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Healthcare utilisation and economic impact of non-treated obesity in Italy: findings from a retrospective administrative and clinical database analysis

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ABSTRACT

Objectives: Aim of this study was to investigate the prevalence of obesity in Italy and to examine its resource consumption and economic impact on the Italian healthcare system.

Design: Retrospective, observational, real-life study

Setting: Data from three Italian local health units from northern, central, and southern Italy.

Participants: 20,159 adult subjects with at least one documented body mass index (BMI) measurement from three local health units. Subjects with BMI ≥30 kg/m^2 were defined as obese.

Interventions: Information retrieved from the databases included primary care data, medical prescriptions, specialist consultations, and hospital discharge records for the period 2009–2013. Costs associated with these data were also calculated. Data are presented for two time periods (1 year after the BMI measurement and at the end of the study).

Primary and secondary outcome measures: The primary outcome was health resources consumption and the associated economic impact on the Italian NHS. Secondary outcome measures were the prevalence and characteristics of subjects in relationship with the BMI category.

Results: The prevalence of obesity was 22.2% (N=4,471) and increased with age. At the 1-year observation period, obese subjects who did not receive treatment for

their obesity experienced longer durations of hospitalisation (median length: 5 vs 3 days), used more prescription drugs (75.0% vs 57.2%), required more specialised outpatient healthcare (mean number: 5.3 vs 4.4), and were associated with greater costs, primarily owing to prescription drugs and hospital admissions (mean annual cost per year per patient: €460.6 vs €290.9 for drug prescriptions, €422.7 vs €279.2 for hospitalisations, and €283.2 vs €251.7 for outpatient care), compared with normal-weight subjects. Similar findings were observed for the period up to data cut-off (mean follow-up of 2.7 years).

Conclusions: Untreated obesity has a significant economic impact on the Italian healthcare system, highlighting the need to raise awareness and proactively treat obese subjects.

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Strengths and limitations of this study

- Large study on more than 20,000 subjects
- Real-world data coming from local health units
- Data retrieved from different geographical areas
- Direct evaluation of costs by integrating multiple data sources
- Limitations due to the retrospective nature of the study

INTRODUCTION

Obesity is now widely regarded as a global epidemic; worldwide, obesity rates have more than doubled since 1980.[1] According to the World Health Organization (WHO), more than 1·9 billion adults were overweight in 2014. Of these, over 600 million (~13% of the world's population) were obese, defined as having a body mass index (BMI) of ≥30 kg/m^2.[1] Obesity is a major risk factor for various chronic diseases, particularly if it remains untreated. Globally, 44% of diabetes, 23% of ischaemic heart disease, and 7–41% of certain cancers are attributable to being overweight or obese.[1] Obesity-associated mortality rates are also alarmingly high, with at least 2.8 million deaths each year resulting from being overweight or obese.[1] Obesity was once considered to be an issue associated with high-income countries only; however, its prevalence is now also increasing in low- and middle-income countries.[2]

In Italy, WHO reports from 2014 showed that the prevalence of obesity was 20.4% among individuals aged ≥18 years.[3] Childhood obesity is a particular concern in the Italian population.[4-6] As in other European countries, there are clear socioeconomic trends: those with a low educational status, from a low-income household, and from the southern regions of Italy are at higher risk of becoming obese.[4 7-13] Possible reasons for these trends are the decreased consumption of a Mediterranean diet and a more sedentary lifestyle.

Previous studies have shown that obesity and its associated comorbidities have a considerable economic impact on healthcare systems, primarily because of high costs for medication and hospitalisations.[14-17] However, in those studies, costs were only estimated indirectly. Alternatively, we report here on the findings from a study of

over 20,000 adults that investigated the prevalence of, and direct costs associated with, untreated obesity in three distinct regions of Italy – which differ in terms of geography and nutritional traditions – in order to understand the healthcare utilisation and economic impact of obesity on the Italian national healthcare system (NHS).

METHODS

Study design and population

This was a retrospective, observational, real-life study. To be eligible, individuals were required to be aged ≥18 years and to have at least one recorded BMI measurement between 1 January 2009 and 31 December 2012. The first recorded BMI was set as the index date. Eligible subjects were identified from registries at three Italian local health units that represent the primary Italian geographical areas: Bergamo, Lombardy (northern Italy), Grosseto, Tuscany (central Italy), and Naples, Campania (southern Italy).

BMI was classified as follows: underweight, <18 kg/m^2; normal weight, ≥18 to <25 kg/m^2; overweight, ≥25 to <30 kg/m^2; obese, ≥30 kg/m^2. Obesity was further classified as mild, moderate, and severe based on BMI levels of ≥30 to <35 kg/m^2, ≥35 to <40 kg/m^2, and ≥40 kg/m^2, respectively.[18]

An anonymous data file is routinely used by regional health authorities for epidemiological and administrative purposes. No identifiers related to subjects were provided to the researchers. In accordance with Italian law regarding data confidentiality,[19] the ethics committee of each local health units was notified about

the study. Neither ethics committee approval nor informed consent was required for using encrypted retrospective information.

Study objective

The primary objective of the study was to estimate health resource consumption and the economic impact of obesity on the Italian NHS. The secondary objective was to assess the prevalence and characteristics of subjects in relationship with the BMI category.

Data sources and analysis

Primary care data for each subject were retrospectively collected from the Health Search Database of the Società Italiana di Medicina Generale (Italian Society of General Medicine) for the period 2009–2013. Using the numeric code assigned to each citizen by the local health units as a unique identifier, this database was linked to the following databases: i) Medications Prescription Database, which includes anatomical–therapeutic–chemical (ATC) codes; ii) Hospital Discharge Database, which includes dates of hospital admission and discharge, as well as discharge diagnosis codes according to the *International Classification of Diseases Ninth Revision, Clinical Modification* (ICD-9-CM); iii) Laboratory Tests and Specialist Visits Database; iv) Mortality Database, from which data on mortality, but not cause of death, were collected; and v) Beneficiaries' Database, from which data regarding date of birth, sex, and place of residence were collected.

Data on drug use, hospitalisations, use of specialist services, and treatment costs were evaluated from the index date until 31 December 2013, corresponding to a

period of at least 12 months and up to 5 years (the date of last enrolment was 31 December 2012). Specialist services encompassed all specialised outpatient healthcare, including diagnostic and laboratory tests (such as X-ray, ultrasound, magnetic resonance imaging, blood, and urinary tests), and consultations by specialist healthcare providers. Costs assigned to medical resources were based on publicly available market prices. Data were presented according to BMI class for the normal-weight, overweight, and obese (total and mild, moderate, and severe) cohorts for two time periods: at 1 year following the index date (1-year observation period) and at the time of data cut-off (31 December 2013). Underweight subjects were included for the prevalence analysis only.

Statistical analysis

To test normality assumption of data distribution, the Skewness-Kurtosis test was used. Continuous variables were reported as mean and standard deviation or median and interquartile range, as appropriate, and compared with analysis of variance (ANOVA) test, whereas categorical variables were expressed as numbers and percentages, and compared with the χ^2 test. Analyses were performed stratified for BMI groups. P-value ≤0.05 were considered statistically significant. All statistical analyses were conducted using Stata software version 12·0 (Stat Corp LP, College Station, TX, USA), data management will be carried out using Microsoft SQL Server 2012.

Role of funding source

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RESULTS

Subjects

Overall, 20,159 adults were included in the study. Table 1 shows the characteristics of subjects who were classified as underweight, normal weight, overweight, and obese at the index date. The prevalence of obesity was 22.2% (N=4471); of these, 3253 (72.8%) were classified as mildly obese, 898 (20.1%) as moderately obese, and 320 (7.2%) as severely obese. The mean length of follow-up was 2.6, 2.7, and 2.8 years for the normal-weight, overweight, and obese groups, respectively (p=NS). Within the obese group, the mean length of follow-up was 2.8 years across each of the mild-, moderate-, and severe-obesity cohorts; 1.1% of subjects died at 1 year following the index date (normal weight 1.1%, overweight 1.2%, obese 1.1%; p=NS).

Table 1. Baseline characteristics and demographics at the index date

	Weight				Total
	Under (BMI <18)	Normal (BMI ≥18 to <25)	Over (BMI ≥25 to <30)	Obese (BMI ≥30)	
Patients, n (%)	282 (1·4)	7861 (39·0)	7545 (37·4)	4471 (22·2)	20,159 (100)
Males:females, n:n	42:240	3002:4859	3996:3549	2048:2423	9088:11,071
Mean age ± SD, years	44.4 ± 21.0*	53.4 ± 17.3†	59.3 ± 15.2‡	58.1 ± 15.1	56.5 ± 16.4

SD, standard deviation

*p<0.001 vs normal weight, overweight, and obese; †p<0.001 vs overweight and obese; ‡p<0.001 vs obese

Prevalence of obesity by age

The proportion of subjects who were overweight or obese increased with age, while it decreased for normal weight subjects (p<0.001) (table 2). Among subjects aged >30 years, more than half were classified as overweight or obese (table 2). In particular, among subjects aged between 30 and 64 years, 36.1 and 22.6% were overweight and obese, respectively; among subjects aged 65+ years, 44 and 23.6% were overweight and obese, respectively (table 2).

Table 2. Proportions of patients classified as being of normal weight, overweight, and obese, stratified by age at the index date

Prevalence	Normal weight	Over weight	Obese	Total
18–29 years, n (%)	786 (63.3)*	267 (21.5)*	189 (15.2)*	1242 (100.0)
30–64 years, n (%)	4801 (41.3)†	4195 (36.1)†	2627 (22.6)†	11623 (100.0)
65+ years, n (%)	2274 (32.4)	3083 (44.0)	1655 (23.6)	7012 (100.0)
Total	7861	7545	4471	

*p<0.0001 vs 30–64 years and +65 years; †p<0.0001 vs +65 years

Use of prescription medication

In total, 13,060 subjects from the normal weight, overweight and obese groups (65.7%) received at least one prescription drug treatment during the 1-year observation period. 3,353 were obese subjects (75%), 4,495 were normal-weight subjects (57.2%) and 5,212 were overweight subjects (69.1%). These differences were significant ($p<0.0001$ among groups); 14,888 (74.9%) subjects had received at least one drug treatment at data cut-off; 3,666 were obese subjects (82%), 5,357 were normal-weight subjects (68.1%) and 5,865 were overweight subjects (77.7%). Again, these differences were significant ($p<0.0001$ among groups). During the 1-year observation period, anti-hypertensive drugs were the most common drug class received (43.5% of subjects); 31.2% of subjects received gastrointestinal drugs, 28.6% received anti-inflammatory drugs, 23.3% received antiplatelet drugs, 17.6% received statins, and 0.7% received antineoplastic drugs. Obese patients received each class of drug more frequently than normal-weight or overweight subjects ($p<0.001$ for all drug classes except antineoplastic among all groups and statins between overweight and obese subjects [p=NS]) (figure 1a). The largest difference in drug use between subjects who were obese and of normal weight was observed for the antidiabetic drug class (301% increase in obese subjects; $p<0.001$). Results were similar for the period up to data cut-off ($p<0.001$ for all drug classes except antineoplastic among all groups and stating between overweight and obese subjects [p=NS]) (figure 1b).

