

# BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis

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**BACKGROUND:** The global obesity epidemic has paralleled a decrease in semen quality. Yet, the association between obesity and sperm parameters remains controversial. The purpose of this report was to update the evidence on the association between BMI and sperm count through a systematic review with meta-analysis.

**METHODS:** A systematic review of available literature (with no language restriction) was performed to investigate the impact of BMI on sperm count. Relevant studies published until June 2012 were identified from a Pubmed and EMBASE search. We also included unpublished data ( $n = 717$  men) obtained from the Infertility Center of Bondy, France. Abstracts of relevant articles were examined and studies that could be included in this review were retrieved. Authors of relevant studies for the meta-analysis were contacted by email and asked to provide standardized data.

**RESULTS:** A total of 21 studies were included in the meta-analysis, resulting in a sample of 13 077 men from the general population and attending fertility clinics. Data were stratified according to the total sperm count as normozoospermia, oligozoospermia and azoospermia. Standardized weighted mean differences in sperm concentration did not differ significantly across BMI categories. There was a J-shaped relationship between BMI categories and risk of oligozoospermia or azoospermia. Compared with men of normal weight, the odds ratio (95% confidence interval) for oligozoospermia or azoospermia was 1.15 (0.93–1.43) for underweight, 1.11 (1.01–1.21) for overweight, 1.28 (1.06–1.55) for obese and 2.04 (1.59–2.62) for morbidly obese men.

**CONCLUSIONS:** Overweight and obesity were associated with an increased prevalence of azoospermia or oligozoospermia. The main limitation of this report is that studied populations varied, with men recruited from both the general population and infertile couples. Whether weight normalization could improve sperm parameters should be evaluated further.

**Key words:** obesity / BMI / sperm concentration / total sperm count / meta-analysis

## Introduction

Subfertility affects ~15% of couples who seek to obtain a pregnancy and a male contribution is identified in 20–50% of the cases (Thonneau et al., 1991). A gradual decrease in sperm quality since the 1970s, particularly of sperm count, has been suggested by two meta-analyses (Carlsen et al., 1992; Swan and Elkin, 1999). This reported secular trend has traditionally been attributed to various methodological (standardization of the techniques, abstinence delay) or environmental (geography, season, genetic, ethnic group, tobacco, toxins) factors (Jouannet et al., 2001) but has also coincided with a worldwide increase in the prevalence of overweight and obesity (Finucane et al., 2011).

The association between high adiposity and subfertility has not been clearly demonstrated in men. Data from three large-scale epidemiological studies suggest an elevated risk for infertility among couples when the male partner is overweight or obese (Sallmen et al., 2006; Nguyen et al., 2007; Ramlau-Hansen et al., 2007). Results of studies investigating the links between BMI and sperm parameters, the gold standard for evaluation of male fertility potential, remain controversial. Several reports have shown an inverse correlation between BMI and sperm concentration or total sperm count (TSC) (Jensen et al., 2004; Paasch et al., 2010) but others have failed to document this association (Aggerholm et al., 2008; Duits et al., 2010). A previous meta-analysis published in 2010 concluded that there was no evidence of an association between BMI and sperm concentration or TSC (MacDonald et al., 2010). However, data from most studies could not be aggregated for the meta-analysis and the conclusion was based on five publications only (Jensen et al., 2004; Koloszar et al.,

2005; Fejes et al., 2006; Qin et al., 2007; Aggerholm et al., 2008). Moreover, ~30 original studies have been published since then. In a preliminary report, we showed that overweight and obesity were associated with an increased risk of presenting with oligozoospermia or azoospermia, compared with normal weight (Sermondade et al., 2012a).

The purpose of the current study is to update the systematic review on the relationship between BMI and sperm count and to perform a meta-analysis.

## Methods

### Literature search

A systematic review of available literature was performed to investigate the impact of BMI on sperm parameters in human males according to the PRISMA statement (Liberati et al., 2009). Relevant studies published until June 2012 were identified from PubMed and EMBASE using a combined free text and the following MeSH search strategy: ('overweight' OR 'weight' OR 'obesity' OR 'BMI' OR 'body fat' OR 'body weight' OR 'body mass index' OR 'adiposity') AND ('sperm' OR 'semen' OR 'spermatozoa' OR 'sperm count' OR 'sperm concentration' OR 'semen quality' OR 'semen parameters' OR 'sperm quantity' OR 'total sperm count' OR 'oligozoospermia' OR 'azoospermia'). References from these studies were also scrutinized to identify other relevant studies. No language restriction was applied.

