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The impact of body mass index on semen parameters and reproductive hormones in human males: a systematic review with meta-analysis

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BACKGROUND: It has been suggested that body mass index (BMI), especially obesity, is associated with subfertility in men. Semen parameters are central to male fertility and reproductive hormones also play a role in spermatogenesis. This review aimed to investigate the association of BMI with semen parameters and reproductive hormones in men of reproductive age.

METHODS: MEDLINE, EMBASE, Biological Abstracts, PsycINFO and CINAHL databases and references from relevant articles were searched in January and February 2009. Outcomes included for semen parameters were sperm concentration, total sperm count, semen volume, motility and morphology. Reproductive hormones included were testosterone, free testosterone, estradiol, FSH, LH, inhibin B and sex hormone binding globulin (SHBG). A meta-analysis was conducted to investigate sperm concentration and total sperm count.

RESULTS: In total, 31 studies were included. Five studies were suitable for pooling and the meta-analysis found no evidence for a relationship between BMI and sperm concentration or total sperm count. Overall review of all studies similarly revealed little evidence for a relationship with semen parameters and increased BMI. There was strong evidence of a negative relationship for testosterone, SHBG and free testosterone with increased BMI.

CONCLUSIONS: This systematic review with meta-analysis has not found evidence of an association between increased BMI and semen parameters. The main limitation of this review is that data from most studies could not be aggregated for meta-analysis. Population-based studies with larger sample sizes and longitudinal studies are required.

Key words: body mass index / semen / reproductive hormones / systematic review / obesity

Introduction

Subfertility is a serious health problem affecting the lives of at least 10% of the population in the developed world (Taylor, 2003). Assisted reproductive technology (ART), mostly in the form of *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI), is now able to treat couples with fertility problems with considerable success. However, it is accepted that ART only bypasses the problem of subfertility and, in many cases, the underlying cause of the patient's impaired fertility may never be determined or treated. Therefore, research into potential modifiable risk factors may ultimately lead to more satisfactory and cost-effective preventative and curative treatments.

Most developed nations are reporting increasing proportions of men and women in their reproductive years who are overweight and obese (Pasquali *et al*., 2007). These proportions are higher with increasing age. There are many negative health consequences of being overweight and reduced fertility is now recognized as one of them. This relationship has been especially well-established in women. Overweight and obese women are more likely to experience ovulatory and menstrual disorders, consequently experiencing delayed fertility (Pasquali *et al*., 2007). Obese women have poorer outcomes when undergoing fertility treatment, experiencing lower pregnancy rates, increased likelihood of miscarriage and requiring higher doses of gonadotrophins (Maheshwari *et al*., 2007). They are also more likely to experience complications during pregnancy, including gestational diabetes and pre-eclampsia.

Research into the impact of body mass index (BMI), or more specifically overweight and obesity, on the reproductive health of males has been limited in comparison to the extensive research undertaken to investigate female subfertility (Pasquali *et al*., 2007). Studies of semen parameters are scarce, yet male factor alone constitutes approximately 25–30% of all cases of subfertility (Hammoud *et al*., 2006). Recently, several large-scale cross-sectional studies have reported results from a general population setting (Jensen *et al*., 2004; Qin *et al*., 2007; Aggerholm *et al*., 2008) alongside a number of studies from subfertile populations (Koloszár *et al*., 2005; Kort *et al*., 2006; Chavarro *et al*., 2008; Hammoud *et al*., 2008b).

Overweight and obesity are expected to be associated with changes to the male reproductive hormone profile. It is already accepted that a high BMI is associated with alterations in the levels of testosterone and estrogens (Pasquali, 2006), as well as sex-hormone binding globulin (SHBG) (Pasquali, 2006). The impact of obesity on free testosterone, gonadotrophins and inhibin B, however, is less well-established.

It has also been proposed that if a relationship between semen parameters and BMI exists, the mechanism for this is likely to involve, at least in part, some alteration or derangement of the male reproductive hormone profile, which might also be related to BMI (Pasquali *et al*., 2007; Qin *et al*., 2007; Hammoud *et al*., 2008a). Reviewing the impact of BMI on both semen parameters and male reproductive hormones may also direct further exploration into the endocrinology of spermatogenesis as well as obesity. The aim of this systematic review was therefore to investigate the impact of BMI on semen parameters and reproductive hormones in men of reproductive age from both general and subfertile populations (Fig. 1).

Methods

A systematic review was undertaken to investigate the impact of BMI on semen parameters and reproductive hormones in human males of reproductive age in developed countries. This has been reported according to the standards of the Quality of Reporting of Meta-analysis of Randomized Controlled Trials and Observational Studies (QUORUM, MOOSE) statements (Moher *et al*., 1999; Stroup *et al*.,. 2000). Published studies and abstracts were included. No restrictions applied for either language or date of publication. Review articles were retrieved as a useful source of references.

Inclusion criteria and outcomes of interest

The inclusion criteria were studies of participants who were all human males of reproductive age, including both adult and adolescent males.

The outcomes included were:

(i) Any measures of sperm concentration, total sperm count, semen volume, sperm motility or sperm morphology, including composite measures of these variables.

(ii) Any basal measurements of the following reproductive hormones: follicle-stimulating hormone (FSH), luteinising hormone (LH), estradiol (E_2), testosterone (T) and free testosterone (free T), inhibin B and SHBG.

The outcome for all eligible studies must have been related to BMI or a similar measure of relative weight, such as ideal body weight (IBW). No exclusions applied to the statistical methods used.

Exclusion criteria

Animal studies and other biomedical and laboratory-based research were excluded. Experimental studies and studies undertaken to assess the effects of any intervention were excluded. Case reports were excluded. For studies investigating the relationship between BMI and reproductive hormones, those with study populations of less than 100 men were excluded from this aspect of the review as it was thought that it was unlikely that they would provide sufficient information to answer the research question. Studies of populations where the mean age was <12 years old or >60 years old were excluded.

Studies of populations that involved primarily men with particular diseases or organic disorders of the reproductive organs were excluded. These included varicocele, abnormal location of the testes, torsion of the testis and history of severe trauma to the genitalia. Studies primarily of azoospermic men were also excluded on the basis that it is not possible to have relationships between semen parameters and BMI with azoospermia, due to the absence of measurable semen parameters. Studies with populations consisting only of men who had previously experienced surgery in the genital and pelvic area, including vasectomy, orchidopexy and hernia surgery, were excluded. Similarly, studies only of men that have been exposed to particular environmental factors known to compromise semen parameters, such as pesticide factory workers or welders, were additionally excluded.

Studies of reproductive hormones that reported only measurements of hormones after stimulation were excluded. Studies with overall fertility or pregnancy rate as the only outcome were excluded. In the cases where duplicate datasets were used for analysis in multiple articles, only one article was included, with those papers with the smallest data sample or the fewest outcome measures being excluded.