Duration of hospitalisation

In total, 1431 subjects (7.2%) were hospitalised at least once during the 1-year observation period and this increased to 3,231 subjects (16.3%) for the period up to data cut-off. In normal-weight, overweight, and obese subjects, hospitalisation rates were 7.4%, 8.7%, and 8.8%, respectively, at 1 year, and 19.0%, 23.0%, and 23.8%, respectively, at data cut-off. Obese and overweight subjects had a higher hospitalisation rate in comparison with normal weight individuals (p=0.006 and 0.03, at 1-year follow-up and data cut-off, respectively). In the 1-year observation period, the mean duration of hospitalisation was 3 (interquartile range; IQR 7) days in normal-weight subjects, 4 (IQR 7) days in overweight subjects, and 5 (IQR 8) days in obese subjects (p=NS). Within the group of obese subjects, median duration of hospitalisation was not different among the severe (4.5 [IQR 8] days), mild- (5 [IQR 8] days) and moderate-obese (4.5 [IQR 9.5] days) groups. The most common reasons for hospitalisation in the mild- and moderate-obese groups were type 2 diabetes and essential hypertension (not specified; 0.8% each). For severe-obese patients, the most common reasons for hospitalisation were severe obesity and benign essential hypertension (1.6% and 0.9%, respectively). Similarly, the median duration of hospitalisation for the period up to data cut-off did not show significant differences among groups (obese subjects, 5 [IQR 7] days; normal-weight subjects, 3 [IQR 7] days; and overweight subjects 4 [IQR 7] days, respectively; p=NS), as well as among obese subgroups (mild-obesity 4 [IQR 7] days; medium-obesity 5 [IQR 9] days; severe obesity 5 [IQR 7.5] days; p=NS).

Use of specialist services

During the 1-year observation period, an average of 5.3 (± 7.0) specialist services were required overall for obese subjects; the mean number of specialist services required was higher in the moderate-obese group (5.8 ± 9.5) than in the other BMI groups (4.4 ± 5.5, 5.0 ± 7.2, 5.2 ± 6.3, and 5.0 ± 5.8 for normal-weight, overweight, mild-obese, and severe-obese groups, respectively, p<0.001). At the point of data cut-off, the mean number of specialist services required was 18.8 (± 26.8) in the moderate-obese group, compared with 12.6 (± 16.0), 15.8 (± 21.3), 16.6 (± 18.8), and 15.9 (± 18.5) for the normal-weight, overweight, mild-obese, and severe-obese groups, respectively, p<0.001.

Costs

During the observation period, the mean annual healthcare costs per subject was €821.80 for normal-weight group, €1,015.19 for overweight group and €1,166.52 for obese group, respectively. The mean healthcare cost per subject for the period up to data-cut-off was €2,468.27 for normal-weight group, €3,417.81 for overweight group and €3,782.21 for obese group, respectively. Mean healthcare costs during the 1-year observation period were higher in obese than in non-obese subjects (p<0.001), while no differences were observed at data cut-off point (p=NS) (figure 2a and figure 2b). During the 1-year observation period, the highest mean annual costs per individual in the obese group were associated with drug prescriptions (€461), followed by hospitalisation costs (€423) and specialised outpatient services (€283). Subjects with moderate obesity generated higher costs than the mild- and severe-obese groups, primarily owing to higher hospitalisation costs (p<0.01). Compared

with normal-weight controls over 1 year, costs were higher by 23.5% for overweight subjects (34.3% when considering drug costs only), 34.8% for patients with mild obesity (47.0% for drug costs only), 70.4% for those with moderate obesity (90.1% for drug costs only), and 33.9% for patients with severe obesity (83.9% for drug costs only) (all values: $p<0.01$). At the point of data cut-off, the mean annual costs in the obese group had increased to €1544,24 for drug prescriptions, €1256,41 for hospitalisation costs, and €981,56 for outpatient services (figure 2b). Similar to the 1-year observation, costs were higher for obese patients in comparison with normal weight controls ($p<0.01$) (figure 2b). Again, patients with moderate obesity generated higher costs, mainly due to outpatient costs ($p<0.05$) (figure 2b).

DISCUSSION

There are still limited data on healthcare resources utilisation for untreated obesity and its economic impact on healthcare systems. We report here on the prevalence and associated costs of obesity in an Italian population of over 20,000 individuals. Our study represents one of the largest European population studies on obesity and provides a real-life assessment of the economic impact of this increasingly prevalent condition. The findings of our study show that obese adults who did not receive treatment for their underlying obesity used more prescription drugs, experienced longer durations of hospitalisation, required more specialised outpatient healthcare and were associated with substantially greater costs compared with normal-weight adults.

Our study directly evaluated the economic impact of comorbidities associated with obesity on the Italian healthcare system by integrating multiple data sources, taking into account the true costs of pharmaceutical treatments, the use of diagnostic and specialist services, and hospitalisations over a period of up to 5 years. Importantly, as a result of the structure of the Italian national healthcare system and the multiple data sources available, the healthcare resources and costs reported in this study are a true and accurate reflection of the real-life costs for each subject. Previous studies have been limited by the fact that they were based on resources used at a single point in time or restricted to a single hospital department. Our study in real-world setting helps to identify the actual consumption of resources by obese patients. However, as with any retrospective observational study, it should be noted that limitations might exist as a result of the variability of professional practice and information bias.

Obese subjects used a wide range of drugs, including antihypertensive, gastrointestinal, anti-inflammatory, antiplatelet, and antidiabetic drugs. Our study showed that obese subjects generally received each class of drug more frequently than normal-weight or overweight subjects, with the exception of antidepressant. This is likely to reflect the various comorbidities that obese subjects commonly experience if their underlying condition remains untreated, such as diabetes and hypertension. Notably, antidiabetic and antihypertensive drugs were used in around twice as many obese as normal-weight subjects. Overall healthcare costs were substantially higher for obese than for non-obese individuals. Prescriptions represented the greatest overall costs, highlighting the economic impact that obesity-related comorbidities have on healthcare systems.

There were also significant costs associated with hospitalisation, particularly for the moderate-obese group; this may be related to the longer mean duration of hospitalisation in these patients compared with severe-obese and non-obese subjects. The relatively short hospital stay observed in the severe-obesity group should be highlighted as this may suggest that many institutions within the Italian healthcare system are not adequately equipped to diagnose and treat morbidly obese subjects, such as radiological instruments not being suitable to host severely obese patients, or a lack of specialists with sufficient experience to prescribe suitable therapies to address the different comorbidities. This could result in these patients being discharged from hospital earlier than should be expected. It is also possible that, as severely obese people are frequently depressed,[20-22] they may refuse to leave home to go to hospital at all, unless they have an acute condition.

The prevalence of obesity reported in this study (22·2%) is in line with the current WHO estimation of the prevalence of obesity in Italy (21·0%),[3] but higher than other estimates (~10%).[7 13] The proportion of subjects who were overweight or obese increased with age, with more than half of adults aged ≥30 years being overweight or obese. Similar findings have previously been reported in Italy;[6] based on data from five surveys conducted between 2006 and 2010, the prevalence ratios for overweight/obesity in individuals aged ≥65 versus 18–24 years were 2·01 in men and 2·65 in women.[7] These data suggest that it may be important to target and educate individuals who are overweight or have mild obesity and are of working age, with the aim of preventing them from becoming more obese later in life.

It is important to raise awareness that the direct treatment of patients who are severely obese would help to reduce the economic impact of the condition on

healthcare systems.[23] The initial costs associated with treatment, such as bariatric surgery, would probably be offset by the subsequent savings made on drug prescriptions, hospitalisation costs, and outpatient care related to the treatment of comorbidities.[24 25] Indeed, a recent meta-analysis, comprising 37,720 patients across 11 studies, showed that bariatric surgery significantly reduces drug use and costs.[26] In addition, the direct treatment of obesity would likely help to reduce the burden on physicians who spend a substantial amount of time treating the comorbidities associated with obesity. The value of preventative strategies for obesity is an important consideration for decision makers, particularly given the increasing concern over the sustainability of the healthcare system and the ageing population. Measures such as advocating the value of a healthy and balanced diet with regular exercise as part of an early obesity prevention strategy are likely to be important.

In conclusion, our data highlight the need to develop public health policies that aim to prevent the development of obesity at an early age and also to proactively and effectively treat severely obese patients, thereby reducing the overall economic burden of this condition.

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CONTRIBUTOR STATEMENT

Chiara Veronesi, Valerio Blini, and Luca Degli Esposti contributed to the design and conduct of the study, data collection and management, analysis and interpretation of the data, and preparation of the manuscript. Annamaria Colao, Marcello Lucchese, Monica D'Adamo, Silvia Savastano, Enrico Facchiano and Paolo Sbraccia contributed to clinical evaluation and data interpretation and investigated all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors critically revised the manuscript for important intellectual content; all authors approved the final version of the manuscript.

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COMPETING INTERESTS

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DATA SHARING

No additional data available.

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FIGURE LEGENDS

Fig 1. Patients exposed to treatment, by BMI category and drug class, during (a) the 1-year observation period and (b) the period up to data cut-off

(a) *p<0.001 vs overweight and obese subjects; †p<0.001 vs obese subjects

(b) *p<0.001 vs overweight and obese subjects; †p<0.001 vs obese subjects

Fig 2. Mean annual costs per surviving individual, by BMI category, during (a) the 1-year observation period and (b) the period up to data cut-off

(a) Overall costs: p<0.001 vs overweight and obese subjects; p<0.01 vs mild and severe obese subjects. Drug costs: p<0.001, p<0.01; Hospitalisation costs: p<0.01, p=NS; Outpatient costs: p<0.01, p=NS

(b) Overall costs: p<0.001 vs overweight and obese subjects; p<0.01 vs mild and severe obese subjects. Drug costs: p<0.001, p=NS; Hospitalisation costs: p<0.001, p=NS; Outpatient costs: p<0.001, p<0.05

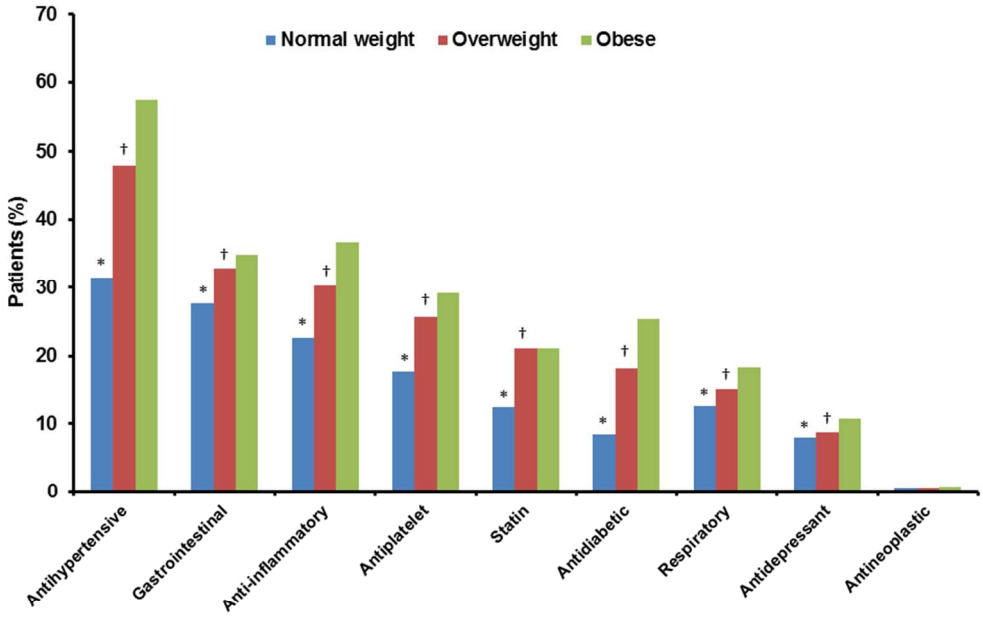

Figure 1a

Patients exposed to treatment, by BMI category and drug class, during (a) the 1-year observation period and (b) the period up to data cut-off ‼ ┼ (a) *p<0.001 vs overweight and obese subjects; †p<0.001 vs obese subjects