### Study selection and data extraction

Titles of all articles retrieved from the database searches were screened. We excluded studies without results on the relationship between BMI and sperm parameters, case reports, reviews, experimental or

interventional studies, studies restricted to men with a particular pathology (such as a varicocele) and studies comparing exposed/non-exposed men. The abstracts of relevant articles investigating the relationship between BMI and sperm parameters were examined and all studies that could potentially be included in this review were retrieved, regardless of population size, origin or age. References from these studies and previous reviews were also scanned for any other relevant articles. Two reviewers independently extracted data (N.S. and C.F.) and there was no disagreement over eligibility of studies.

Owing to the wide variety of statistical methods and outcomes used in published studies (different BMI categories, mean or median, sperm concentration or TSC), authors of studies selected to be included in the present meta-analysis were contacted by email and asked to complete a standardized data extraction form indicating TSCs according to BMI categories, as specified by the World Health Organization (WHO; [World Health Organization, 2000](#)). We also included previously unpublished data obtained from all patients seen at the Infertility Center of Jean Verdier Hospital, Bondy, France, between January 2007 and December 2010, assigned as 'Levy *et al.* (unpublished)' study in the following text, table and figures.

## Data synthesis and analysis

Analyses were performed using the following BMI categories: <18.5 (underweight), 18.5–24.9 (normal weight), 25.0–29.9 (overweight), 30.0–39.9 (obesity) and  $\geq 40.0$  (morbid obesity)  $\text{kg/m}^2$  ([World Health Organization, 2000](#)). Participants with a BMI between 18.5 and 24.9  $\text{kg/m}^2$  were considered as the reference group. Random effects models were used to obtain summary estimates in order to account for inter-study variation. Studies were weighted according to an estimate of statistical size defined as the inverse of the variance of the log odds ratio (OR; [Woodward, 2005](#)). Prevalence ORs and their 95% confidence intervals (95% CIs) were obtained by comparing the prevalence of abnormal sperm count in each BMI category with the BMI reference category (see above). Statistical significances were obtained using the  $\chi^2$  test. The percentage of variability across studies attributable to heterogeneity was estimated using the  $I^2$  statistic ([Higgins and Thompson, 2002](#); [Higgins \*et al.\*, 2003](#)).

First, mean sperm concentrations and TSC were compared using standardized weighted mean differences (SMD) across BMI categories. Secondly, data were stratified according to TSC as normozoospermia ( $\geq 40 \times 10^6$  spermatozoa per ejaculate), oligozoospermia ( $< 40 \times 10^6$  but  $> 0$  spermatozoa per ejaculate) and azoospermia (absence of spermatozoa) according to WHO guidelines ([World Health Organization, 1999](#)). We tested whether the association between BMI and abnormal sperm count was the same for men with oligozoospermia or azoospermia by performing separate analyses on each of these outcomes. As there was no significant heterogeneity, further analyses were performed by combining oligozoospermia and azoospermia as a single outcome in order to increase the statistical power of the analyses. The prevalence of subjects having abnormal sperm count was compared across BMI categories as described above, as well as the prevalence of men having decreased sperm concentration according to WHO guidelines ( $< 15 \text{ M/ml}$ ; [Cooper \*et al.\*, 2010](#); [World Health Organization, 2010](#)). The Egger regression test was performed to assess publication bias ([Egger \*et al.\*, 1997](#)). All analyses were performed using STATA software (Release 10; STATA Corporation, College Station, TX, USA).