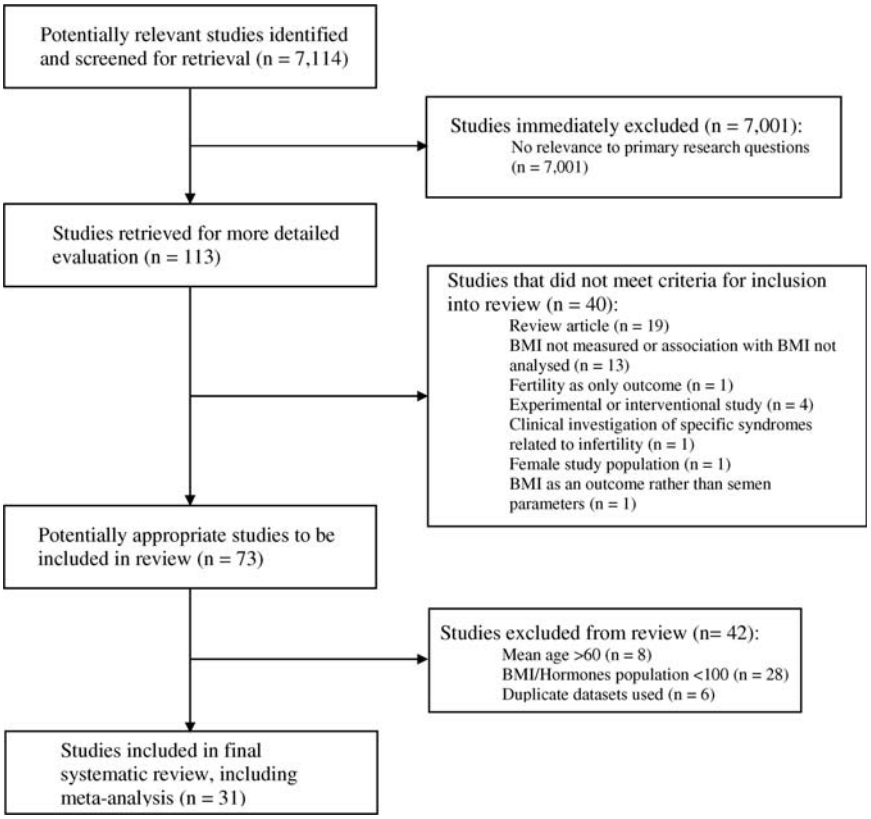

Figure 1 QUOROM statement flow diagram for systematic review of BMI, semen parameters and reproductive hormones, including meta-analysis of relationship between BMI and semen parameters.

Search strategy

MEDLINE (1950 to January, 2009), EMBASE (1980 to December, 2008), Biological Abstracts (1969 to December, 2008), PsycINFO (1806 to January, 2009) and the CINAHL database (1981 to January, 2009) were comprehensively searched. Two searches were completed for each database, one independent search conducted for each relationship being reviewed (BMI and semen parameters; BMI and reproductive hormones). All databases were searched from their start date to their most recent entries. Full search strings are included in Supplementary Material.

Search terms used for BMI were: BMI, body weight, overweight, obesity, IBW, ideal weight. Search terms used for semen parameters were: semen, semen quality, semen volume, spermatozoa, sperm, sperm count, sperm concentration, sperm quantity, sperm motility, sperm morphology, sperm head, sperm midpiece, sperm tail, spermatids, spermatocytes, spermatogonia, antisperm antibodies, sperm chromatin integrity, DNA fragmentation index (DFI), oligospermia.

Search terms used for the male reproductive hormones were: male reproductive hormone, male hormone profile, reproductive hormone, testosterone, free testosterone, free testosterone index, free androgen, free androgen index (FAI), unbound testosterone, estradiol, estrogen, FSH, LH, gonadotrophins, pituitary gonadotrophins, gonadotrophin-realeasing hormone, GnRH, inhibin, gonadal hormone, gonadal steroid hormone, sex steroid, sex steroid hormone, progesterone, sex hormone-binding globulin, SHBG, testosterone-estradiol ratio.

The field term 'textword' was used for all search terms and Medical Subject Headings (MeSH) were used where available. Appropriate synonyms, variant spellings and truncations were included for each search term where appropriate. No language limits were applied. Limits were applied for humans and males in all searches.

Search methods

All titles in database results were screened for relevance to this review. The abstracts of relevant titles were then read and all studies that potentially met the inclusion criteria were retrieved. The reference lists of all retrieved studies, both included and excluded and relevant reviews were hand-searched to identify any additional studies that may have met the inclusion criteria.

Data extraction

The conclusions of each study with regard to the investigated association with BMI were recorded. Quantitative results were not systematically reported in this review. Due to the wide variety of statistical methods and outcomes used in these studies, it was not anticipated that quantitative data would itself be useful in reviewing the studies published so far, except for the meta-analysis described below.

The characteristics of each study recorded were: number and type of participants, the BMI distribution if BMI categories were used, the BMI distribution of the study population and the statistical methods used to investigate the relationship between BMI and semen parameters or reproductive hormones. The age distribution was also recorded if the mean age was within 15 years of the age exclusion threshold.

Meta-analysis

Meta-analysis of observational data by means of weighted regression was undertaken using only cross-sectional studies that reported mean or median sperm concentration or mean or median total sperm count in BMI categories as an outcome. Semen parameters used in the meta-analysis were: mean sperm concentration, median sperm concentration, mean total sperm count, median total sperm count, mean semen volume and sperm motility.

Data were organized so that each study had up to four entries, one for each BMI category. Each entry included the study, semen parameter, BMI group and the number of observations. BMI category was coded from one to four to denote the standard BMI classifications of underweight (<20), normal weight (20–25), overweight (25–30) and obese (>30), except in studies that had wider ranges for the BMI categories. In these studies, an intermediate code was assigned to represent that BMI category.

Analysis was by weighted linear regression in Stata 10 (Stata 10, StataCorp, Texas, USA) for each of the semen parameters using BMI category as a continuous variable. These regressions were weighted by the number of people in the group to give more weight to larger studies. They were also clustered by study to allow for different correlations within and between studies.

Results

In total, 31 articles were included in this review: six studies investigated the relationship between BMI and semen parameters, 18 investigated the relationship between BMI and male hormone profile. A further seven investigated both relationships, although four of these studies had study population sizes of less than 100 men and were therefore not included in the reproductive hormones aspect of this review, but were still included in the results for semen parameters. The characteristics and findings of all of these studies are presented in Table I (semen parameters) and Table II (reproductive hormones).

Description of studies

Thirteen studies were included in the BMI and semen parameters aspect of this review, providing cross-sectional data on a total of 6793 men. All of these were cross-sectional studies, except for one, which was a case–control study. Twenty-one studies were reviewed in the BMI and male reproductive hormones aspect of this review, providing cross-sectional data on a total of 15 060 men. All were cross-sectional studies, except for one longitudinal study and one interventional study. The longitudinal study (Mohr *et al.*, 2005) reported cross-sectional data at separate intervals and the interventional study (Hautanen *et al.*, 1994) performed cross-sectional analysis only on the placebo group of men that had been randomly allocated and had not received any intervention. One study was published in German (Kley and Krüskemper, 1979) and this was translated into English by a German medical student from the University of Auckland's School of Medicine.

Of all included studies, three studies reported IBW instead of BMI (Kley and Krüskemper, 1979; Strain *et al.*, 1982; Jarow *et al.*, 1993). All three were small studies, with population sizes of between 45 and 120. For calculation of BMI, three studies used self-reported measurements of weight and height (Allen *et al.*, 2002; Aggerholm *et al.*, 2008; Hammoud *et al.*, 2008b), whereas height and weight were measured by investigators in the remaining studies.