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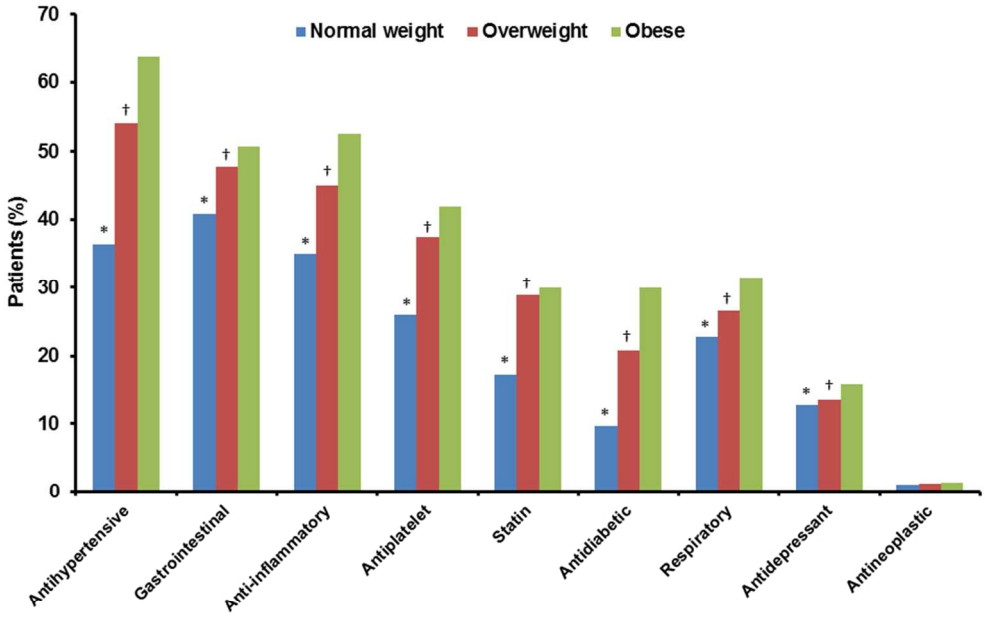

Figure 1b

Patients exposed to treatment, by BMI category and drug class, during (a) the 1-year observation period and (b) the period up to data cut-off ‼ ┼ (b) *p<0.001 vs overweight and obese subjects; †p<0.001 vs obese subjects

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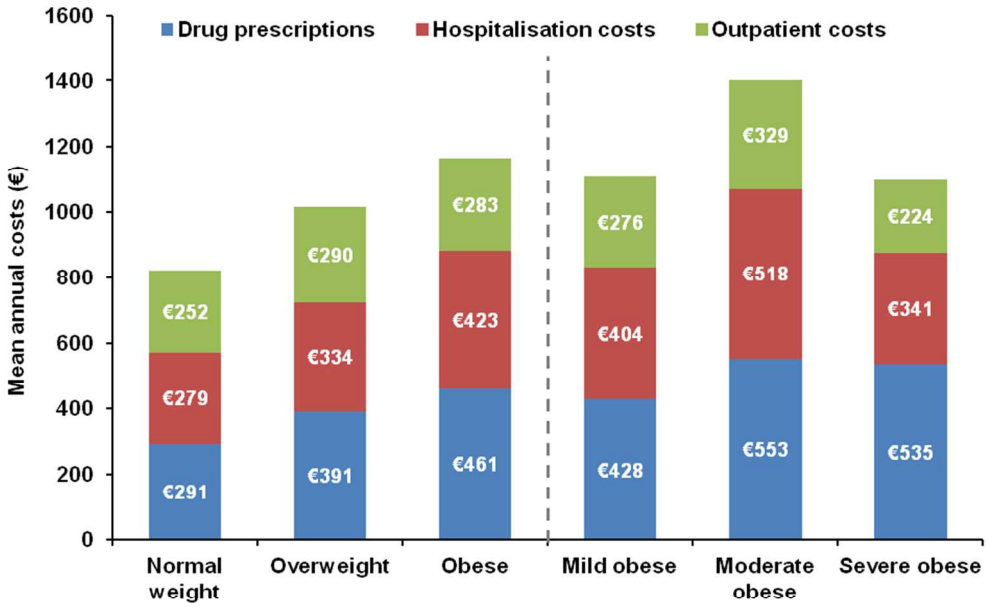

Figure 2a

Mean annual costs per surviving individual, by BMI category, during (a) the 1-year observation period and (b) the period up to data cut-off (a) Overall costs: p<0.001 vs overweight and obese subjects; p<0.01 vs mild and severe obese subjects. Drug costs: p<0.001, p<0.01; Hospitalisation costs: p<0.01, p=NS; Outpatient costs: p<0.01, p=NS

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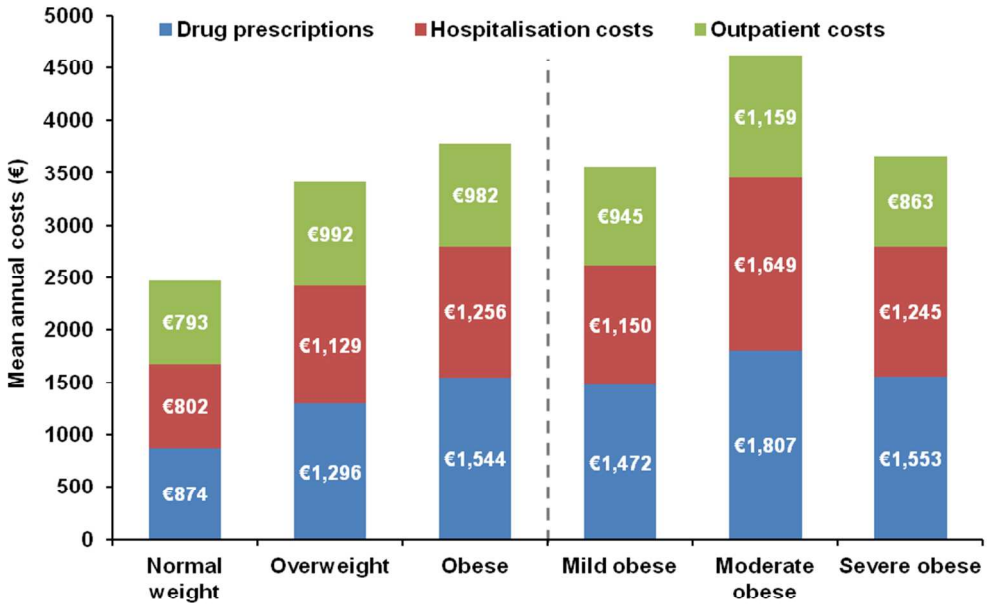

Figure 2b

Mean annual costs per surviving individual, by BMI category, during (a) the 1-year observation period and (b) the period up to data cut-off (b) Overall costs: p<0.001 vs overweight and obese subjects; p<0.01 vs mild and severe obese subjects. Drug costs: p<0.001, p=NS; Hospitalisation costs: p<0.001, p=NS; Outpatient costs: p<0.001, p<0.05

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Healthcare utilisation and economic impact of non-treated obesity in Italy: findings from a retrospective administrative and clinical database analysis

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Healthcare utilisation and economic impact of non-treated obesity in Italy: findings from a retrospective administrative and clinical database analysis

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ABSTRACT

Objectives: Investigate the prevalence of obesity in Italy and examine its resource consumption and economic impact on the Italian healthcare system.

Design: Retrospective, observational, real-life study

Setting: Data from three health units from Northern (Bergamo, Lombardy), Central (Grosseto, Tuscany), and Southern (Naples, Campania) Italy.

Participants: All patients aged ≥18 years with at least one recorded BMI measurement between January 1st 2009 and December 31st 2012 were included.

Interventions: Information retrieved from the databases included primary care data, medical prescriptions, specialist consultations, and hospital discharge records from 2009–2013. Costs associated with these data were also calculated. Data are presented for two time periods (1 year after BMI measurement and study end).

Primary and secondary outcome measures: Primary – to estimate health resources consumption and the associated economic impact on the Italian NHS. Secondary – the prevalence and characteristics of subjects by BMI category.

Results: 20,159 adult subjects with at least one documented BMI measurement. Subjects with BMI ≥30 kg/m^2 were defined as obese. The prevalence of obesity was 22.2% (N=4,471) and increased with age. At the 1-year observation period, obese subjects who did not receive treatment for their obesity experienced longer durations of hospitalisation (median length: 5 vs 3 days), used more prescription drugs (75.0% vs 57.7%), required more specialised outpatient healthcare (mean number: 5.3 vs

4.4), and were associated with greater costs, primarily owing to prescription drugs and hospital admissions (mean annual cost per year per patient: €460.6 vs €288.0 for drug prescriptions, €422.7 vs € 279.2 for hospitalisations, and €283.2 vs €251.7 for outpatient care), compared with normal-weight subjects. Similar findings were observed for the period up to data cut-off (mean follow-up of 2.7 years).

Conclusions: Untreated obesity has a significant economic impact on the Italian healthcare system, highlighting the need to raise awareness and proactively treat obese subjects.

Strengths and limitations of this study

- Large study on more than 20,000 subjects
- Real-world data coming from local health units
- Data retrieved from different geographical areas
- Direct evaluation of costs by integrating multiple data sources
- Limitations due to the retrospective nature of the study

INTRODUCTION

Obesity is now widely regarded as a global epidemic; worldwide, obesity rates have more than doubled since 1980.[1 2] According to the World Health Organization (WHO), more than 1·9 billion adults were overweight in 2014. Of these, over 600 million (~13% of the world's population) were obese, defined as having a body mass index (BMI) of ≥30 kg/m^2.[1] In Italy, WHO reports from 2014 showed that the prevalence of obesity was 20.4% among individuals aged ≥18 years.[3] Obesity is a major risk factor for various chronic diseases, particularly if it remains untreated. Globally, 44% of diabetes, 23% of ischaemic heart disease, and 7–41% of certain cancers are attributable to being overweight or obese.[1] Obesity-associated mortality rates are also alarmingly high, with at least 2.8 million deaths each year resulting from being overweight or obese.[1] Obesity was once considered to be an issue associated with high-income countries only; however, its prevalence is now also increasing in low- and middle-income countries.[4]

Previous studies have shown that obesity and its associated comorbidities have a considerable economic impact on healthcare systems, primarily because of high costs for medication and hospitalisations.[5-8] However, in those studies, costs were only estimated indirectly. In contrast, we report here on the findings from a study of over 20,000 adults that investigated the prevalence of, and direct costs associated with, untreated obesity in three distinct regions of Italy – which differ in terms of geography and nutritional traditions – in order to understand the healthcare utilisation and economic impact of obesity on the Italian national healthcare system (NHS).

METHODS

Study design and population

This was a retrospective, observational, real-life study. To be eligible, individuals were required to be aged ≥18 years and to have at least one recorded BMI measurement between 1 January 2009 and 31 December 2012. The first recorded BMI was set as the index date. Eligible subjects were identified from registries at three Italian local health units that represent the primary Italian geographical areas: Bergamo, Lombardy (northern Italy), Grosseto, Tuscany (central Italy), and Naples, Campania (southern Italy).

BMI was classified as follows: underweight, <18.5 kg/m^2; normal weight, ≥18.5 to <25 kg/m^2; overweight, ≥25 to <30 kg/m^2; obese, ≥30 kg/m^2. Obesity was further classified as grade I, II and III based on BMI levels of ≥30 to <35 kg/m^2, ≥35 to <40 kg/m^2, and ≥40 kg/m^2, respectively.[9]

An anonymous data file is routinely used by regional health authorities for epidemiological and administrative purposes. No identifiers related to subjects were provided to the researchers. In accordance with Italian law regarding data confidentiality,[10] the ethics committee of each local health units was notified about the study. Neither ethics committee approval nor informed consent was required for using encrypted retrospective information.

Study objective

The primary objective of the study was to estimate health resource consumption and the economic impact of obesity on the Italian NHS. The secondary objective was to

assess the prevalence and characteristics of subjects in relationship with the BMI category.