## Results

### Study characteristics

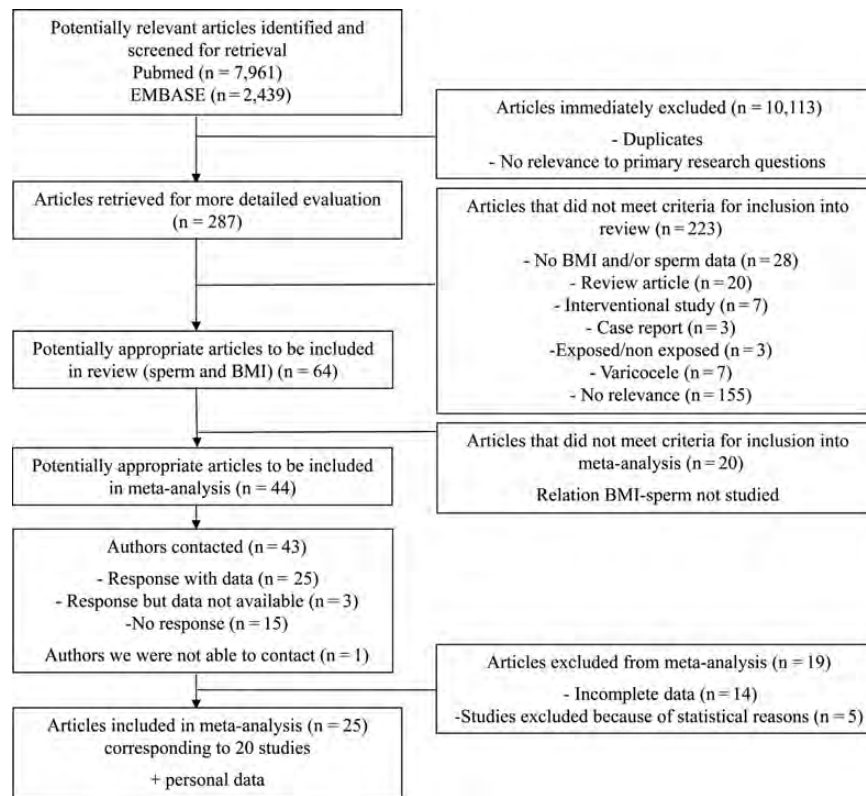
The search strategy identified a total of 10 400 articles, including duplicates and articles that had no relevance to the primary research

questions. After review of 287 abstracts, 64 articles providing BMI and sperm data were selected. Among them, 44 articles investigating the relationship between BMI and sperm parameters seemed potentially appropriate to be included in the meta-analysis (Fig. 1). We were able to contact 43 of the 44 authors by email (one email address was not available), allowing us to obtain original and complete data for 20 studies corresponding to 25 published articles ([Eskenazi \*et al.\*, 2003](#); [Jensen \*et al.\*, 2004](#); [Fejes \*et al.\*, 2005, 2006](#); [Koloszar \*et al.\*, 2005](#); [Magnusdottir \*et al.\*, 2005](#); [Zorn \*et al.\*, 2007, 2012](#); [Aggerholm \*et al.\*, 2008](#); [Li \*et al.\*, 2009](#); [Vujkovic \*et al.\*, 2009](#); [Chavarro \*et al.\*, 2010](#); [Duits \*et al.\*, 2010](#); [Keltz \*et al.\*, 2010](#); [Martini \*et al.\*, 2010](#); [Ramlau-Hansen \*et al.\*, 2010](#); [Hammiche \*et al.\*, 2011, 2012](#); [Lotti \*et al.\*, 2011](#); [Relwani \*et al.\*, 2011](#); [Shayeb \*et al.\*, 2011](#); [Tunc \*et al.\*, 2011](#); [Braga \*et al.\*, 2012](#); [Eskandar \*et al.\*, 2012](#); [La Vignera \*et al.\*, 2012](#)). Three authors could not contribute to the meta-analysis because of incomplete data ([Strain \*et al.\*, 1982](#); [Nicopoulou \*et al.\*, 2009](#); [Paasch \*et al.\*, 2010](#)). We included previously unpublished data obtained from Jean Verdier Infertility Center, Bondy, France. Data from 19 articles, totaling 8359 men, which addressed the association between BMI and sperm parameters could not be analyzed ([Strain \*et al.\*, 1982](#); [Parazzini \*et al.\*, 1993](#); [Kort \*et al.\*, 2006](#); [Gao \*et al.\*, 2007](#); [Qin \*et al.\*, 2007](#); [Hammoud \*et al.\*, 2008, 2010](#); [Pauli \*et al.\*, 2008](#); [Robeva \*et al.\*, 2008](#); [Nicopoulou \*et al.\*, 2009](#); [Stewart \*et al.\*, 2009](#); [Bak \*et al.\*, 2010](#); [Hofny \*et al.\*, 2010](#); [Paasch \*et al.\*, 2010](#); [Sekhavat and Moein, 2010](#); [Wegner \*et al.\*, 2010](#); [Egwurugwu \*et al.\*, 2011](#); [Rybar \*et al.\*, 2011](#); [Fariello \*et al.\*, 2012](#)).