Participants in these studies were sampled from both a general population setting as well as from subfertile populations, recruited from patients attending fertility clinics for investigation or treatment of infertility. For the 13 studies of semen parameters, only six used general population samples, with the remaining seven recruiting men from fertility clinics. The three largest of these studies consisted of men sampled from a general population setting. Eighteen studies of reproductive hormones were solely of men from the general population, with the remaining three studies specifically including subfertile men in their sample. Studies from all population backgrounds were reviewed together without distinction based on factors such as the type of population sampled.

Five studies investigating semen parameters reported data in a manner suitable for data pooling and meta-analysis according to the outcomes specified in the Methods section above. Studies also reported a variety of other outcomes that were either uncommonly reported, such as sperm morphology, or combined semen parameters into a single composite measure, such as normal-motile sperm (NMS) count (Kort *et al.*, 2006), relative risk of dyspermia (Parazzini *et al.*, 1993) and progressively motile sperm count (Hammoud *et al.*, 2008b). Six studies reported results with a regression analysis or correlation coefficient to assess the relationship of semen parameters with BMI.

For the reproductive hormones, studies reported either average hormone levels for different BMI categories or correlation or regression coefficients, both of which allow for the assessment of the relationship between reproductive hormone levels and BMI. Of the 21 studies included, testosterone was measured in 20, SHBG in 15, estradiol in 10, inhibin B in 3, FSH in 6 and LH in 9. Free testosterone was measured in 12 studies, with a further two measuring the related FAI.

Twenty-eight studies investigating only the relationship between BMI and reproductive hormones were excluded on the basis that their study population was of insufficient size (100 men or less). A further eight articles were excluded due to having a mean age >60 years. One study that investigated BMI and semen parameters was excluded on the basis that it used BMI as an outcome to compare normozoospermic and oligozoospermic men rather than using a semen parameter as an outcome. Additionally, six published studies were excluded on the basis that they used data from identical sources as three other included studies (Jankowska *et al.*, 2000; Mohr *et al.*, 2005; Kort *et al.*, 2006). All excluded studies and their reasons for exclusion are listed in Supplementary Material, Table S1.

Meta-analysis of BMI and semen parameters

In this review, a total of six cross-sectional studies were included with sperm concentration or total sperm count as an outcome. The meta-analysis used five of these, with data from one study unable to be pooled as it did not report the BMI distribution of its study population (Chavarro *et al.*, 2008). Data used from these studies is compiled in Table III and the regression coefficients calculated in the meta-analysis are presented in Table IV. There was no evidence from this meta-analysis that there is a relationship between BMI category and mean sperm concentration, median sperm concentration, mean total sperm count, median total sperm count, mean semen volume or average sperm motility.

Table I Characteristics and results of studies investigating BMI and semen parameters

Study	Participants	BMI distribution	Statistical methods	Conclusions: relationship with BMI	Notes
Studies included in meta-analysis					
Aggerholm *et al.* (2008)	1989 European men. Data from five population-based environmental studies in Denmark, Belgium, UK, Italy, Greenland, Sweden, Ukraine and Poland (1992–2005)	<20 ($n = 67$)	Regression analysis	No statistically significant association for sperm concentration, total sperm count or sperm motility ($P = 0.139$, $P = 0.102$, $P = 0.062$, respectively)	Largest study undertaken that investigates BMI and semen
		20–25 ($n = 986$)	Comparison of mean semen parameters between men from 4 BMI categories (shown to left)		Participants recruited from a general population setting
		25–30 ($n = 773$) >30 ($n = 171$) Mean = unreported			Multi-national study (eight European countries) Weight and height self-reported Study sample had a wide age range (range = 18–66)
Jensen *et al.* (2004)	1558 young Danish men attending compulsory physical examination for military conscription.	<20 ($n = 217$)	Regression analysis	Significant negative relationships were found for sperm concentration and total sperm count	Narrow population—mostly young men with normal BMI. Very few had BMI > 25. 1170 (75%) aged 18–20 years
		20–25 ($n = 1042$)	Comparison of median semen parameters between men from three BMI categories (shown to left)	No significant associations were found for semen volume or sperm motility, except in underweight men where these semen parameters were lower than in normal weight men. No association was found for sperm morphology	Men with chronic diseases excluded
		>25 ($n = 299$) Median (95% CI) = 22.4 (20.4, 24.3)			
Qin *et al.* (2007)	990 men enrolled from general population in China	<18.5 ($n = 42$)	Comparison of mean semen parameters between men from four BMI categories (shown to left)	Significant positive relationships were found for sperm concentration ($r = 0.1120$, $P < 0.01$) total sperm count ($r = 0.0930$, $P < 0.01$) and normal sperm morphology ($r = 0.1030$, $P < 0.01$)	Only 1.7% had a BMI > 30, too few to include in some analyses

Continued

Table I *Continued*

Study	Participants	BMI distribution	Statistical methods	Conclusions: relationship with BMI	Notes
		18.5–25 ($n = 690$)	Comparison of odds-ratios for low sperm concentration, total sperm count and sperm motility between men from three BMI categories (shown to left, with obese men excluded from this analysis).	When semen values were compared between BMI categories, only the underweight group (BMI < 18.5) had significantly different mean values to that of the normal weight group (BMI 18.5–25)	Men with genital diseases, chronic diseases, heaving smoking and regular alcohol consumption excluded
		25–30 ($n = 241$)		A significant negative relationship was found for sperm motility ($r = -0.1100$, $P < 0.01$), although this did not remain statistically significant when adjusted for study centre, age, diseases of the reproductive organs, smoking, alcohol and period of abstinence.	Suggests that overweight may be protective against low sperm concentration and total sperm count.
		>30 ($n = 17$)		Odds-ratios for low sperm concentration, total sperm count or sperm motility was not significantly different between BMI categories	
		Mean ($\pm$SD) = 23.2 $\pm$ 2.9		No statistically significant associations between BMI and semen volume	
Koloszár *et al.* (2005)	274 normozoospermic males presenting at fertility clinic in Hungary	<20 ($n = 29$)	Comparison of mean semen parameters between men from four BMI categories (shown to left)	Found a significant negative relationship for sperm concentration, although the lower sperm concentration was only statistically significant in obese men compared with normal weight men ($P < 0.05$)	Only reported relationship with sperm concentration
		20–25 ($n = 96$) 25–30 ($n = 91$) >30 ($n = 58$) Mean ($\pm$SD) = 27.6 $\pm$ 4.9 Range = 17–39			Semen analyses repeated once
Fejes *et al.* (2006)	42 oligozoospermic men presenting at a fertility clinic in Hungary.	$\leq$25 ($n = 17$)	Comparison of mean semen parameters between men from two BMI categories (shown to left)	Sperm concentration found to be significantly lower in men with a BMI > 25 than men with a BMI < 25	Study population was only of oligozoospermic men (no controls)
		>25 ($n = 25$)		No association found for semen volume, sperm motility and sperm morphology	Only used two BMI categories (>25 and $\leq$25)
		Mean ($\pm$SD) = 27.6 $\pm$ 4.6 Range = 18–37			Semen analyses repeated once
Studies not included in meta-analysis					
Kort *et al.* (2006)	520 men presenting at a fertility clinic in Georgia, USA	20–25 ($n =$ unreported)	Regression analysis	Significant negative relationship found with normal-motile sperm (NMS) count (NMS = $-1.534 \times$ BMI $- 49.028$, $P < 0.05$)	Limited outcome data (note: NMS = volume $\times$ concentration $\times$ %motility $\times$ %morphology)