Data sources and analysis

Primary care data for each subject were retrospectively collected from the Health Search Database of the Società Italiana di Medicina Generale (Italian Society of General Medicine) for the period 2009–2013. Using the numeric code assigned to each citizen by the local health units as a unique identifier, this database was linked to the following databases: i) Medications Prescription Database, which includes anatomical–therapeutic–chemical (ATC) codes; ii) Hospital Discharge Database, which includes dates of hospital admission and discharge, as well as discharge diagnosis codes according to the *International Classification of Diseases Ninth Revision, Clinical Modification* (ICD-9-CM); iii) Laboratory Tests and Specialist Visits Database; iv) Mortality Database, from which data on mortality, but not cause of death, were collected; and v) Beneficiaries' Database, from which data regarding date of birth, sex, and place of residence were collected.

Data on drug use, hospitalisations, use of specialist services, and treatment costs were evaluated from the index date until 31 December 2013, corresponding to a period of at least 12 months and up to 5 years (the date of last enrolment was 31 December 2012). Specialist services encompassed all specialised outpatient healthcare, including diagnostic and laboratory tests (such as X-ray, ultrasound, magnetic resonance imaging, blood, and urinary tests), and consultations by specialist healthcare providers. The cost analysis was conducted from the perspective of the NHS. Costs are reported in Euros (€). Drug costs were evaluated

based on the Italian NHS costs at the time of the analysis. Outpatient services costs were evaluated according to regional tariffs. Hospitalisation costs were calculated using the Diagnosis-Related Group (DRG) tariff. Data were presented according to BMI class for the normal-weight, overweight, and obese (total and grade I, II and III) cohorts for two time periods: at 1 year following the index date (1-year observation period) and at the time of data cut-off (31 December 2013). Underweight subjects were included for the prevalence analysis only. Costs were also analysed according to age (using a cut-off of 65 years).

Statistical analysis

To test normality assumption of data distribution, the Skewness-Kurtosis test was used. Continuous variables were reported as mean and standard deviation or median and interquartile range, as appropriate, and compared with analysis of variance (ANOVA) test, whereas categorical variables were expressed as numbers and percentages, and compared with the χ^2 test. Analyses were performed stratified for BMI groups. P-value ≤0.05 were considered statistically significant. All statistical analyses were conducted using Stata software version 12·0 (Stat Corp LP, College Station, TX, USA), data management was carried out using Microsoft SQL Server 2012.

Role of funding source

Unrestricted financial support for the collection of data and for medical editorial assistance was provided by Johnson & Johnson Medical.

RESULTS

Subjects

Overall, 20,159 adults were included in the study. Table 1 shows the characteristics of subjects who were classified as underweight, normal weight, overweight, and obese at the index date. The prevalence of obesity was 22.2% (N=4471); of these, 3253 (72.8%) were classified as grade I obesity, 898 (20.1%) as grade II obesity, and 320 (7.2%) as grade III obesity. The mean length of follow-up was 2.6, 2.7, and 2.8 years for the normal-weight, overweight, and obese groups, respectively (p=NS). Within the obese group, the mean length of follow-up was 2.8 years across each of the grade I, II and III obesity cohorts; 1.1% of subjects died at 1 year following the index date (normal weight 1.1%, overweight 1.2%, obese 1.1%; p=NS).

Table 1. Baseline characteristics and demographics at the index date

	Weight				Total
	Under (BMI <18.5)	Normal (BMI ≥18.5 to <25)	Over (BMI ≥25 to <30)	Obese (BMI ≥30)	
Patients, n (%)	475 (2.3)	7686 (38.1)	7545 (37·4)	4471 (22·2)	20,159 (100)
Males:females, n:n	67:390	2977:4709	3996:3549	2048:2423	9088:11,071
Mean age ± SD, years	44.6 ± 20.4*	53.6 ± 17.2†	59.3 ± 15.2‡	58.1 ± 15.1	56.5 ± 16.4

SD, standard deviation

*p<0.001 vs normal weight, overweight, and obese; †p<0.001 vs overweight and obese; ‡p<0.001 vs obese

Prevalence of obesity by age

The proportion of subjects who were overweight or obese increased with age, while it decreased for normal weight subjects (p<0.001) (table 2). Among subjects aged >30 years, more than half were classified as overweight or obese (table 2). In particular, among subjects aged between 30 and 64 years, 36.4 and 22.8% were overweight and obese, respectively; among subjects aged 65+ years, 44.2 and 23.7% were overweight and obese, respectively (table 2).

Table 2. Proportions of patients classified as being of normal weight, overweight, and obese, stratified by age at the index date

Prevalence	Normal weight	Over weight	Obese	Total
18–29 years, n (%)	743 (62.0)*	267 (22.3)*	189 (15.8)*	1199 (100.0)
30–64 years, n (%)	4701 (40.8)†	4195 (36.4)†	2627 (22.8)†	11523 (100.0)
65+ years, n (%)	2242 (32.1)	3083 (44.2)	1655 (23.7)	6980 (100.0)
Total	7686	7545	4471	

*p<0.0001 vs 30–64 years and +65 years; †p<0.0001 vs +65 years

Use of prescription medication

In total, 13,002 subjects from the normal weight, overweight and obese groups (66%) received at least one prescription drug treatment during the 1-year observation period. 3,353 were obese subjects (75%), 4,437 were normal-weight subjects (57.7%) and 5,212 were overweight subjects (69.1%). These differences were significant ($p<0.0001$ among groups); 14,807 (75.2%) subjects had received at least one drug treatment at data cut-off; 3,666 were obese subjects (82%), 5,276 were normal-weight subjects (68.6%) and 5,865 were overweight subjects (77.7%). Again, these differences were significant ($p<0.0001$ among groups). During the 1-year observation period, anti-hypertensive drugs were the most common drug class received (43.8% of subjects); 31.3% of subjects received gastrointestinal drugs, 28.8% received anti-inflammatory drugs, 23.4% received antiplatelet drugs, 17.7% received statins, and 0.7% received antineoplastic drugs. Obese patients received each class of drug more frequently than normal-weight or overweight subjects ($p<0.001$ for all drug classes except antineoplastic among all groups and statins between overweight and obese subjects [p=NS]) (figure 1a). The largest difference in drug use between subjects who were obese and of normal weight was observed for the antidiabetic drug class (30.1% increase in obese subjects; $p<0.001$). Results were similar for the period up to data cut-off ($p<0.001$ for all drug classes except antineoplastic among all groups and stating between overweight and obese subjects [p=NS]) (figure 1b).

Duration of hospitalisation

In total, 1416 subjects (7.2%) were hospitalised at least once during the 1-year observation period and this increased to 3,204 subjects (16.3%) for the period up to data cut-off. In normal-weight, overweight, and obese subjects, hospitalisation rates were 6.5%, 7.7%, and 7.6%, respectively, at 1 year, and 14.8%, 17.3%, and 17.0%, respectively, at data cut-off. Obese and overweight subjects had a higher hospitalisation rate in comparison with normal weight individuals (p=0.006 and 0.03, at 1-year follow-up and data cut-off, respectively). In the 1-year observation period, the mean duration of hospitalisation was 3 (interquartile range; IQR 7) days in normal-weight subjects, 4 (IQR 7) days in overweight subjects, and 5 (IQR 8) days in obese subjects (p=NS). Within the group of obese subjects, median duration of hospitalisation was not different among the grade III (4.5 [IQR 8] days), grade I (5 [IQR 8] days) and grade II obese (4.5 [IQR 9.5] days) groups. The most common reasons for hospitalisation in the grade I and II obese groups were type 2 diabetes and essential hypertension (not specified; 0.8% each). For grade III obese patients, the most common reasons for hospitalisation were severe obesity and benign essential hypertension (1.6% and 0.9%, respectively). Similarly, the median duration of hospitalisation for the period up to data cut-off did not show significant differences among groups (obese subjects, 5 [IQR 7] days; normal-weight subjects, 3 [IQR 7] days; and overweight subjects 4 [IQR 7] days, respectively; p=NS), as well as among obese subgroups (grade I obesity 4 [IQR 7] days; grade II obesity 5 [IQR 9] days; grade III obesity 5 [IQR 7.5] days; p=NS).

Use of specialist services

During the 1-year observation period, an average of 5.3 (± 7.0) specialist services were required overall for obese subjects; the mean number of specialist services required was higher in the II grade obese group (5.8 ± 9.5) than in the other BMI groups (4.4 ± 5.5, 5.0 ± 7.2, 5.2 ± 6.3, and 5.0 ± 5.8 for normal-weight, overweight, grade I obese, and grade III obese groups, respectively, p<0.001). At the point of data cut-off, the mean number of specialist services required was 18.8 (± 26.8) in the grade II obese group, compared with 12.7 (± 16.1), 15.8 (± 21.3), 16.6 (± 18.8), and 15.9 (± 18.5) for the normal-weight, overweight, grade I and II obese groups, respectively, p<0.001.

Costs

During the observation period, the mean annual healthcare costs per subject was €819.03 for normal-weight group, €1,015.19 for overweight group and €1,166.52 for obese group, respectively. The mean healthcare cost per subject for the period up to data-cut-off was €2,465.01 for normal-weight group, €3,417.81 for overweight group and €3,782.21 for obese group, respectively. Mean healthcare costs during the 1-year observation period were higher in obese than in non-obese subjects (p<0.001), while no differences were observed at data cut-off point (p=NS) (figure 2a and figure 2b). During the 1-year observation period, the highest mean annual costs per individual in the obese group were associated with drug prescriptions (€461), followed by hospitalisation costs (€423) and specialised outpatient services (€283). Subjects with grade II obesity generated higher costs than the grade I and grade III obese groups, primarily owing to higher hospitalisation costs (p<0.01). Compared

with normal-weight controls over 1 year, costs were higher by 23.5% for overweight subjects (34.3% when considering drug costs only), 34.8% for patients with grade I obesity (47.0% for drug costs only), 70.4% for those with grade II obesity (90.1% for drug costs only), and 33.9% for patients with grade III obesity (83.9% for drug costs only) (all values: $p<0.01$). At the point of data cut-off, the mean annual costs in the obese group had increased to €1544,24 for drug prescriptions, €1256,41 for hospitalisation costs, and €981,56 for outpatient services (figure 2b). Similar to the 1-year observation, costs were higher for obese patients in comparison with normal weight controls ($p<0.01$) (figure 2b). Again, patients with grade II obesity generated higher costs, mainly due to outpatient costs ($p<0.05$) (figure 2b).

The possible effect of age, when comparing the impact of obesity on healthcare costs, is reported in Figure 3.

DISCUSSION

There are still limited data on healthcare resources utilisation for untreated obesity and its economic impact on healthcare systems. We report here on the prevalence and associated costs of obesity in an Italian population of over 20,000 individuals. Our study represents one of the largest European population studies on obesity and provides a real-life assessment of the economic impact of this increasingly prevalent condition. The findings of our study show that obese adults who did not receive treatment for their underlying obesity used more prescription drugs, experienced longer durations of hospitalisation, required more specialised outpatient healthcare

and were associated with substantially greater costs compared with normal-weight adults.

Our study directly evaluated the economic impact of comorbidities associated with obesity on the Italian healthcare system by integrating multiple data sources, taking into account the true costs of pharmaceutical treatments, the use of diagnostic and specialist services, and hospitalisations over a period of up to 5 years. Importantly, as a result of the structure of the Italian national healthcare system and the multiple data sources available, the healthcare resources and costs reported in this study are a true and accurate reflection of the real-life costs for each subject. To our knowledge, at present only few studies have evaluated data on real-life healthcare costs from obesity associated with BMI.[11-13] Previous studies have been limited by the fact that they were based on resources used at a single point in time or restricted to a single hospital department. Our study in real-world setting helps to identify the actual consumption of resources by obese patients. However, as with any retrospective observational study, it should be noted that limitations might exist as a result of the variability of professional practice and information bias.