The present meta-analysis included a total of 21 eligible studies. All were cross-sectional studies, except two prospective cohort studies ([Vujkovic \*et al.\*, 2009](#); [Hammiche \*et al.\*, 2011, 2012](#)). The study sample sizes ranged from 72 ([Magnusdottir \*et al.\*, 2005](#)) to 1966 ([Shayeb \*et al.\*, 2011](#)) and totaled 13 077 individuals, including men from Jean Verdier Hospital Infertility Center ( $n = 717$ ) (Table 1). Study participants were from diverse countries, including Australia ([Tunc \*et al.\*, 2011](#)), China ([Li \*et al.\*, 2009](#)), Saudi Arabia ([Eskandar \*et al.\*, 2012](#)), Argentina ([Martini \*et al.\*, 2010](#)), Brazil ([Braga \*et al.\*, 2012](#)), USA ([Eskenazi \*et al.\*, 2003](#); [Chavarro \*et al.\*, 2010](#); [Keltz \*et al.\*, 2010](#); [Relwani \*et al.\*, 2011](#)), Denmark ([Jensen \*et al.\*, 2004](#); [Aggerholm \*et al.\*, 2008](#); [Ramlau-Hansen \*et al.\*, 2010](#)), Hungary ([Fejes \*et al.\*, 2005, 2006](#); [Koloszar \*et al.\*, 2005](#)), Iceland ([Magnusdottir \*et al.\*, 2005](#)), Italy ([Lotti \*et al.\*, 2011](#); [La Vignera \*et al.\*, 2012](#)), the Netherlands ([Vujkovic \*et al.\*, 2009](#); [Duits \*et al.\*, 2010](#); [Hammiche \*et al.\*, 2011, 2012](#)), Slovenia ([Zorn \*et al.\*, 2007, 2012](#)), UK ([Shayeb \*et al.\*, 2011](#)) and France ([Levy \*et al.\*, unpublished data](#)). They were recruited from the general population, including volunteers during military conscription, or fertility clinics (Table 1). Sperm analysis was performed according to WHO 1999 guidelines ([World Health Organization, 1999](#)) for all studies, except one ([Hammiche \*et al.\*, 2012](#)) which followed WHO 2010 guidelines ([World Health Organization, 2010](#)).

### Association between BMI and sperm count abnormality

With azoospermia and oligozoospermia considered as a single outcome, a J-shaped association was found between BMI and abnormal sperm count ( $< 40 \text{ M/ejaculate}$ ) (Fig. 2;  $n = 13\,077$  men analyzed). Compared with normal weight men, the ORs (95% CI) for oligozoospermia or azoospermia were 1.15 (0.93–1.43) for underweight men,



**Figure 1** Flow chart of screening for relevant articles in systematic review and meta-analysis of data on BMI and sperm count.

1.11 (1.01–1.21) for overweight men, 1.28 (1.06–1.55) for obese men and 2.04 (1.59–2.62) for morbidly obese men (see also Supplementary data, Figs S1–IV).

A similar J-shaped association was observed between BMI and abnormal sperm concentration ( $<15$  M/ml;  $n = 13\,453$  men analyzed). Compared with normal weight men, the ORs (95% CI) for oligozoospermia or azoospermia were 1.46 (1.14–1.88) for underweight men, 1.06 (0.95–1.18) for overweight men, 1.31 (1.07–1.61) for obese men and 1.97 (1.27–3.07) for morbidly obese men.

### Sensitivity analyses

Using fixed effects models did not substantially modify the results (underweight: 1.03, 0.83–1.28; overweight: 1.12, 1.05–1.19; obese: 1.26, 1.15–1.38; morbidly obese: 2.36, 1.93–2.89). Also, excluding data from Levy *et al.* (unpublished) did not influence the results: when this study was excluded, the ORs (95% CI) for abnormal sperm count were 1.10 (0.89–1.37) for underweight, 1.10 (1.00–1.22) for overweight, 1.31 (1.08–1.60) for obesity and 2.11 (1.59–2.80) for morbid obesity.