		25–30 (n = unreported) >30 (n = unreported) Mean ($\pm$SEM) = 27.5 $\pm$ 0.49	Comparison of mean semen parameters between men from three BMI categories (shown to left) (DFI = 1.145 × [BMI] − 6.079, $P < 0.05$)	Significant positive relationship with DNA Fragmentation Index (DFI)	
Chavarro *et al*. (2008)	483 men presenting at a fertility clinic in Massachusetts, USA	18.5–25 (n = unreported) 25–30 (n = unreported) 30–35 (n = unreported) >35 (n = unreported) Mean = unreported	Comparison of median semen parameters between men from four BMI categories (shown to left)	A significant negative relationship was found for total sperm count ($P = 0.04$) and semen volume (no data reported) No association found between BMI and sperm concentration, sperm morphology or sperm motility	Published in abstract form only No indication of BMI distribution Unknown exclusion criteria
Hammoud *et al*. (2008b)	390 men presenting at a fertility clinic in Utah, USA.	20–25 (n = 94) 25–30 (n = 168) >30 (n = 128) Mean ($\pm$SEM) = 28.5 $\pm$ 0.26	Comparison of prevalence and odds-ratio of oligozoospermia and low progressively motile sperm count between men from three BMI categories (shown to left).	The prevalence of oligozoospermia (sperm concentration <20 M/ml) and low progressively motile sperm count (progressively motile sperm <10 M) increased significantly with higher BMI The odds ratios of oligozoospermia and low progressively motile sperm count in obese men compared with non-obese (BMI < 25) men were 3.3 (95% CI = 1.19, 9.14) and 3.4 (95% CI = 1.12, 10.60), respectively. The odds ratio of a high proportion of abnormal sperm morphology in obese men compared with non-obese men (BMI < 30) was 1.6 (95% CI = 1.05, 2.59).	Height and weight self-reported Patients with known male factor infertility were excluded
Parazzini *et al*. (1993)	323 men in Italy	<23 (n = 108)	Comparison of age-adjusted relative risk of dyspermia between men of three BMI categories (shown to left) using dyspermic cases and normozoospermic controls	No significant relationship between BMI and the risk of dyspermia (sperm concentration of 5–10 M/ml, sperm motility <30%, abnormal sperm morphology >30%)	Case–control study.

Continued

Table I *Continued*

Study	Participants	BMI distribution	Statistical methods	Conclusions: relationship with BMI	Notes
	105 were fertile men (unknown semen parameters), 97 infertile men with dyspermia, 121 normozoospermic infertile men	23–25 ($n = 108$)			Used dyspermia, which is not a conventional outcome measure and has a very narrow definition (similar to oligoasthenoteratozoospermia)
		>25 ($n = 105$) Mean = unreported			
Pauli *et al.* (2008)	87 men in Pennsylvania, USA	Mean ($\pm$SD) = 29.3 $\pm$ 6.5	Regression analysis	No relationship with sperm concentration, semen volume, sperm motility or total motile sperm count	
		Range = 16.1–47.0			
Magnusdottir *et al.* (2005)	72 men presenting at the fertility clinic in Iceland	Did not use categories	Regression analysis	A statistically significant negative association was found between BMI and sperm concentration as well as total sperm count	Participants recruited from a general population setting
	Mean (95% CI) = 26.3 (19.7,14.5)			This was not statistically significant for men with male-factor subfertility	Very small study population
					Study mainly focused on evaluating the effects of environmental factors (organochlorine pesticides) on fertility
Strain *et al.* (1982)	45 men in New York, USA	21 = obese men (52–332% above IBW)	Semen parameters compared with normal population values derived from a prior population study	Obese men found to have a distribution of semen volumes and sperm concentrations almost identical to that of a normal population sample	Used IBW (Ideal Body Weight) according to Metropolitan Life Insurance Company tables
		24 = non-obese men (unreported weights) Mean = unreported			No known exclusion criteria, although all men were stated to be 'healthy'
Ayers *et al.* (1985)	20 male marathon athletes in Michigan, USA	Mean = 24.4	Regression analysis	No correlation between BMI and total sperm count (no data published)	All participants were marathon runners
		Range = 17.8–25.4			Narrow BMI range, very few overweight and none obese

Table II Characteristics and results of studies investigating BMI and reproductive hormones

Study	Population	BMI distribution	Statistical methods	Conclusions: relationship with BMI	Notes
Wu *et al.* (2008)	3200 European men participating in the European Male Aging Study (EMAS), made up of a random sample of men from the UK, Belgium, Sweden, Estonia, Poland, Hungary and Italy	Mean (95% CI) = 27.7 (27.5–27.8)	Regression analysis	Significant negative relationships found for T, free T and SHBG	Participants recruited from general population
			Comparison of mean hormone levels between men of three BMI categories (<25, 25–30, >30)	No statistically significant association found for LH	Multi-national study (seven European countries)
					Mainly a study of ageing men Mean age = 59.7 (59.3–60.1) [mean (95% CI)] Age range = 40–79
Aggerholm *et al.* (2008)	1989 men in Europe (Table I)	<20 ($n = 67$)	Comparison of mean semen parameters between men of four BMI categories (shown to left)	Significant negative relationships found for T and SHBG ($P < 0.001$ for both relationships)	Weight and height self-reported
		20–25 ($n = 986$)		Inhibin B was found to be significantly lower at BMI values above or below the normal BMI range of 20–25 (inverse U shaped association), $P = 0.02$)	Participants recruited from general population
		25–30 ($n = 773$)		No statistically significant relationships were found for E_2, LH or FSH ($P = 0.732$, $P = 0.689$, $P = 0.836$, respectively)	Multi-national study (eight European countries)
		>30 ($n = 171$)			
Mohr *et al.* (2005)	1677 men in Massachusetts, USA participating in the Massachusetts Male Ageing Study (MMAS). Used only cross sectional data from initial sample (T1: 1987–1989)	<29 ($n = 460$)	Comparison of mean hormone levels between men of two BMI categories (shown to left)	T, free T and bioavailable T were found to be significantly lower in men with a BMI > 29 than those with a BMI < 29 ($P < 0.001$, $P < 0.01$ and $P < 0.01$, respectively)	Participants recruited from general population
		>29 ($n = 1217$)			Mainly a study of ageing men Mean age of men in initial sample = 55.2 ± 8.7 Age range = 40–70 Data from follow-up samples (T2: 1995–1997 and T3: 2002–2004) excluded from this review due to mean age of these samples being >60. However, the same relationships were identified in these later samples as well No exclusion criteria