Obese subjects used a wide range of drugs, including antihypertensive, gastrointestinal, anti-inflammatory, antiplatelet, and antidiabetic drugs. Our study showed that obese subjects generally received each class of drug more frequently than normal-weight or overweight subjects, with the exception of antidepressant. This is likely to reflect the various comorbidities that obese subjects commonly experience if their underlying condition remains untreated, such as diabetes and hypertension. Notably, antidiabetic and antihypertensive drugs were used in around twice as many obese as normal-weight subjects. Overall healthcare costs were

substantially higher for obese than for non-obese individuals. Prescriptions represented the greatest overall costs, highlighting the economic impact that obesity-related comorbidities have on healthcare systems.

There were also significant costs associated with hospitalisation, particularly for the grade II obese group; this may be related to the longer mean duration of hospitalisation in these patients compared with grade III obese and non-obese subjects. The relatively short hospital stay observed in the grade III obesity group should be highlighted as this may suggest that many institutions within the Italian healthcare system are not adequately equipped to diagnose and treat morbidly obese subjects, such as radiological instruments not being suitable to host severely obese patients, or a lack of specialists with sufficient experience to prescribe suitable therapies to address the different comorbidities. This could result in these patients being discharged from hospital earlier than should be expected. It is also possible that, as severely obese people are frequently depressed,[14-16] they may refuse to leave home to go to hospital at all, unless they have an acute condition.

The prevalence of obesity reported in this study (22·2%) is in line with the current WHO estimation of the prevalence of obesity in Italy (21·0%),[3] but higher than other estimates (~10%).[17 18] The proportion of subjects who were overweight or obese increased with age, with more than half of adults aged ≥30 years being overweight or obese. Similar findings have previously been reported in Italy;[19] based on data from five surveys conducted between 2006 and 2010, the prevalence ratios for overweight/obesity in individuals aged ≥65 versus 18–24 years were 2·01 in men and 2·65 in women.[17] These data suggest that it may be important to target and

educate individuals who are overweight or have grade I obesity and are of working age, with the aim of preventing them from becoming more obese later in life.

Since older subjects are likely to consume more healthcare resources, we have also analysed the possible effect of age when comparing the impact of obesity on healthcare costs. The results highlight that healthcare costs did not increase just because obese patients were older than normal weight patients, but that in each age group, the costs of obese patients were higher than other patients.

It is important to raise awareness that the direct treatment of patients who are severely obese would help to reduce the economic impact of the condition on healthcare systems.[20] The initial costs associated with treatment, such as bariatric surgery, would probably be offset by the subsequent savings made on drug prescriptions, hospitalisation costs, and outpatient care related to the treatment of comorbidities.[21 22] Indeed, a recent meta-analysis, comprising 37,720 patients across 11 studies, showed that bariatric surgery significantly reduces drug use and costs.[23] In addition, the direct treatment of obesity would likely help to reduce the burden on physicians who spend a substantial amount of time treating the comorbidities associated with obesity. The value of preventative strategies for obesity is an important consideration for decision makers, particularly given the increasing concern over the sustainability of the healthcare system and the ageing population. Measures such as advocating the value of a healthy and balanced diet with regular exercise as part of an early obesity prevention strategy are likely to be important.

Although in our study we used the healthcare databases of Lombardy, Tuscany and Campania, three Italian Regions localised from north to south of Italy, including data

for a total population of about 2.3 million, and Health Search Database of the Società Italiana di Medicina Generale, larger studies are needed to confirm and to enhance the generalisability of the findings.

In conclusion, our data highlight the need to develop public health policies that aim to prevent the development of obesity at an early age and also to proactively and effectively treat severely obese patients, thereby reducing the overall economic burden of this condition.

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CONTRIBUTOR STATEMENT

Chiara Veronesi, Valerio Blini, and Luca Degli Esposti contributed to the design and conduct of the study, data collection and management, analysis and interpretation of the data, and preparation of the manuscript. Annamaria Colao, Marcello Lucchese, Monica D'Adamo, Silvia Savastano, Enrico Facchiano and Paolo Sbraccia contributed to clinical evaluation and data interpretation and investigated all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors critically revised the manuscript for important intellectual content; all authors approved the final version of the manuscript.

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COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: all authors had financial support from Johnson & Johnson Medical for the submitted work; no financial relationship with any organisations that might have an interest in the submitted work in the previous three years; no other relationship or activities that could appear to have influenced the submitted work.

DATA SHARING

No additional data available.

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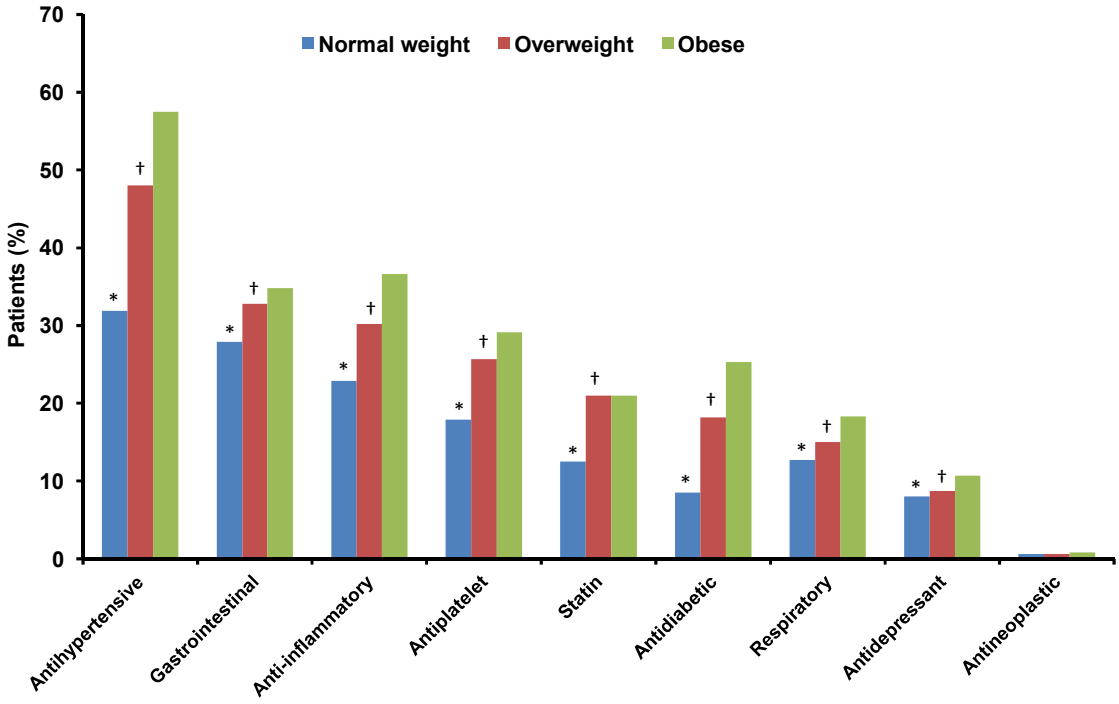
FIGURE LEGENDS

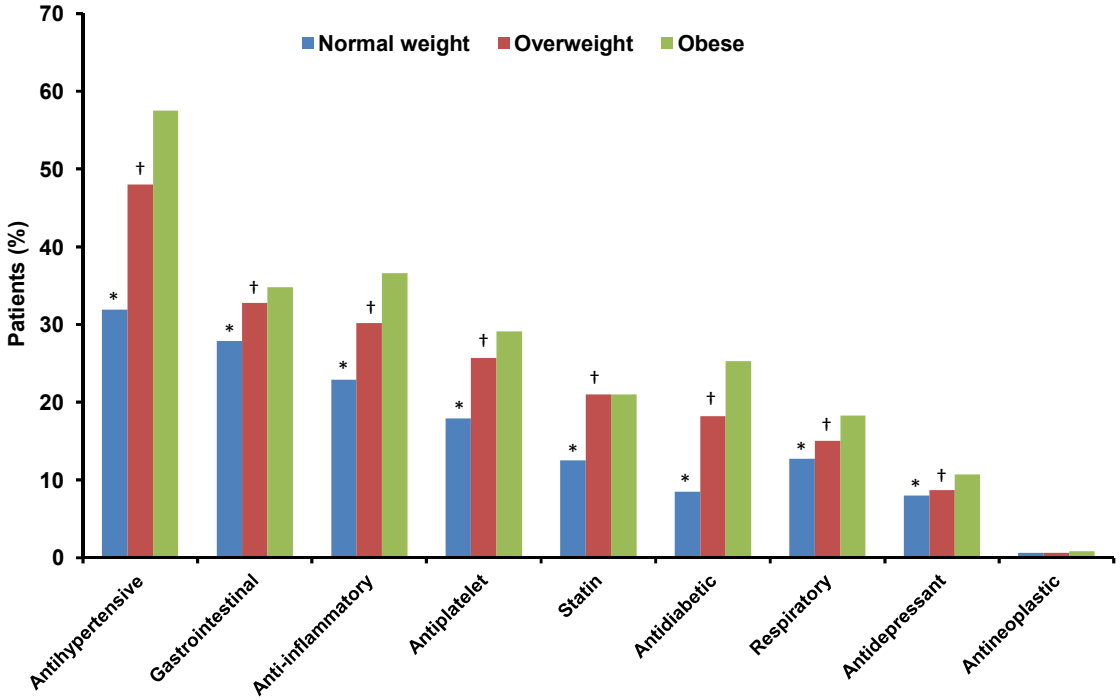
Fig 1. Patients exposed to treatment, by BMI category and drug class, during (a) the 1-year observation period and (b) the period up to data cut-off

(a)



*p<0.001 vs overweight and obese subjects; †p<0.001 vs obese subjects

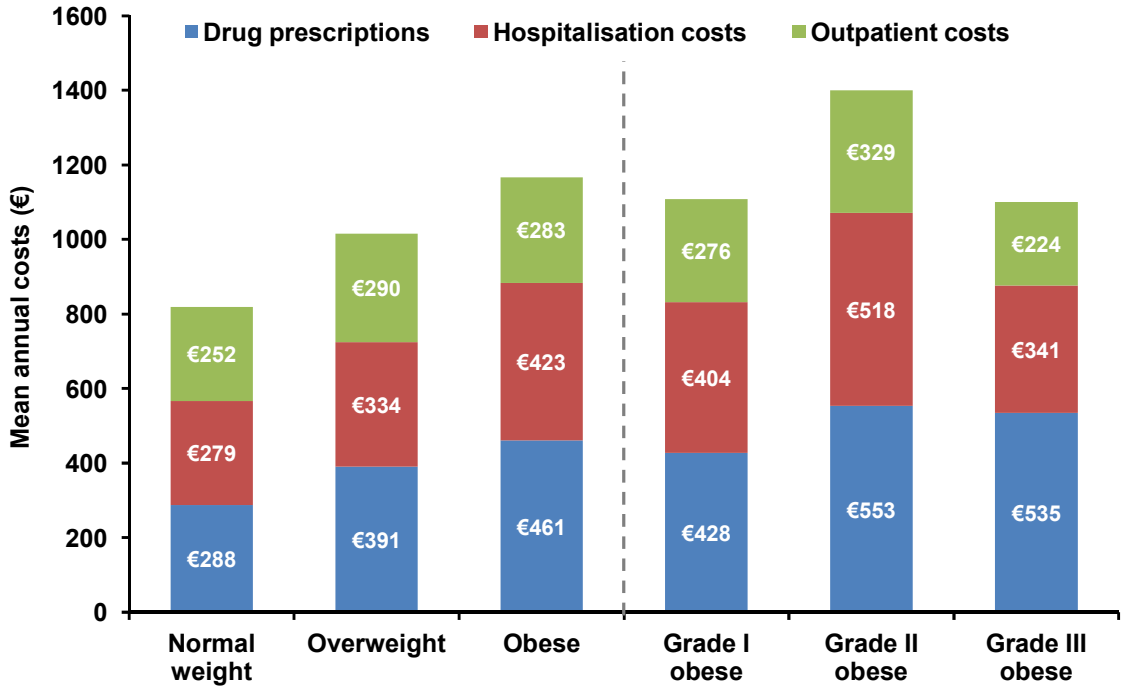
(b)