Possible sources of heterogeneity were investigated by stratifying the studies according to study population type (general population or clinical population, see Supplementary data, Fig. S5).

### Assessment of publication bias

The Egger test provided no evidence of publication bias when analyses were performed for underweight ( $P = 0.92$ ), overweight ( $P = 0.66$ )

or obesity ( $P = 0.79$ ) using ‘oligozoospermia or azoospermia’ as abnormal sperm count. Similar results were obtained for oligozoospermia or azoospermia analyzed separately.

## Discussion

This meta-analysis based on 13 077 men showed a J-shaped association between BMI and abnormal sperm count: underweight was associated with an increased but non-significant risk of abnormal sperm count, whereas overweight and obese men had a significantly elevated risk of abnormal sperm count compared with normal weight men.

The relationship between obesity and alteration of sperm parameters or male subfertility is likely to be multifactorial, and different pathophysiological hypotheses have been raised. First, alterations of the hypothalamic–pituitary–gonadal axis have been suggested to be involved in this process. Indeed, aromatization of steroids to estrogens in peripheral tissues leads to the hypogonadotropic hyperestrogenic hypogonadism previously described in obese men (Schneider *et al.*, 1979), with a significant decrease in total and free testosterone levels and increase in estradiol ( $E_2$ ), both leading to deleterious effects on spermatogenesis. Moreover, studies showed a decrease of sex hormone-binding globulin among obese men, notably mediated by hyperinsulinemia, emphasizing the negative feedback effect of elevated total  $E_2$  levels (Stellato *et al.*, 2000). Obesity is also associated with an increase of endorphins leading to a both lower LH pulse amplitude and GnRH production (Blank *et al.*, 1994). Some authors have also suggested that obesity may directly alter spermatogenesis and

**Table I** Characteristics of studies included in the meta-analysis.

Study	Population <sup>a</sup>	Ascertainment of BMI	Repeated semen collection	Age (years, mean $\pm$ SD)	Percentage by BMI category (kg/m <sup>2</sup> )					Percentage by TSC category		
					<18.5	18.5–24.9 (%)	25–29.9 (%)	30–39.9 (%)	$\geq 40$ (%)	Azoospermia	Oligozoospermia (%)	Normozoospermia (%)
Aggerholm <i>et al.</i> (2008), Denmark	1669 male volunteers from general population	Self-reported	Once	33.9 $\pm$ 8.8	0.5%	52.0	39.4	8.1	0	1.2%	11.1	87.7
Jensen <i>et al.</i> (2004), Denmark	1558 young male military recruits	Measured on site	Once	19.5 $\pm$ 1.3	3.5%	77.3	15.4	3.7	0.1	0.3%	45.2	54.5
Li <i>et al.</i> (2009), China	1338 healthy male volunteers	Measured on site	Once	32.4 $\pm$ 5.5	6.9%	74.1	17.8	1.2	0	0%	8.4	91.6
Ramlau-Hansen <i>et al.</i> (2010), Denmark	259 sons of mothers recruited during their pregnancy in 1984–1987	Self-reported	Once	20.1 $\pm$ 0.8	3.9%	72.2	17.8	6.1	0	0.8%	20.5	78.7
La Vignera <i>et al.</i> (2012), Italy	150 healthy non-smoking male volunteers	Self-reported	Twice	31.4 $\pm$ 2.3	0%	33.3	33.3	26.7	6.7	2.7%	41.3	56.0
Eskenazi <i>et al.</i> (2003), USA	97 non-smoking male volunteers without known fertility problems	Self-reported	Once	46.4 $\pm$ 15.9	0%	50.5	42.3	7.2	0	4.1%	12.4	83.5
Shayeb <i>et al.</i> (2011), UK	1966 male partners from subfertile couples presenting in fertility center	Measured on site	Once	33.1 $\pm$ 6.0	0.9%	40.8	44.9	12.5	0.9	EXC	18.2	81.8
Duits <i>et al.</i> (2010), The Netherlands	1401 male partners from subfertile couples presenting in fertility center	Self-reported	Twice	36.4 $\pm$ 6.5	0.4%	47.3	41.9	9.7	0.7	6.3%	17.5	76.2
Martini <i>et al.</i> (2010), Argentina	793 male partners from subfertile couples presenting in fertility center	Measured on site	Once	34.9 $\pm$ 6.2	EXC	31.0	49.4	18.5	1.1	1.9%	52.7	45.4