Continued

Table II *Continued*

Study	Population	BMI distribution	Statistical methods	Conclusions: relationship with BMI	Notes
Jensen *et al.* (2004)	1558 young men in Denmark (Table I)	<20 ($n = 217$)	Comparison of median hormone levels between men of three BMI categories (shown to left)	Significant negative relationships found for T, SHBG and inhibin B (especially strong in SHBG). A negative relationship was also found for FSH, which was significantly higher in slim men (BMI < 20)	Narrow population—mostly young men with normal BMI. Very few had BMI > 25
		20–25 ($n = 1042$)		Significant positive association found for E_2 and free androgen index (FAI)	Mean age = 19. 1170 men (75%) were aged 18–20 years
		>25 ($n = 299$)		No statistically significant relationship reported for LH	Men with chronic diseases excluded
		Median (95% CI) = 22.4 (20.4, 24.3)			
Svartberg *et al.* (2004)	1548 men in Tromso, Italy participating in the Tromso population-based health survey	Mean (± SD) = 26.1 ± 3.4	Correlation coefficients	Significant negative relationships found for T ($r = -0.31$, $P < 0.001$), free T ($r = -0.07$, $P < 0.01$) and SHBG ($r - -0.42$, $P < 0.001$)	Participants recruited from general population
					Included older men. Mean age (± SD) = 60.3 ± 10. Age range = 55–74
Qin *et al.* (2007)	990 men in China (Table I)	<18.5 ($n = 42$)	Comparison of mean hormone levels between men of four BMI categories (shown to left)	Negative relationship found for T. Positive relationship found for FSH	Men with genital diseases, chronic diseases, heaving smoking and regular alcohol consumption excluded
		18.5–25 ($n = 690$) 25–30 ($n = 241$) >30 ($n = 17$) Mean (± SD) = 23.2 ± 2.9		E_2 and LH were not related to BMI	
Allen *et al.* (2002)	696 men in the UK recruited from the general population for a study investigating the effect of lifestyle and nutrition, particularly vegetarianism and veganism, on male hormones	<20 ($n = 53$)	Comparison of mean hormone levels between men of four BMI categories (shown to left)	Significant negative association found for T ($P < 0.0001$). There was a statistically significant negative association for free T ($P = 0.031$), although this was not strong, with obese men having only 5% lower free T than lean men	Participants recruited from general population
		20–25 ($n = 422$)		Significant negative association found for SHBG and LH ($P < 0.0001$ and $P = 0.007$, respectively)	Height and weight self-reported
		25–30 ($n = 180$) >30 (n–41) Median (IQR) = 23.5 (21.6–25.7)			Included some older men Mean age (IQR) = 46.0 (38–58) Age range = 20–70

Schatzl *et al.* (2003)	561 men in Vienna, Austria	Unreported	Correlation coefficients	Significant negative relationships found for T ($r = -0.428$, $P < 0.001$) and free T ($r = -0.446$, $P < 0.001$)	Participants recruited from general population
	526 were recruited through health screening projects organized at workplaces 35 were recruited from the general population according to the SENIEUR protocol				Included some older men. Mean age ($\pm$SD) = 45.6 $\pm$ 15.7. Age range = 20–89 No exclusion criteria except those recruited under the SENIEUR protocol ($n = 35$), which excluded men with any signs of underlying disease
Muller *et al.* (2003)	400 men in the Netherlands recruited from the general population	Mean = 26.3	Regression analysis	Significant negative relationships found for T, bioavailable T and SHBG ($P < 0.001$ for all relationships)	Participants recruited from general population
		Range = 17–43		Significant positive relationship found for E_2 ($P = 0.003$)	Mainly a study of ageing men Mean age = 60.2. Age range = 40–80 No exclusion criteria
Meeker *et al.* (2007)	388 men presenting at a fertility clinic in Massachusetts, USA	Mean ($\pm$SD) = 28 $\pm$ 4.6	Regression analysis	Negative relationship for T, SHBG and inhibin B Positive relationship for FAI	Data for BMI not presented (no *P*-values) Excluded men with vasectomy
Ukkola *et al.* (2001)	324 men enrolled in the HERITAGE Family Study, a multicentre study of healthy adults in the USA and Canada (hormone data available on between 295 and 324 men, depending on hormone)	Mean = 27.1	Regression analysis	Significant negative relationships for T and SHBG ($P \leq 0.003$ for both relationships)	Excluded men with a BMI > 40
			Correlation coefficients	No significant association found for E_2 BMI was found to be the most important predictor of both T and SHBG concentrations compared with all other variables, including age	Men with chronic diseases excluded Participants recruited from general population Multi-national study (two North American countries)
Meikle *et al.* (1989)	323 men of twin or triplet births living in Utah, USA (160 twin pairs and one set of triplets)	Range = 80–140% IBW	Factor analysis of the effect of BMI on hormone levels in twin pairs	Found that BMI had significant negative effect on T and SHBG BMI had no significant effect on free T, LH, FSH and T/E_2 ratio	Used IBW (Ideal Body Weight) according to Metropolitan Life Insurance Company tables No exclusion criteria
Jankowska *et al.* (2000)	236 men in Poland recruited from the general population. 95 formed a younger group of men (aged 22–33). 141 formed an older group of men (aged 40–67)	<27 ($n = 175$)	Regression analysis	Significant positive association found for T in younger, but not older, men	Men recruited from general population
		≥27 ($n = 61$)	Comparison of BMI ranges in groups of men with different hormone levels	No associations found for free T or E_2 in younger or older men	Included some older men
		Mean = 25.2			Men with gonadal dysfunction excluded

Continued

Table II *Continued*

Study	Population	BMI distribution	Statistical methods	Conclusions: relationship with BMI	Notes
Andersson *et al.* (2004)	178 men in Denmark. 100 were proven fertile men and 78 were idiopathic oligozoospermic men referred to a fertility clinic	Median (2.5, 97.5 percentile) = 24.2 (19.4, 31.3) in fertile men	Regression analysis	No relationships found for inhibin b or FSH (relationship data not reported)	Only measured FSH and inhibin B
		Median (2.5, 97.5 percentile) = 25.3 (19.4, 34.5) in oligozoospermic men			Measurement procedures for BMI unreported
		Range = 19.4–34.5			Men with obstructive azoospermia, orchitis or possible iatrogenic causes of infertility were excluded
Haffner *et al.* (1993)	178 men in the San Antonio Heart Study, a population-based study consisting of randomly selected Mexican American ($n = 75$) and white men ($n = 103$) in Texas, USA	Mean ($\pm$SD) = 27.6 $\pm$ 0.6 in Mexican Americans	Correlation coefficients	Negative relationship found for T ($r = -0.335$, $P < 0.001$), free T ($r = -0.248$, $P < 0.001$) and SHBG ($r = -0.177$, $P < 0.05$)	Participants recruited from general population
		Mean ($\pm$SD) = 27.1 $\pm$ 0.5 in white Americans		No significant relationship found for E_2	Included some older men. Mean ($\pm$SD) ages were 53.0 $\pm$ 1.2 in Mexican Americans and 52.1 $\pm$ 1.2 in whites No exclusion criteria
Hofstra *et al.* (2008)	160 obese men in the Netherlands	30–35 ($n = 27$)	Regression analysis	Significant negative relationships found for T and free T ($P < 0.001$ for all relationships)	Included only obese men (all men had a BMI > 30). Therefore no normal weight controls
		35–40 ($n = 38$)	Comparison of mean hormone levels between men of five BMI categories (shown to left)	Significant positive relationship found for E_2 ($P < 0.001$)	Excluded men with renal insufficiency, pituitary disease and hypogonadotrophic hypogonadism
		45–50 ($n = 24$)	Comparison of prevalence of subnormal testosterone between men of five BMI categories (shown to left)	No associations found for LH or FSH	Concluded that male obesity leads to a reduction of testosterone levels well into the hypogonadal range
		>50 ($n = 27$)	Comparison of mean BMI between men with low testosterone (hypogonadal) and men with normal testosterone (eugonadal)	No relationship found for SHBG, although this was in the lower end of the normal reference range for all obese men	Propose that SHBG probably does decrease with BMI, except that there is a possible plateau effect at BMI > 30
		Mean ($\pm$SD) = 42.7 $\pm$ 0.7 Range = 30.0–65.7			
Hautanen *et al.* (1994)	159 men enrolled in the placebo group of the Helsinki Heart Study (HHS), a randomized, placebo controlled trial of gemfibrozil to reduce cardiovascular risk in dyslipidaemic men	Unreported.	Correlation coefficients	Significant negative relationships found for T ($r = -0.231$, $P < 0.01$) and SHBG ($r = -0.282$, $P < 0.001$)	All men dyslipidaemic (HDL cholesterol $\geq$5.2 mmol/l)
					BMI distribution unreported Mean age ($\pm$SD) = 47.0 $\pm$ 4.7