*p<0.001 vs overweight and obese subjects; †p<0.001 vs obese subjects

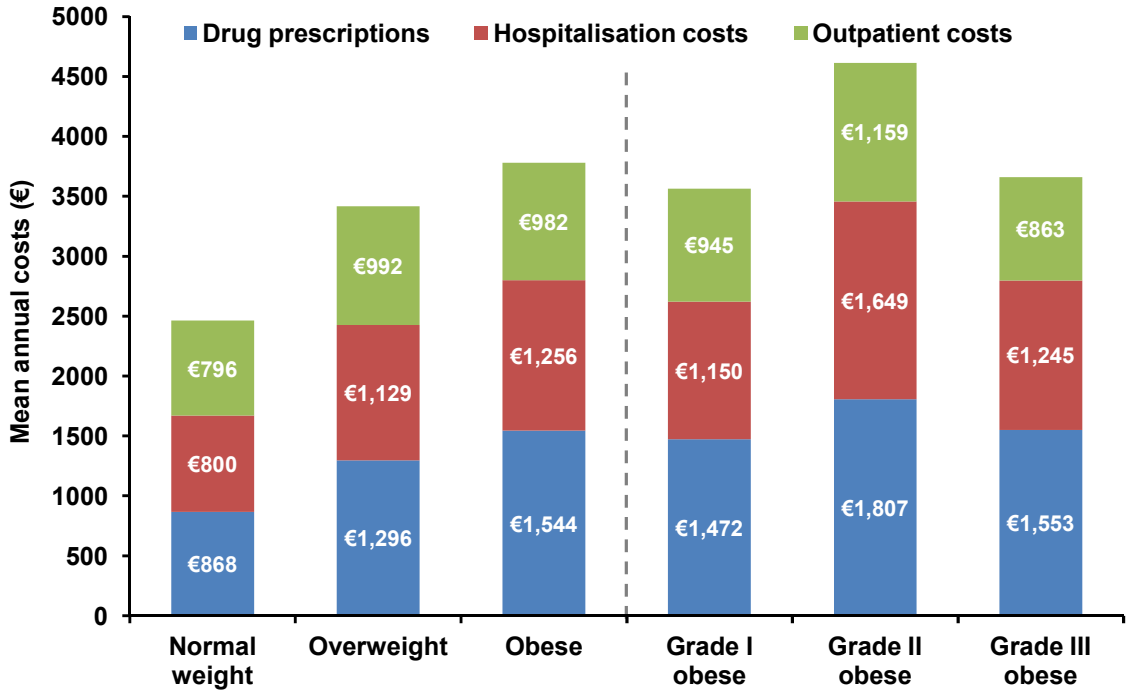
Fig 2. Mean annual costs per surviving individual, by BMI category, during (a) the 1-year observation period and (b) the period up to data cut-off

(a)



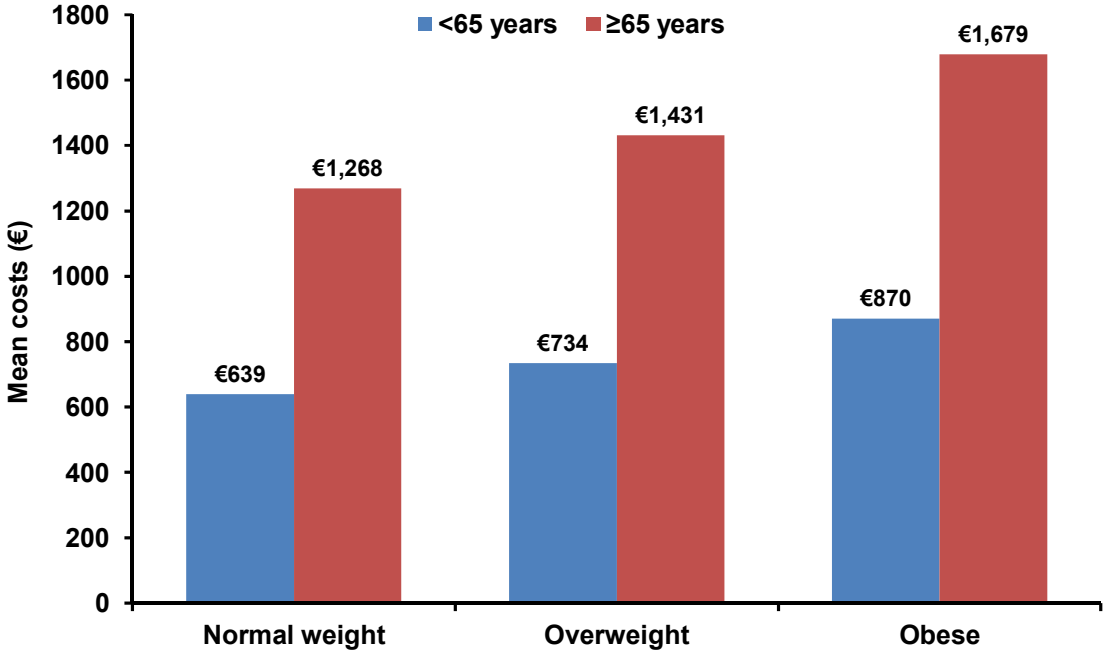
Overall costs: p<0.001 vs overweight and obese subjects; p<0.01 vs grade I and grade II obese subjects. Drug costs: p<0.001, p<0.01; Hospitalisation costs: p<0.01, p=NS; Outpatient costs: p<0.01, p=NS

(b)



Overall costs: p<0.001 vs overweight and obese subjects; p<0.01 vs grade I and grade II obese subjects. Drug costs: p<0.001, p=NS; Hospitalisation costs: p<0.001, p=NS; Outpatient costs: p<0.001, p<0.05

Fig 3. Mean cost according to age and BMI



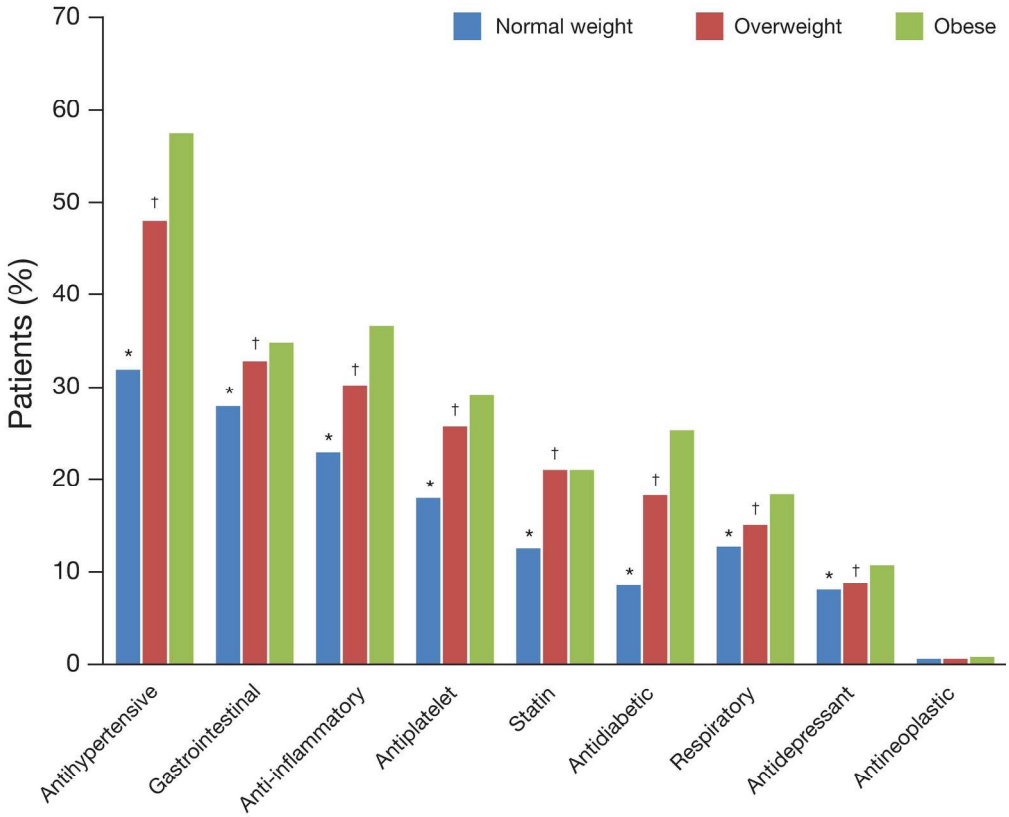


Figure 1a

Fig 1a

173x150mm (300 x 300 DPI)

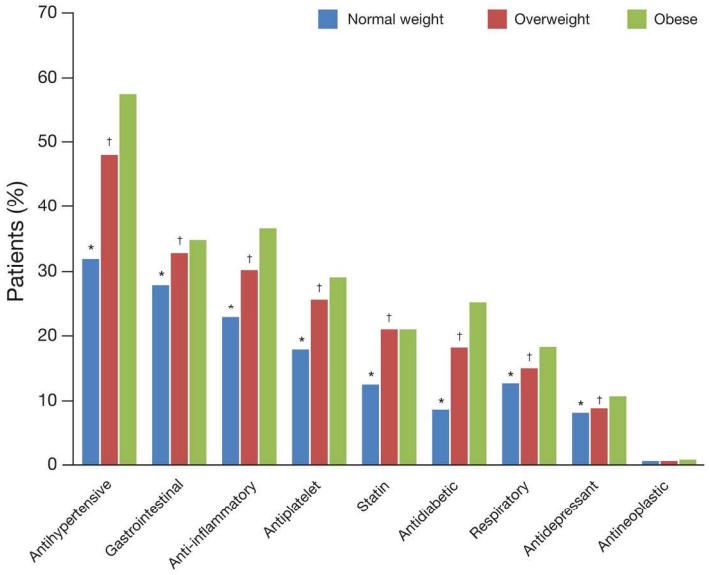


Figure 1b

Fig 1b

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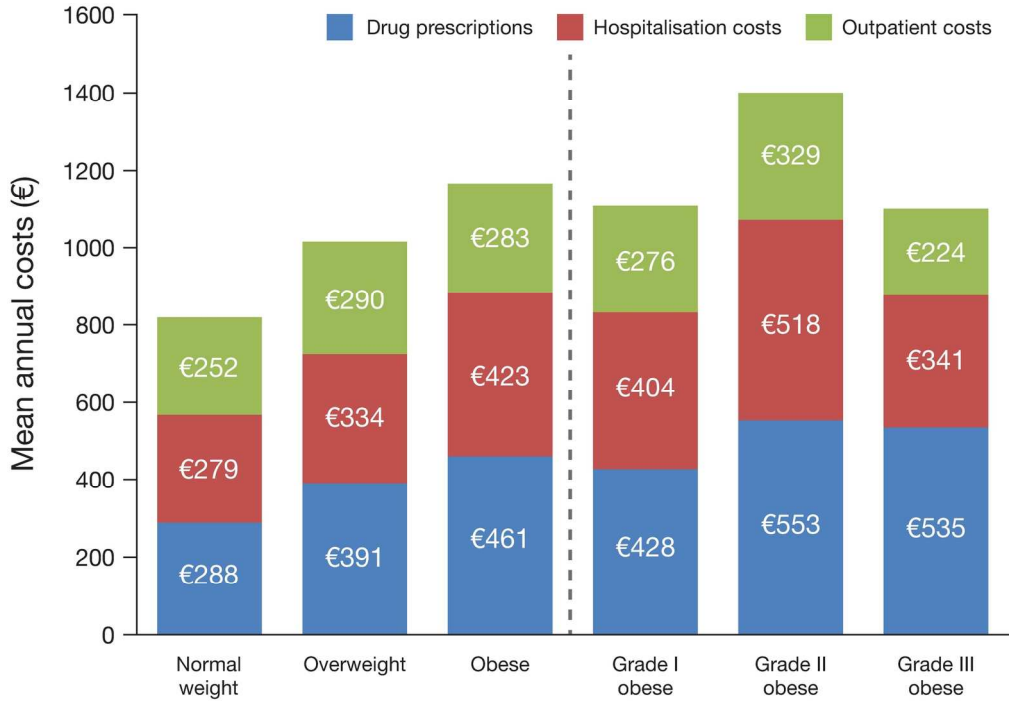