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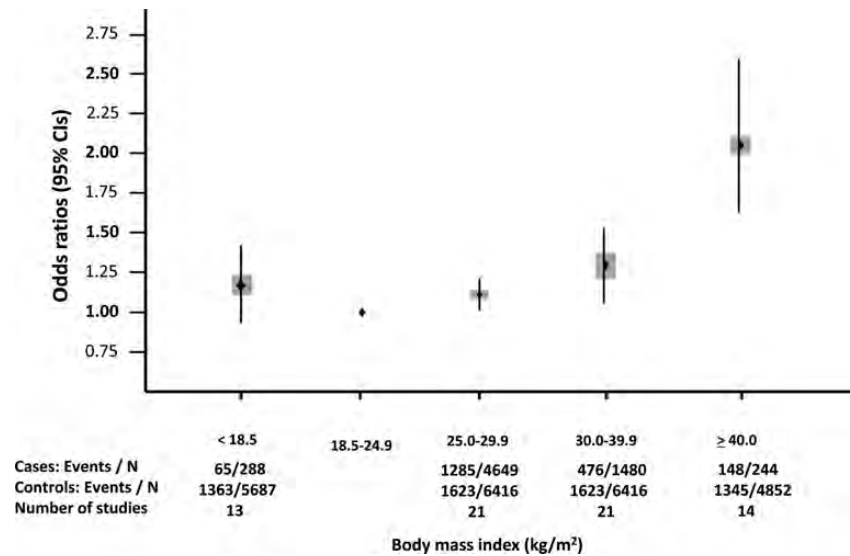
Table I Continued

Study	Population <sup>a</sup>	Ascertainment of BMI	Repeated semen collection	Age (years, mean $\pm$ SD)	Percentage by BMI category (kg/m <sup>2</sup> )					Percentage by TSC category		
					<18.5	18.5–24.9 (%)	25–29.9 (%)	30–39.9 (%)	$\geq 40$ (%)	Azoospermia	Oligozoospermia (%)	Normozoospermia (%)
Lévy <i>et al.</i> (unpublished data), France	717 male partners from subfertile couples presenting in fertility center	Self-reported	Once	37.4 $\pm$ 7.5	0.4%	45.5	38.9	13.5	1.7	8.2%	27.6	64.2
Eskandar <i>et al.</i> (2012), Saudi Arabia	500 male partners from subfertile couples presenting in fertility center	Measured on site	Twice	34.8 $\pm$ 7.7	11.0%	13.4	24.0	26.4	25.2	1.4%	29.0	69.6
Chavarro <i>et al.</i> (2010), USA	483 male partners from subfertile couples presenting in fertility center	Measured on site	Once	36.3 $\pm$ 5.4	EXC	25.5	48.2	23.8	2.5	EXC	10.8	89.2
Koloszar <i>et al.</i> (2005) and Fejes <i>et al.</i> (2005, 2006), Hungary	473 male partners from subfertile couples presenting in fertility center	Measured on site	Twice	29.5 $\pm$ 3.6	6.3%	33.6	32.4	22.0	5.7	4.4%	30.0	65.6
Hammiche <i>et al.</i> (2012), The Netherlands	449 male partners from subfertile couples presenting in fertility center	Measured on site	Once	35.4 $\pm$ 6.5	1.1%	34.1	49.2	15.2	0.4	5.8%	35.2	59.0
Braga <i>et al.</i> (2012), Brazil	250 male partners from subfertile couples during IVF/ICSI cycles	Measured on site	Once	38.4 $\pm$ 9.3	2.0%	50.0	40.0	4.0	4.0	EXC	34.4	65.6
Vujkovic <i>et al.</i> (2009) and Hammiche <i>et al.</i> (2011), The Netherlands	225 male partners from subfertile couples during IVF/ICSI cycles	Self-reported	Once	37.4 $\pm$ 5.3	0.9%	45.3	45.3	8.5	0	EXC	40.9	59.1