Gomez *et al.* (2007)	134 men randomly selected from the population of Llobregat, Spain	Mean = 27.3	Correlation coefficients	Significant negative relationship found for SHBG ($r = -0.254$, $P = 0.005$) No significant correlation found for T ($r = -0.11$, $P = 0.16$)	Participants recruited from general population Included some older men. Mean age = 41.4. Age range = 15–70 Men with thyroid dysfunction excluded
Jarow *et al.* (1993)	120 men in North Carolina, USA	≤135% IBW ($n = 90$)	Comparison of mean hormone levels between men of two IBW categories (<135%, >135%)	Significant negative relationships for T, SHBG and T/E_2 in infertile, but not fertile, men	Used IBW (Ideal Body Weight) according to Metropolitan Life Insurance Company tables
	30 fertile men recruited as volunteers and 90 infertile men recruited from a fertility clinic	>135% IBW ($n = 30$)		No statistically significant associations found for E_2 or LH	Very small numbers of obese men ($n = 30$) No exclusion criteria Relationships found in infertile men only (not fertile men)
Kley and Krüskemper, (1979)	116 men recruited in Germany	100–120% IBW ($n = 40$)	Comparison of mean hormone levels between men of 4 IBW categories: 100–120, 160–180, 180–200, >200%	Significant negative relationships found for T and free T	Used IBW (Ideal Body Weight) according to Metropolitan Life Insurance Company tables
	76 were overweight men (>120% IBW) awaiting calorie-reduction diet. 40 were normal weight controls (IBW 100–120%) of volunteer medical staff and students	160–200% IBW ($n = 20$)		Compared with the normal-weight control group, the mean T was 73, 40 and 32% in the IBW categories of 180–200, 200–220 and >220%, respectively	Excluded men with history of cryptorchidism and hypogonadism
		>200% IBW ($n = 16$)		Compared with the normal weight control group, the mean free T was 68.5 and 60% in the IBW categories of 200–200 and >220%, respectively	Found no clinical signs of hypogonadism in overweight men, even with testosterone levels several times lower than the normal-weight control levels Published in German (translated)
		Range = 80–256% IBW			
Giagulli *et al.* (1994)	110 men recruited as volunteers in Belgium 45 were obese (BMI > 30), 70 were age-matched non-obese controls (BMI < 26)	<26 ($n = 70$)	Regression analysis	Significant negative relationship for T ($P < 0.01$) and SHBG ($P < 0.01$)	Source of recruitment unreported
		30–35 ($n = 22$)	Comparison of mean hormone levels between men of three BMI categories (shown to left)	Free T was normal in the moderately obese men (BMI of 30–35 kg m^{-2}) but significantly decreased in severely obese men (BMI > 40) ($P < 0.05$)	Proposes that in overweight and moderate obesity, SHBG and T are both decreased but free T and LH remain normal (therefore not an expression of hypogonadism). In severely obese men, LH and free T are decreased as well, resulting in hypogonadotrophic hypogonadism
		>40 ($n = 18$)		LH was normal in moderately obese men but significantly decreased in severely obese men ($P < 0.05$) Significant positive relationship for E_2 ($P < 0.01$)	

Table III Data extracted from all studies for use in meta-analysis

	BMI Category	Aggerholm et al. (2008)	Jensen et al. (2004)	Qin et al. (2007)	Koloszár et al. (2005)	Fejes et al. (2006)
Study population	Total	1989	1558	990	274	42
	<20	67	217	*42*[a]	29	25
	20–25	986	1042	*690*[b]	96	
	25–30	773	299	241	91	17
	>30	171		17	58	
Mean sperm concentration (M/ml)	Total					
	<20	82		*45.2 ± 4.74*[a]	38 ± 14	11.2
	20–25	74		*69.1 ± 1.35*[b]	39 ± 14	
	25–30	70		76.2 ± 3.35	37 ± 14	8.1
	>30	80		70.6 ± 10.35	29 ± 12	
Median sperm concentration (M/mL)	Total		44 [21–79]			
	<20	67 [25 102]	40 [17, 75]			
	20–25	55 [9,99]	46 [23, 84]			
	25–30	53 [27,90]	39 [20, 69]			
	>30	65 [33 114]				
Mean total sperm count (M)	Total					
	<20	256		*117.8 ± 14.25*[a]		
	20–25	231		*175.3 ± 4.63*[b]		
	25–30	216		196.6 ± 9.51		
	>30	265		149.5 ± 25.47		
Median total sperm count (M)	Total		128 [55, 246]			
	<20	165 [86, 351]	105 [47, 240]			
	20–25	161 [77, 309]	138 [59, 259]			
	25–30	153 [67, 286]	116 [46, 213]			
	>30	156 [75, 317]				
Mean semen volume (mL)	Total					4.3 ± 0.7
	<20	3.1	3.0 ± 1.5	2.8 ± 0.20[a]		
	20–25	3.2	3.2 ± 1.4	2.5 ± 0.04[b]		
	25–30	3.2	3.2 ± 1.6	2.5 ± 0.07		
	>30	3.2		2.5 ± 0.29		
Average sperm motility (%)	Total					
	<20	42	63.7 ± 14.5	*74.5 ± 1.58*[a]		
	20–25	41	65.4 ± 12.4	*70.2 ± 0.45*[b]		
	25–30	48	65.5 ± 12.5	69.1 ± 0.87		
	>30	54		72.4 ± 2.83		

Note: Median values = median [25th, 75th percentiles]; Mean values = mean ± SD.
Data in *italics* is part of an unconventional BMI category (not as reported in BMI category column).
[a]Underweight BMI category of <18.5.
[b]Normal weight BMI category of 18.5–25.

The remaining seven studies investigating semen parameters could not be included in the meta-analysis because they did not report average values of sperm concentration or total sperm count across BMI categories. Instead they reported a range of different composite outcomes and measures of effect to relate various semen parameters to BMI. Sperm morphology and other composite semen parameters were not incorporated in the meta-analysis because of variable and inconsistent reporting of data that was not suitable for data pooling.

Review of BMI and semen parameters

Ten of the included studies examined sperm concentration as an outcome. Five of these studies were suitable for inclusion in the meta-analysis above. The three largest studies examining the relationship between BMI and sperm concentration came to three completely different conclusions. The largest study (Aggerholm *et al.*, 2008), found no statistically significant relationship whatsoever between BMI and sperm concentration. Jensen *et al.* (2004) found a negative relationship between BMI and sperm concentration (Jensen *et al.*, 2004). To the contrary, Qin *et al.* (2007) found a positive relationship in their study, where a high BMI was in fact protective against a low sperm count (Qin *et al.*, 2007).