Figure 2a

Fig 2a

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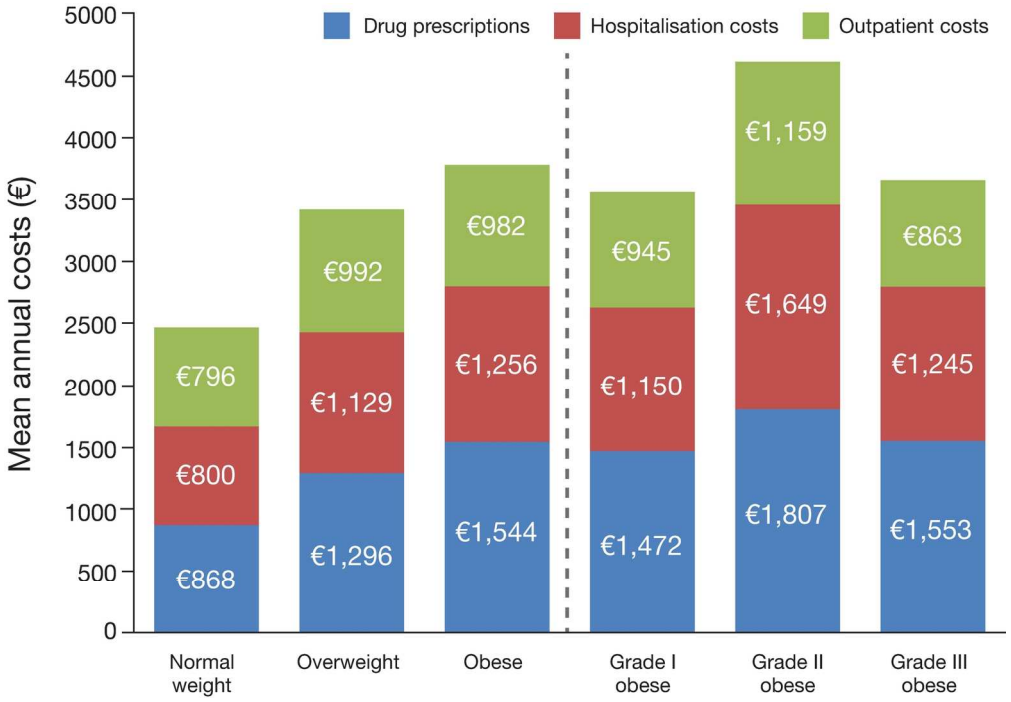

Figure 2b

Fig 2b

161x124mm (300 x 300 DPI)

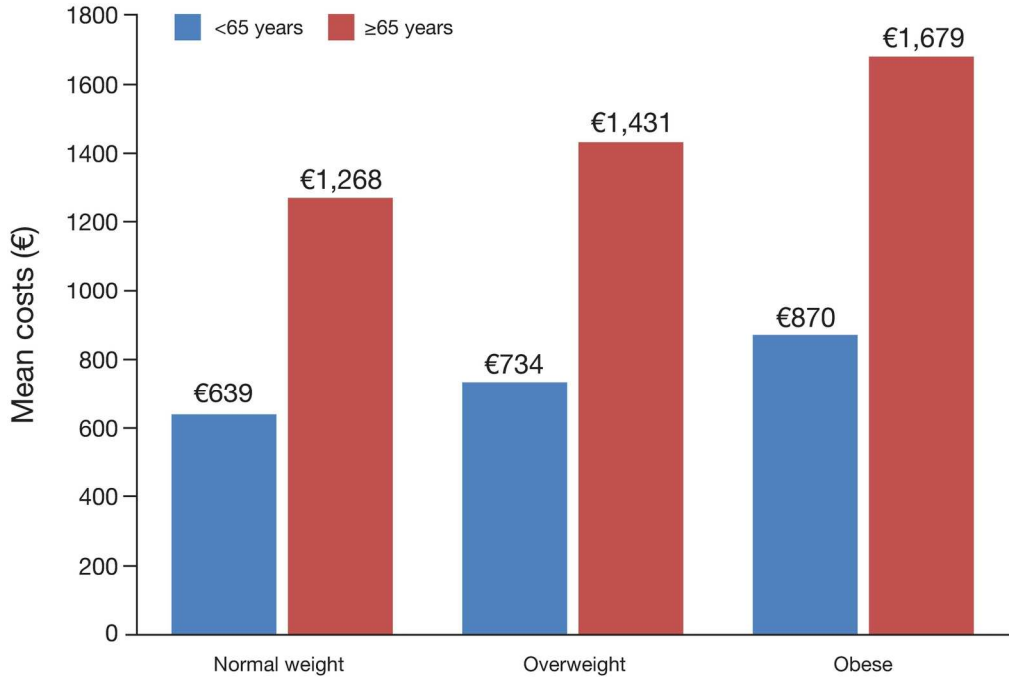

Figure 3

Fig 3

161x124mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page no.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **The title on page 1 in the main manuscript states the study design:** *"Healthcare utilisation and economic impact of non-treated obesity in Italy: findings from a retrospective administrative and clinical database analysis"*	**1**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **The Abstract in the main manuscript provides a balanced summary of what was done and what was found:** ***ABSTRACT*** ***Objective:*** *Aim of this study was to investigate the prevalence of obesity in Italy and to examine its resource consumption and economic impact on the Italian healthcare system.* ***Design:*** *Retrospective, observational, real-life study* ***Setting:*** *Analysis of data performed by integrating administrative databases that included a total of approximately 2.3 million health-assisted individuals from three Italian Local Health Units from northern (Bergamo, Lombardy), central (Grosseto, Tuscany), and southern (Naples, Campania) Italy.* ***Participants:*** *All patients aged ≥18 years with at least one recorded BMI measurement between January 1st 2009 and December 31st 2012 were included.* ***Main outcome measures:*** *The primary outcome was health resources consumption and the associated economic impact on the Italian NHS. Secondary outcome measures were the prevalence and characteristics of subjects in relationship with the BMI category.* ***Results:*** *20,159 adult subjects with at least one documented body mass index (BMI) measurement from three local health units. Subjects with BMI ≥30 kg/m^2 were defined as obese. The prevalence of obesity was 22.2% (N=4,471) and increased with age. At the 1-year observation period, obese subjects who did not receive treatment for their obesity experienced longer durations of hospitalisation (median length: 5 vs 3 days), used more prescription drugs (75.2% vs 57.7%), required more specialised outpatient healthcare (mean number: 5.3 vs 4.4), and were associated with greater costs, primarily owing to prescription drugs and hospital admissions (mean annual cost per year per patient: €460.6 vs €288.0 for drug prescriptions, €422.7 vs €279.2 for hospitalisations, and €283 vs €251.7 for outpatient care), compared with normal-weight subjects. Similar findings were observed*	**2, 3**

for the period up to data cut-off (mean follow-up of 2.7 years).

Conclusions: *Untreated obesity has a significant economic impact on the Italian healthcare system, highlighting the need to raise awareness and proactively treat obese subjects.*

Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported **In the introduction in the main manuscript a scientific background and rationale is provided:** *Obesity is now widely regarded as a global epidemic; worldwide, obesity rates have more than doubled since 1980.[1 2] According to the World Health Organization (WHO), more than 1·9 billion adults were overweight in 2014. Of these, over 600 million (~13% of the world's population) were obese, defined as having a body mass index (BMI) of ≥30 kg/m^2.[2 1] In Italy, WHO reports from 2014 showed that the prevalence of obesity was 20.4% among individuals aged ≥18 years.[3] Obesity is a major risk factor for various chronic diseases, particularly if it remains untreated. Globally, 44% of diabetes, 23% of ischaemic heart disease, and 7–41% of certain cancers are attributable to being overweight or obese.[1] Obesity-associated mortality rates are also alarmingly high, with at least 2.8 million deaths each year resulting from being overweight or obese.[1] Obesity was once considered to be an issue associated with high-income countries only; however, its prevalence is now also increasing in low- and middle-income countries.[4]* *Previous studies have shown that obesity and its associated comorbidities have a considerable economic impact on healthcare systems, primarily because of high costs for medication and hospitalisations.[5-8] However, in those studies, costs were only estimated indirectly. In contrast, we report here on the findings from a study of over 20,000 adults that investigated the prevalence of, and direct costs associated with, untreated obesity in three distinct regions of Italy – which differ in terms of geography and nutritional traditions – in order to understand the healthcare utilisation and economic impact of obesity on the Italian national healthcare system (NHS).*	**4, 5**
Objectives	3	State specific objectives, including any prespecified hypotheses **The objectives are stated in both the Introduction and Methods sections***:* *…we report here on the findings from a study of over 20,000 adults that investigated the prevalence of, and direct costs associated with, untreated obesity in three distinct regions of Italy – which differ in terms of geography and nutritional traditions – in order to understand the healthcare utilisation and economic impact of obesity on the Italian national healthcare system (NHS).*	**5**

		The primary objective of the study was to estimate health resource consumption and the economic impact of obesity on the Italian NHS. The secondary objective was to assess the prevalence and characteristics of subjects in relationship with the BMI category.	**6**
Methods			
Study design	4	Present key elements of study design early in the paper	
		The key elements are presented in the method section of the main manuscript:	
		Study design and population	**5, 6**
		This was a retrospective, observational, real-life study. To be eligible, individuals were required to be aged ≥18 years and to have at least one recorded BMI measurement between 1 January 2009 and 31 December 2012. The first recorded BMI was set as the index date. Eligible subjects were identified from registries at three Italian local health units that represent the primary Italian geographical areas: Bergamo, Lombardy (northern Italy), Grosseto, Tuscany (central Italy), and Naples, Campania (southern Italy).	
		BMI was classified as follows: underweight, <18.5 kg/m^2; normal weight, ≥18.5 to <25 kg/m^2; overweight, ≥25 to <30 kg/m^2; obese, ≥30 kg/m^2. Obesity was further classified as grade I, II and III based on BMI levels of ≥30 to <35 kg/m^2, ≥35 to <40 kg/m^2, and ≥40 kg/m^2, respectively.[9]	
		An anonymous data file is routinely used by regional health authorities for epidemiological and administrative purposes. No identifiers related to subjects were provided to the researchers. In accordance with Italian law regarding data confidentiality,[10] *the ethics committee of each local health units was notified about the study. Neither ethics committee approval nor informed consent was required for using encrypted retrospective information.*	
		Data sources and analysis	**6, 7**
		Primary care data for each subject were retrospectively collected from the Health Search Database of the Società Italiana di Medicina Generale (Italian Society of General Medicine) for the period 2009–2013. Using the numeric code assigned to each citizen by the local health units as a unique identifier, this database was linked to the following databases: i) Medications Prescription Database, which includes anatomical–therapeutic–chemical (ATC) codes; ii) Hospital Discharge Database, which includes dates of hospital admission and discharge, as well as discharge diagnosis codes according to the International Classification of Diseases Ninth Revision, Clinical Modification (ICD-9-CM); iii) Laboratory Tests and Specialist Visits Database; iv) Mortality Database, from which data on mortality, but not cause of death, were collected; and v) Beneficiaries' Database, from which data regarding date of birth, sex, and place of residence were collected.	
		Data on drug use, hospitalisations, use of specialist services, and treatment costs were evaluated from the index date until 31 December 2013,	

