained by a common underlying inflammatory status that may reciprocally influence the outcome of the diseases [32]. However, the reported number of patients with this dental comorbidity was significantly lower than that observed in several large epidemiological studies [33]. This data let us to speculate that GPs are not well trained to focus on this aspect. No BMI value was recorded in 29.4 % of patients, although they were identified as obese during the study period. Moreover, BMI values more than 30 kg/m<sup>2</sup> were recorded in at least one third of patients, without any related diagnosis of obesity. Also smoking status or alcohol consumption were never recorded for most of the obese patients, although both habits might be important to evaluate the risk.

These observations suggest that GPs do not believe that obesity is a condition that deserves attention and they do not acknowledge obesity as a modifiable risk factor. Obese patients are likely considered as a waste of time by GPs and the management of the clinical condition is underestimated, even if patients have high cardiovascular risk and are out of LDL target. The data obtained so far showed that orlistat or the association of naltrexone/bupropion were not prescribed by GPs in the time frame of at least 2 years of the study, in accordance with the data of the anti-obesity drug sales. Specifically, only seven patients received a prescription of liraglutide, due to the concomitant presence of type 2 diabetes. Indeed, several anorectic substances, several dietary supplements (anorectic or fiber-based) and off-label drugs are used for the treatment of obesity. However, these therapeutic alternatives were not available on file and therefore this could represent a limitation of our study. The present data lead us to hypothesize that GPs believe that anti-obesity pharmacotherapy is not useful and appropriate to improve the health status of obese patients. However, this attitude is in disagreement with the guidelines and with the huge amount of data supporting the efficacy and the low rate of adverse effects of approved weight-loss medicines. Additional reasoning might explain the reluctance of GPs to prescribe the anti-obesity drugs. It could be that GPs have concerns on the compliance and adherence to the pharmacotherapy, being obese patients stigmatized as unreliable and unavailable to follow physician's directions and considered as to have less self-discipline. In addition, it could be that GPs believe that an obese subject is personally responsible for his/her clinical condition and that if he/she would reduce the amount of food and increase physical exercise, the problem would be solved. However, this is a wrong judgement call: in fact, they are unaware that obesity is a chronic disease that arises from a disturbance in the energy balance system that is under the tight control of sophisticated and interlinked central and peripheral mechanisms.

In conclusion, whatever it is the barrier to the prescription of anti-obesity drugs, GPs should be trained and advised to accept anti-obesity



medicines. In addition, they should be available and open to discuss the cost-benefit of the drugs to facilitate the understanding and the addressing of the non-prescribing concerns.

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## Declaration of competing interest

The authors declare that there are no conflicts of interest.

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