For Jensen *et al.* (2004), there was a wide variation of sperm concentrations and total sperm counts throughout the BMI range, but especially in men within the normal BMI range of 20–25. In this BMI range, sperm concentration ranged from 0 M/ml to over 400 M/ml. The overall median sperm concentration of 44 M/ml had a 25th to 75th percentile interval of 21–79 M/ml, a difference in

Table IV Regression coefficients from meta-analysis

Semen Parameter	Number of studies used	Number of data entries used	Regression coefficient	95% Confidence Interval
Mean sperm concentration	4	14	−0.02	−8.24, 8.18
Median sperm concentration	2	7	1.57	−7.39, 10.53
Mean total sperm count	2	8	12.43	−164.95, 189.81
Median total sperm count	2	7	2.09	−35.79, 39.97
Semen volume	3	11	0.05	−0.05, 0.15
Average sperm motility	3	11	−1.07	−7.39, 5.25

sperm concentration of 276%. For men with a BMI >25, 75.6% had a sperm concentration of 20–200 M/ml, whereas in the normal weight range 78.3% of men had a sperm concentration of >20 M/ml. BMI did not seem to significantly affect the prevalence of oligozoospermia. Among men with a normal BMI, oligozoospermia was found in 21.7% of men, whereas in men with a BMI >25, the prevalence of oligozoospermia was 24.4%.

Although Qin *et al*. (2007) did find a positive relationship using simple linear correlations, these results were not consistent across their analyses. When the mean semen parameter values of each BMI category were compared, overweight and obese groups did not have significantly different means to those of the normal weight group. Furthermore, odds ratios for low sperm concentration were also not significantly different across the BMI categories.

Other reasonably large studies found only weak relationships or no relationship at all between BMI and sperm concentration. This was the conclusion of Chavarro *et al*. (2008) and the study by Koloszár *et al*. (2005) reported no significant differences in sperm concentration between men of different BMI categories except for those with a BMI >30 (Koloszár *et al*., 2005). Results were mixed in the smallest studies of less than 100 men.

Seven of the included studies examined total sperm count. The three largest studies found relationships in line with their results for sperm concentration (Jensen *et al*., 2004; Qin *et al*., 2007; Aggerholm *et al*., 2008). Chavarro *et al*. (2008) found a significant negative relationship (Chavarro *et al*., 2008), whereas Magnusdottir *et al*. (2005) only found such a relationship in the subfertile group of men, but not in fertile men (Magnusdottir *et al*., 2005).

Six of the included studies measured semen volume. Five of these studies found no significant relationship between BMI and semen volume, including two of the largest studies in this review (Jensen *et al*., 2004; Qin *et al*., 2007). Only one study reported a statistically significant association for semen volume, although these results were not accompanied by any data (Chavarro *et al*., 2008).

Five studies reported sperm motility as an outcome, with all of these concluding that there is no relationship between BMI and sperm motility, including the two largest studies investigating BMI and semen parameters (Jensen *et al*., 2004; Aggerholm *et al*., 2008). Only four studies reported sperm morphology as an outcome. The largest of these found no significant association between BMI and sperm morphology (Jensen *et al*., 2004), although results from smaller studies were mixed.

Three studies reported primary outcomes that were composite measures of semen parameters (Parazzini *et al*., 1993; Kort *et al*., 2006; Hammoud *et al*., 2008b). Parazzini *et al*. (1993) did not find any relationship between BMI and risk of dyspermia, a condition defined similarly to oligoasthenoteratozoospermia. In contrast, Kort *et al*. (2006) found a significant negative relationship between BMI and NMS count and Hammoud *et al*. (2008b) found a similar trend for the odds ratio of low progressively-motile sperm count. These latter results indicate that, in their studies, BMI was related to poorer semen quality in terms of one or more semen parameters.

Review of BMI and male reproductive hormones

The results of all studies investigating reproductive hormones are summarized in Table V. Eighteen of the twenty studies measuring testosterone and 15 of the 16 studies measuring SHBG reported negative relationships between BMI and these hormones. Of 12 studies that investigated free testosterone, 10 reported a negative relationship with BMI. It was commonly reported that, whereas free testosterone was negatively correlated with BMI, this relationship was not as strong as that for testosterone or SHBG (Kley and Krüskemper, 1979; Giagulli *et al*., 1994; Allen *et al*., 2002). Other studies also observed this trend, with one reporting a correlation coefficient of only $r = -0.07$, $P < 0.01$ (Svartberg *et al*., 2004) and another finding the obese group of men had mean free testosterone levels only 5% lower than normal weight men (Allen *et al*., 2002).

Four of the ten studies measuring estradiol found a positive relationship between BMI and estradiol, with the remaining not finding any statistically significant association. The largest of these studies in fact found unadjusted mean estradiol concentrations to be essentially identical across all four standard BMI categories (Aggerholm *et al*., 2008).

Most studies did not find any significant relationship between BMI and the gonadotrophins. Four studies investigated inhibin B, with most finding that a high BMI has a negative effect on inhibin B levels. Two studies found simple negative relationships, whereas one study (Aggerholm *et al*., 2008) found a more complicated relationship

Table V Summarized results of studies investigating BMI and reproductive hormones

Study	Size	Relationship between BMI and reproductive hormone						
		T	Free T	SHBG	E_2	Inhibin B	FSH	LH
Wu *et al.* (2008)	3200	Negative	Negative	Negative				None
Aggerholm *et al.* (2008)	1989	Negative		Negative	None	Inverse U curve	None	None
Mohr *et al.* (2005)	1677	Negative	Negative					
Jensen *et al.* (2004)	1558	Negative	Positive (FAI)	Negative	Positive	Negative	None	None*
Svartberg *et al.* (2004)	1548	Negative	Negative	Negative				
Qin *et al.* (2007)	990	Negative*			None		Positive*	None
Allen *et al.* (2002)	696	Negative	Negative	Negative				Negative
Schatzl *et al.* (2003)	561	Negative	Negative					
Muller *et al.* (2003)	400	Negative	Negative (Bio T)	Negative	Positive			
Meeker *et al.* (2007)	388	Negative*	Positive (FAI)*	Negative*		Negative*		
Ukkola *et al.* (2001)	324	Negative		Negative	None			
Meikle *et al.* (1989)	323	Negative	None	Negative			None	None
Jankowska *et al.* (2000)	236	Positive[a]	None		None			
Andersson *et al.* (2004)	178					None	None	
Haffner *et al.* (1993)	178	Negative	Negative	Negative	None			
Hofstra *et al.* (2008)	160	Negative	Negative	None	Positive		None	None
Hautanen *et al.* (1994)	159	Negative		Negative				
Gomez *et al.* (2007)	134	None		Negative				
Jarow *et al.* (1993)	120	Negative[b]		Negative[b]	None			None
Kley and Krüskemper, (1979)	116	Negative	Negative					
Giagulli *et al.* (1994)	110	Negative	Negative[c]	Negative	Positive			Negative[c]

Note: All relationships stated are statistically significant ($P \leq 0.05$) unless otherwise noted.
Bio T = bioavailable testosterone, FAI = Free Androgen Index.
*No *P*-values or confidence intervals published, therefore statistical significance of these trends not reported.
[a]Relationship was statistically significant in younger men (aged 22–39) but not older men (aged 40–67).
[b]These relationships found only in infertile groups of men (not fertile men).
[c]Levels of these hormones were only significantly reduced in severely obese men (BMI > 40).

where inhibin B decreased progressively with a BMI higher or lower than the normal BMI range of 20–25.