		corresponding to a period of at least 12 months and up to 5 years (the date of last enrolment was 31 December 2012). Specialist services encompassed all specialised outpatient healthcare, including diagnostic and laboratory tests (such as X-ray, ultrasound, magnetic resonance imaging, blood, and urinary tests), and consultations by specialist healthcare providers. The cost analysis was conducted with the perspective of the National Health System. Costs are reported in Euros (€) currency. Drug costs were evaluated using the Italian National Health Service purchase both at the time of analysis. Outpatient services costs were evaluated according to regional tariffs. Hospitalization costs were calculated using the Diagnosis-Related Group (DRG) tariff. Data were presented according to BMI class for the normal-weight, overweight, and obese (total and grade I, II and III of obesity) cohorts for two time periods: at 1 year following the index date (1-year observation period) and at the time of data cut-off (31 December 2013). Underweight subjects were included for the prevalence analysis only. Costs were also analysed according to age (using a cut off of 65-years).	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **The setting, locations and relevant dates are presented in the method section (paragraphs "Study design and population" "Data sources and analysis") of the main manuscript:** *The data used for the analysis were obtained from the healthcare databases of three Local Health Units (LHUs), whose databases included a total population of about 2.3 million health-assisted individuals, in the Italian regions of Lombardy, Tuscany and Campania.*	**5**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	**NA**
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed **The participants are described in the methods section (paragraph "Study design and populations") of the main manuscript:** *This was a retrospective, observational, real-life study. To be eligible, individuals were required to be aged ≥18 years and to have at least one recorded BMI measurement between 1 January 2009 and 31 December 2012. The first recorded BMI was set as the index date. (…) BMI was classified as follows: underweight, <18.5 kg/m^2; normal weight, ≥18.5 to <25 kg/m^2; overweight, ≥25 to <30 kg/m^2; obese, ≥30 kg/m^2. Obesity was further classified as grade I, II and III based on BMI levels of ≥30 to <35 kg/m^2, ≥35 to <40 kg/m^2, and ≥40 kg/m^2, respectively.* **The methods of follow-up are described in the methods section (paragraph "Data sources and analysis") of the main manuscript:** *Data on drug use, hospitalisations, use of specialist services, and treatment costs were evaluated from the index date until 31 December 2013,*	**5** **7**

		corresponding to a period of at least 12 months and up to 5 years (the date of last enrolment was 31 December 2012). (….) Data were presented according to BMI class for the normal-weight, overweight, and obese (total and grade I, II and III) cohorts for two time periods: at 1 year following the index date (1-year observation period) and at the time of data cut-off (31 December 2013). Underweight subjects were included for the prevalence analysis only. Costs were also analysed according to age (using a cut off of 65-years).	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **The outcomes are described in the methods section of the main manuscript:** *Data on drug use, hospitalisations, use of specialist services, and treatment costs were evaluated from the index date until 31 December 2013, corresponding to a period of at least 12 months and up to 5 years (the date of last enrolment was 31 December 2012). Specialist services encompassed all specialised outpatient healthcare, including diagnostic and laboratory tests (such as X-ray, ultrasound, magnetic resonance imaging, blood, and urinary tests), and consultations by specialist healthcare providers. The cost analysis was conducted with the perspective of the National Health System. Costs are reported in Euros (€) currency. (….) Data were presented according to BMI class for the normal-weight, overweight, and obese (total and grade I, II and III) cohorts for two time periods: at 1 year following the index date (1-year observation period) and at the time of data cut-off (31 December 2013). Underweight subjects were included for the prevalence analysis only. Costs were also analysed according to age (using a cut off of 65-years).*	**7**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Data sources and details of methods of assessment are given in the methods section:** *This was a retrospective, observational, real-life study. To be eligible, individuals were required to be aged ≥18 years and to have at least one recorded BMI measurement between 1 January 2009 and 31 December 2012. The first recorded BMI was set as the index date. Eligible subjects were identified from registries at three Italian local health units that represent the primary Italian geographical areas: Bergamo, Lombardy (northern Italy), Grosseto, Tuscany (central Italy), and Naples, Campania (southern Italy).* *BMI was classified as follows: underweight, <18.5 kg/m^2; normal weight, ≥18.5 to <25 kg/m^2; overweight, ≥25 to <30 kg/m^2; obese, ≥30 kg/m^2. Obesity was further classified as grade I, II and III based on BMI levels of ≥30 to <35 kg/m^2, ≥35 to <40 kg/m^2, and ≥40 kg/m^2, respectively.* *Primary care data for each subject were retrospectively collected from the Health Search Database of the Società Italiana di Medicina Generale (Italian*	**5** **6**

		Society of General Medicine) for the period 2009–2013. (…) *Data on drug use, hospitalisations, use of specialist services, and treatment costs were evaluated from the index date until 31 December 2013, corresponding to a period of at least 12 months and up to 5 years (the date of last enrolment was 31 December 2012). Specialist services encompassed all specialised outpatient healthcare, including diagnostic and laboratory tests (such as X-ray, ultrasound, magnetic resonance imaging, blood, and urinary tests), and consultations by specialist healthcare providers. The cost analysis was conducted with the perspective of the National Health System. Costs are reported in Euros (€) currency. Drug costs were evaluated using the Italian National Health Service purchase both at the time of analysis. Outpatient services costs were evaluated according to regional tariffs. Hospitalization costs were calculated using the Diagnosis-Related Group (DRG) tariff. Data were presented according to BMI class for the normal-weight, overweight, and obese (total and grade I, II and III) cohorts for two time periods: at 1 year following the index date (1-year observation period) and at the time of data cut-off (31 December 2013). Underweight subjects were included for the prevalence analysis only. Costs were also analysed according to age (using a cut off of 65-years).*	**7**
Bias	9	Describe any efforts to address potential sources of bias **This is addressed by the design of the study and the clearly defined data selection specifications**	**NA**
Study size	10	Explain how the study size was arrived at *How the study size was arrived at is described in the methods section* **Sample size dictated by the source databases**	**NA**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **The handling of the variables is described in the "Statistical analysis" paragraph:** *To test normality assumption of data distribution, the Skewness-Kurtosis test was used. Continuous variables were reported as mean and standard deviation or median and interquartile range, as appropriate, and compared with analysis of variance (ANOVA) test, whereas categorical variables were expressed as numbers and percentages, and compared with the χ^2 test.*	**7, 8**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	**7, 8**
		(*b*) Describe any methods used to examine subgroups and interactions	**7, 8**
		(*c*) Explain how missing data were addressed	**NA**
		(*d*) If applicable, explain how loss to follow-up was addressed	**NA**

		(*e*) Describe any sensitivity analyses	**7, 8**
		The statistical methods are given in the "Statistical analysis" paragraph: *To test normality assumption of data distribution, the Skewness-Kurtosis test was used. Continuous variables were reported as mean and standard deviation or median and interquartile range, as appropriate, and compared with analysis of variance (ANOVA) test, whereas categorical variables were expressed as numbers and percentages, and compared with the χ^2 test. Analyses were performed stratified for BMI groups. P-value ≤0.05 were considered statistically significant. All statistical analyses were conducted using Stata software version 12·0 (Stat Corp LP, College Station, TX, USA), data management will be carried out using Microsoft SQL Server 2012.*	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **The numbers of individuals are given in the Results section**	**9–14**
		(b) Give reasons for non-participation at each stage	**NA**
		(c) Consider use of a flow diagram	**NA**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **The characteristics of study participants are given in Tables 1 and 2.**	**9, 10**
		(b) Indicate number of participants with missing data for each variable of interest	**NA**
		(c) Summarise follow-up time (eg, average and total amount) **(…) cohorts for two time periods: at 1 year following the index date (1-year observation period) and at the time of data cut-off (31 December 2013). (follow-up period)**	**7**
		The mean length of follow-up was 2.6, 2.7, and 2.8 years for the normal-weight, overweight, and obese groups, respectively	**8**
Outcome data	15*	Report numbers of outcome events or summary measures over time **Numbers of outcome events were reported in the Results section, and in Figures 1 and 2**	**8, 9, 11, 13, 14**
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	**7, 8**

		Variables defined in Statistical analysis section and analyses reported in Figure 1 and 2	**11,13, 14, 26–29**
		(*b*) Report category boundaries when continuous variables were categorized	**NA**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	**NA**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	**8, 11,12**
Discussion			
Key results	18	Summarise key results with reference to study objectives **Key results are summarized as follows in the Discussion:** *(…) The findings of our study show that obese adults who did not receive treatment for their underlying obesity used more prescription drugs, experienced longer durations of hospitalisation, required more specialised outpatient healthcare and were associated with substantially greater costs compared with normal-weight adults.*	**14,15**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Limitations are summarized as follows in the Discussion:** *… as with any retrospective observational study, it should be noted that limitations might exist as a result of the variability of professional practice and information bias.* *Although in our study we used the healthcare databases of Lombardy, Tuscany and Campania, three Italian Regions localized from north to south of Italy, including data for a total population of about 2.3 million, and Health Search Database of the Società Italiana di Medicina Generale larger studies are needed to confirm and to enhance the generalizability of the findings.*	**15** **18**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **The interpretation is given as follows in the Discussion:** *There are still limited data on healthcare resources utilisation for untreated obesity and its economic impact on healthcare systems. We report here on the prevalence and associated costs of obesity in an Italian population of over 20,000 individuals. Our study represents one of the largest European population studies on obesity and provides a real-life assessment of the economic impact of this increasingly prevalent condition. (….) The findings of*	**14–17**

our study show that obese adults who did not receive treatment for their underlying obesity used more prescription drugs, experienced longer durations of hospitalisation, required more specialised outpatient healthcare and were associated with substantially greater costs compared with normal-weight adults.

Our study directly evaluated the economic impact of comorbidities associated with obesity on the Italian healthcare system by integrating multiple data sources, taking into account the true costs of pharmaceutical treatments, the use of diagnostic and specialist services, and hospitalisations over a period of up to 5 years. Importantly, as a result of the structure of the Italian national healthcare system and the multiple data sources available, the healthcare resources and costs reported in this study are a true and accurate reflection of the real-life costs for each subject. To our knowledge, at present only few studies have evaluated data on real-life healthcare costs from obesity associated with body mass index (BMI).[11-13] Previous studies have been limited by the fact that they were based on resources used at a single point in time or restricted to a single hospital department. Our study in real-world setting helps to identify the actual consumption of resources by obese patients. However, as with any retrospective observational study, it should be noted that limitations might exist as a result of the variability of professional practice and information bias.

These data suggest that it may be important to target and educate individuals who are overweight or have grade I obesity and are of working age, with the aim of preventing them from becoming more obese later in life.

It is important to raise awareness that the direct treatment of patients who are severely obese would help to reduce the economic impact of the condition on healthcare systems.[14] (….) In addition, the direct treatment of obesity would likely help to reduce the burden on physicians who spend a substantial amount of time treating the comorbidities associated with obesity. The value of preventative strategies for obesity is an important consideration for decision makers, particularly given the increasing concern over the sustainability of the healthcare system and the ageing population. Measures such as advocating the value of a healthy and balanced diet with regular exercise as part of an early obesity prevention strategy are likely to be important.

Generalisability	21	Discuss the generalisability (external validity) of the study results	
		The issue of generalisability is addressed as follows in the Discussion:	**18**
		Although in our study we used the healthcare databases of Lombardy, Tuscany and Campania, three Italian Regions localized from north to south of Italy, including data for a total population of about 2.3 million, and Health Search Database of the Società Italiana di Medicina Generale larger studies are needed to confirm and to enhance the generalizability of the findings.	
		Despite these limitations, our study indicates that in a "real-world" setting,	

		our data highlight the need to develop public health policies that aim to prevent the development of obesity at an early age and also to proactively and effectively treat severely obese patients, thereby reducing the overall economic burden of this condition.	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Such information is given in the Funding section:** ***Role of funding source*** *Unrestricted financial support for the collection of data and for medical editorial assistance was provided by Johnson & Johnson Medical.*	**21**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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