Lotti <i>et al.</i> (2011), Italy	222 male partners from subfertile couples presenting in fertility center	Measured on site	Once	$35.3 \pm 7.0$	0%	59.0	32.0	9.0	0	20.3%	37.8	41.9
Zorn <i>et al.</i> (2007), Slovenia	189 male partners from subfertile couples presenting in fertility center	Self-reported	Once	$34.4 \pm 5.8$	0%	43.9	41.8	14.3	0	22.2%	11.7	66.1
Keltz <i>et al.</i> (2010) and Relwani <i>et al.</i> (2011), USA	185 male partners from subfertile couples during IVF/ICSI cycles	Self-reported	Once	$37.5 \pm 8.0$	0.5%	22.2	47.0	29.2	1.1	EXC	44.9	55.1
Tunc <i>et al.</i> (2011), Australia	81 male partners from subfertile couples presenting in fertility center	Self-reported	Once	$36.8 \pm 5.2$	0%	25.9	45.7	28.4	0	EXC	28.4	71.6
Magnusdottir <i>et al.</i> (2005), Iceland	72 male partners from subfertile couples presenting in fertility center	Self-reported	Once	$37.0 \pm 5.4$	0%	36.1	44.4	15.3	4.2	2.8%	27.8	69.4

EXC, excluded; TSC, total sperm count.

<sup>a</sup>Size of the population corresponds to the size used for the main studied outcome.



**Figure 2** Association between BMI and abnormal TCS (oligozoospermia or azoospermia) according to categories of BMI.

Sertoli cell function (Winters *et al.*, 2006), as indicated by the more severe decrease of inhibin B levels compared with the decrease of FSH. Another hypothesis is the increase of scrotal temperature caused by hip and abdominal fat tissue accumulation, or even scrotal fat deposition (Shafik and Olfat, 1981), which would involve spermatogenesis disturbances. Preferential accumulation in fatty tissue of toxic substances and liposoluble endocrine disruptors would amplify those alterations, as indicated by serum organochlorine levels being correlated with BMI (Magnusdottir *et al.*, 2005).

When mean sperm concentrations were compared using SMD across BMI categories, no significant difference was observed (data not shown) in agreement with a previous meta-analysis (MacDonald *et al.*, 2010). Our analysis based on dichotomized sperm count or concentration, however, is in sharp contrast with the previous meta-analysis. We believe the current meta-analysis overcomes many of the limitations of previous attempts to summarize the association between BMI and semen quality. First, because sperm count has a highly skewed distribution, it is not unexpected that our analyses comparing means across BMI categories or previous analyses based on correlation statistics suggested no association between BMI and sperm count. We believe our alternative approach of dichotomizing sperm count at a prespecified and clinically relevant cutoff is more informative clinically and more adequate analytically. Secondly, ~30 articles assessing the association of BMI with sperm parameters have been published since the previous meta-analysis by MacDonald *et al.* (2010). Lastly, given the wide variety of statistical methods, BMI categories and outcomes used in published studies, we obtained individual patient data rather than relying on published information only. Thanks to this strategy, we achieve a more homogeneous meta-analysis.

Our study has several limitations. First, despite our efforts, incomplete data or absence of response from contacted authors led to the exclusion of 19 studies (Strain *et al.*, 1982; Parazzini *et al.*, 1993; Kort *et al.*, 2006; Gao *et al.*, 2007; Qin *et al.*, 2007; Hammoud *et al.*, 2008,