Discussion

There is no strong evidence for a relationship between BMI and sperm concentration or total sperm count on the basis of the studies in this systematic review. Although several studies did report statistically significant relationships for these semen parameters, the overall body of research does not support such conclusions. At the very least, we conclude that if such a relationship does exist it is not significant enough to be detected by review and meta-analysis of cross-sectional studies of 6800 men. The strongest evidence for this conclusion is drawn from the meta-analysis, which found no evidence for a relationship between BMI and average sperm concentration and average total sperm count.

The study by Aggerholm *et al.* (2008) is arguably the most important study to investigate BMI and semen parameters. It has the largest sample size ($n = 1989$) and also the broadest study population, with men from eight European countries. Men were recruited from a general population setting, rather than from a fertility clinic, and the sample included significant proportions of overweight and obese men as well as a wide age range. Therefore this study sample was likely to be representative of men in most developed countries. The main limitation of this study was that weight and height were self-reported. Although this is not ideal, self-reported BMI has been independently verified to be sufficiently valid for identifying relationships in epidemiological research (Spencer *et al.*, 2002). The results of this study were entirely consistent with the meta-analysis and conclusions of this review.

In contrast, Jensen *et al.* (2004) reported a statistically significant negative relationship between BMI and both sperm concentration and total sperm count. However, the men sampled in this study were younger and of a healthy weight range and are therefore not representative of the general male population of most developed countries. Further to this, sperm concentrations and total sperm counts showed wide variation, especially for men in the normal BMI range, and a high BMI did not significantly impact on the prevalence of oligozoospermia. Therefore, if BMI does impact on sperm quantity, these results suggest that it has only a small, and clinically insignificant, effect.

The study of Qin *et al.* (2007) was the only study to report a positive relationship between BMI and sperm concentration or total sperm count. These conflicting results may be explained by the BMI

distribution of the study population, with obese men making up only 1.7% of the sample. This study also employed stringent exclusion criteria, excluding regular alcohol drinkers, heavy smokers and men with chronic diseases for example, which may have introduced significant bias. Overall, however, the results of this study were mixed and are still consistent with the conclusion that there is a lack of evidence for any relationship between BMI and semen parameters.

Studies are almost uniformly consistent in finding no relationship between BMI and sperm motility. Results for sperm morphology are less conclusive, although the large study by Jensen *et al*. (2004) did find that there was no association between BMI and sperm morphology.

Although this systematic review has not found an association between increased BMI and semen parameters, other research findings do suggest an impact of increased BMI on fertility outcomes. Data from the Agricultural Health Study in the USA, analysing 1329 couples, reported that male BMI is an independent risk factor for infertility in couples trying to conceive (Sallmen *et al*., 2006). More specifically, obesity has been repeatedly associated with erectile dysfunction and it has been demonstrated in at least one study that erectile function can be improved with weight loss (Pasquali *et al*., 2007). In addition, the severe impact that a high BMI has on general adult morbidity and mortality has already been firmly established. Finally, one study of BMI and DFI, a measure of the genetic integrity of sperm, suggests a negative relationship (Kort *et al*., 2006), although further research is awaited. Therefore, although this systematic review has not reported an association between BMI and semen parameters, despite the outcome of this review, overweight and obese men should still be advised to normalize their BMI when couples present with fertility problems for the reasons outlined above.

This review finds strong evidence for a negative relationship between BMI and both testosterone and SHBG. The strength and consistency of relationships for these hormones across different populations, age ranges and BMI samples supports this conclusion. For SHBG, this relationship is probably explained by reduced hepatic globulin synthesis due to inhibition by excessive circulating insulin in men with a higher BMI (Pasquali *et al*., 2007). There is also evidence that there is a negative relationship between free testosterone and BMI. However, this relationship appears to be weak. One small study has gone as far as to suggest that free testosterone remains within normal ranges in overweight and even moderately obese men, although in severely obese men the levels are sub-normal (Giagulli *et al*., 1994). It is of interest that the few studies that undertook more comprehensive clinical examination did not observe clinical signs of hypogonadism, even in those with significantly reduced free testosterone (Kley and Krüskemper, 1979; Strain *et al*., 1982). It is therefore suggested that a reduction in free testosterone in overweight and obese men has little biological effect, consistent with our finding that there is no detectable relationship between BMI and semen parameters.

The majority of articles find no relationship between estradiol and BMI, including the large population study by Aggerholm *et al*. (2008). However, four studies did find statistically significant positive relationships. Such a relationship is biologically plausible due to increased peripheral conversion of androgen to estrogen associated with the increased adipose tissue present at a higher BMI (Schneider *et al*., 1979; Pasquali *et al*., 2007), although this relationship has yet to be proven consistently in population studies.

It is an interesting finding that BMI appears to have little relationship with semen parameters yet is strongly related to alterations in the male reproductive hormone profile, especially reduction in testosterone. Spermatogenesis is driven mainly by the action of testosterone, in the form of free testosterone, and FSH. This discrepancy might by explained by two other findings: firstly, although testosterone decreased significantly in obese men, free testosterone was decreased to a smaller extent and secondly, there was no evidence for a relationship between BMI and FSH. Therefore, it is possible that the homeostasis of endocrine control of spermatogenesis is maintained to some degree, even in obese men. Additionally, this possibly reflects that the rate of spermatogenesis is not precisely controlled by hormonal regulation. Instead, it may be a biological process whose output has only a prerequisite minimum endocrine drive and is otherwise independent of precise hormone levels.

There are limitations to this systematic review. First, there were few studies that reported the outcomes of interest. The statistical aggregation and analysis of data from all of the included studies was thus restricted to five studies that reported comparable outcome measures. The remaining studies were excluded from the meta-analysis even though they may have found useful evidence. In spite of this, the meta-analysis did still include the three largest studies of BMI and semen parameters so far published.

Second, we were reliant on BMI as a surrogate measure of body fat content. BMI is an imperfect measure of this and the validity of BMI, and particularly its thresholds for overweight and obesity, have been questioned (Prentice and Jebb, 2001). The sensitivity of BMI in estimating an individual's body fat suffers from its inability to distinguish variability in body composition and body fat distribution (Akpinar *et al*., 2007). However, it has been shown that BMI is positively correlated with body fat (Gallagher *et al*., 1996; Neovius *et al*., 2005; Akpinar *et al*., 2007) and BMI is still a satisfactory indicator of adiposity in large-scale population studies (Keys *et al*. 1972; Gallagher *et al*., 1996; Neovius *et al*., 2005). BMI was used in this review as it is the predominant measure of adiposity used in studies, especially large population studies. In these and additional searches, no published studies were found that investigated the relationship between semen parameters and alternative measures of obesity or adiposity. As BMI is still the standard system for classifying obesity at a population level, relationships reported with BMI still remain the most relevant to public health. Future research would greatly benefit from employing more accurate surrogate measures of adiposity such as waist circumference (Chan *et al*., 2003; Neovius *et al*., 2005) or direct measures of body fat content such as bioimpedance (Prentice and Jebb, 2001).

Further research should ensure sample sizes are sufficient to answer the question of the association of obesity and semen parameters. With the increasing utilization of fertility clinics worldwide, studies with large enough samples of men should be possible. Longitudinal studies and clinical trials involving weight loss will greatly improve our insight into the impact of BMI and semen parameters. In terms of reproductive hormones, further population studies with inhibin B, LH and FSH are warranted to better analyse their relationship with BMI.

Supplementary data

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

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