2010; Pauli *et al.*, 2008; Robeva *et al.*, 2008; Nicopoulou *et al.*, 2009; Stewart *et al.*, 2009; Bak *et al.*, 2010; Hofny *et al.*, 2010; Paasch *et al.*, 2010; Sekhvat and Moein, 2010; Wegner *et al.*, 2010; Egwurugwu *et al.*, 2011; Rybar *et al.*, 2011; Fariello *et al.*, 2012). Among them, 10 studies corresponding to 4809 men (Kort *et al.*, 2006; Hammoud *et al.*, 2008, 2010; Robeva *et al.*, 2008; Stewart *et al.*, 2009; Bak *et al.*, 2010; Hofny *et al.*, 2010; Paasch *et al.*, 2010; Sekhvat and Moein, 2010; Egwurugwu *et al.*, 2011) argued for a relationship between BMI and sperm parameters, whereas 9 studies investigating 3550 men (Strain *et al.*, 1982; Parazzini *et al.*, 1993; Gao *et al.*, 2007; Qin *et al.*, 2007; Pauli *et al.*, 2008; Nicopoulou *et al.*, 2009; Wegner *et al.*, 2010; Rybar *et al.*, 2011; Fariello *et al.*, 2012) did not. A selective outcome reporting can then probably be rejected and, owing to the high number of excluded studies showing an inverse association between BMI and sperm parameters, it is likely that this exclusion led to an underestimation of the computed ORs. Secondly, study populations varied, with men recruited from the general population or infertile couples. However, this variability also suggests that both the clinical population and the general population would benefit from our findings. Thirdly, BMI and conventional semen parameters were considered relevant enough to estimate body fat content and assess male fertility. BMI may not be the best indicator, as suggested by the questions about thresholds (Prentice and Jebb, 2001) and its inability to distinguish body fat composition or distribution, such as with waist circumference or waist-to-hip ratio (Fejes *et al.*, 2005; Akpinar *et al.*, 2007; Hammiche *et al.*, 2012). Nevertheless, our findings will prove easy to apply, as BMI is a marker widely used in clinical and research settings. Similarly, conventional semen parameters suffer from high uncertainty of measurement and only provide partial information about sperm functions. For example, functional tests, such as the hemizona assay or zona-binding test, have been suggested to be more relevant to predict fertilization outcome (Sifer *et al.*, 2005). Cutoff values for sperm parameters have also been blamed to be of insufficient clinical relevance because of



variations in semen analysis results, related to both physiological variations and limitations of the techniques used (Björndahl, 2011). However, conventional semen parameters remain the gold standard for primary clinical evaluation of male fertility. Notably sperm count is a relatively consensual and objective semen parameter (Auger *et al.*, 2000; Eustache and Auger, 2003) and TSC is a readily available parameter that most laboratories would assess fairly consistently with a WHO cutoff that can be used. We believe that, beyond controversies about reference limits, our meta-analysis offers several strengths, including the largest sample size ever published and the original use of standardized aggregated data.

In conclusion, a J-shaped association was found between BMI and the risk of abnormal sperm count, defined as oligozoospermia or azoospermia. Our systematic review with meta-analysis is in contradiction with a previous one that did not find associations of overweight and obesity with sperm concentration and TSC. Several methodological issues and updates in the literature have helped in understanding such a discrepancy. Although the risk may remain moderate at an individual level, our data indicate that high BMI affects sperm production. It is currently unclear whether weight loss can reverse this effect. Whereas weight loss was associated with an increase in TSC in a recent pilot cohort study (Hakonsen *et al.*, 2011), others reported a severe worsening of semen parameters during the months after bariatric surgery (Sermondade *et al.*, 2012b). Longitudinal studies and randomized controlled trials will then be required to evaluate whether weight normalization through diet modification and physical activity or bariatric surgery could improve sperm parameters and therefore male fertility.

## Supplementary data

Supplementary data are available at <http://humupd.oxfordjournals.org/>.

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## Authors' roles

N.S., C.F. and S.C. have full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analyses. R.L., S.C., N.S., L.F. studied the concept and designed the same. N.S., C.F., A.G.S., J.P.B., T.K.J., M.V.W., J.C., A.C.M., M.E., J.E.C., S.K., J.M.T., C.H.R.-H., E.B., F.L., R.P.M.S.-T., B.Z., A.J.P., S.L.V., B.E., K.T., E.V.M., I.F. were involved in acquisition of data. R.L., S.C., N.S., C.F., L.F., S.H. performed the analysis and interpretation of data. N.S., S.C., L.F. were helpful in the drafting of the manuscript. N.S., C.F., L.F., A.G.S., J.P.B., T.K.J., M.V.W., J.C., A.C.M., M.E., J.E.C., S.K., J.M.T., C.H.R.-H., E.B., F.L., R.P.M.S.-T., B.Z., A.J.P., S.L.V., B.E., K.T., E.V.M., I.F., S.H., R.L., S.C. contributed to the critical revision of the manuscript for important intellectual content. L.F. made the statistical analyses. S.C. supervised the study.

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## Conflicts of interest

None declared.

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