Reduced Fertility Among Overweight and Obese Men

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Background: Overweight and obese men have been reported to have lower sperm counts and hormonal changes, but data are lacking regarding effects on couple fertility.

Methods: We examined the relationship between male body mass index (BMI) and infertility in couples enrolled in the Agricultural Health Study in the United States. The analysis sample was limited to couples (wife <40 years old) with an attempt at pregnancy in the last 4 years based on pregnancy and fertility data provided by wives. Infertility was defined as not conceiving a pregnancy after at least 12 months of unprotected intercourse regardless of whether or not a pregnancy ultimately occurred. Self-reported weight and height were used to calculate BMI (kg/m^2). Adjusted odds ratios (aORs) for infertility associated with increases in male BMI were calculated with logistic regression.

Results: Adjusting for potential confounders, a 3-unit increase in male BMI was associated with infertility (aOR = 1.12; 95% confidence interval = 1.01–1.25; n = 1329). There was a dose–response relationship, and the BMI effect was stronger when the data were limited to couples with the highest-quality infertility data. The association between BMI and infertility was similar for older and younger men, suggesting that erectile dysfunction in older men does not explain the association.

Conclusions: This report of lower fertility in overweight and obese men needs replication. If the findings are robust, programs to prevent obesity may improve men's reproductive health and save medical costs for infertility treatment.

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High body mass index (BMI) in men may reduce fertility. High BMI has been associated with reduced semen quality and hormone alterations.[1–4] In addition, overweight men may be at greater risk of erectile dysfunction,[5] which could reduce fertility. To our knowledge, there are no studies that report the relationship between male BMI and couple fertility. We examined this association in men who enrolled in the Agricultural Health Study, a large study of pesticide applicators and their spouses.[6]

METHODS

Study Population and Data Collection

The Agricultural Health Study is composed of certified pesticide applicators and their spouses in Iowa and North Carolina.[6] Male private applicators, largely farmers (n = 52,395), and 32,347 spouses (approximately 75% of eligible spouses) enrolled between 1993 and 1997. The study protocol was approved by the Human Subjects Review Boards of the National Institutes of Health and each of the collaborating field stations, and informed consent was obtained from study participants before data collection. The present study is restricted to families in which the wife completed the Female and Family Health questionnaire (n = 20,620), a self-administered questionnaire (available at www.aghealth.org). To exclude perimenopausal women, we further restricted to premenopausal women age <40 years at the time of enrollment (n = 5526).

Infertility was defined as taking more than 12 months to conceive regardless of whether or not a pregnancy ultimately was achieved. The focus of our analysis was on the most recent attempt to conceive to be as concurrent as possible with the BMI data that were collected at enrollment. We could clearly ascertain the infertility status for those who had never been pregnant but had tried, those who tried after the last pregnancy, and those with only one pregnancy. Ascertainment of infertility status for multigravid women was more complicated because women were not asked about infertility for each separate pregnancy (rather, they were asked if they ever took more than 12 months to conceive). Therefore, multigravid women who reported ever taking >12 months to conceive a prior pregnancy were assumed to have experienced a period of infertility with their last pregnancy if the nonpregnant interval before their last pregnancy was sufficiently long (at least 16 months after a birth and at least 14 months after a pregnancy loss). Data were analyzed with and without these women to evaluate their impact on the overall findings.

Eligible participants were couples who had had an attempt at pregnancy estimated to have started no more than 4 years before enrollment that could be classified as fertile or infertile (>12 months to conceive). The inclusion of couples was based on the estimated start of a pregnancy attempt, and not on the dates of pregnancies, to maintain similar distribu-

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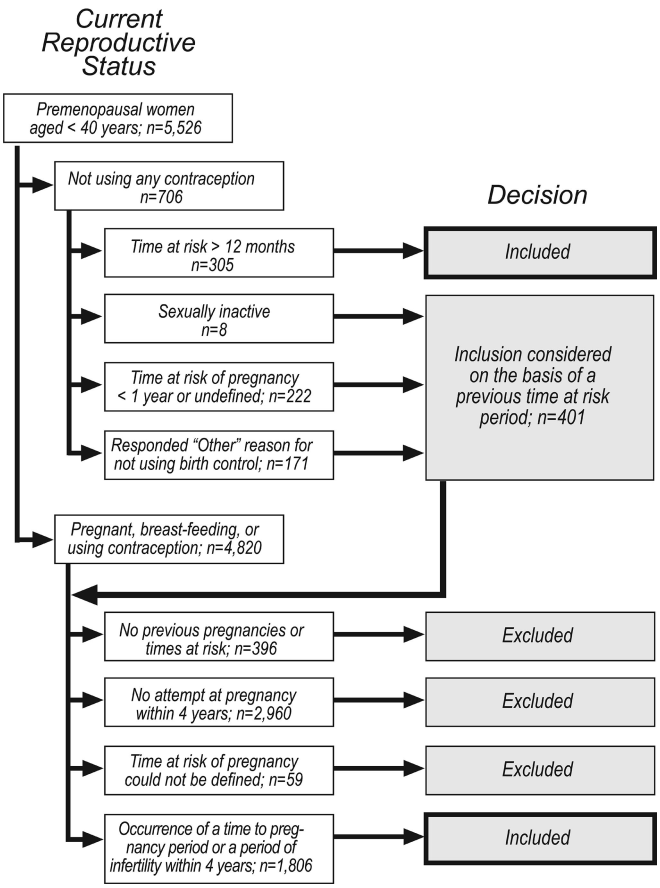

FIGURE 1. Description of the inclusion criteria for analysis based on reproductive history and current reproductive status among couples in the Agricultural Health Study.

tions between fertile and infertile couples for the start times of their pregnancy attempts.[7] Figure 1 shows the scheme for identifying eligible couples. Women who were not using birth control at the time of enrollment were included if they had not used birth control for more than 12 months and their reason for not using suggested they were at risk for pregnancy (n = 305: 98 "trying to become pregnant," 71 "not trying but OK if pregnant," 98 "do not think I can become pregnant," 4 "stopped one method of birth control and have not started another," 27 "do not use birth control," and 7 with missing information); those saying "other reason" were evaluated for inclusion in the analysis on the basis of a prior attempt. Fertility status of a current attempt could not be assessed for those who reported not using birth control for <12 months. Thus, 5221 couples (Fig. 1) were evaluated for inclusion in analysis on the basis of any prior attempt. The fertility status of a prior attempt was determined, and a start time for that attempt was estimated. We used estimates of median attempt time: 18 months for infertile couples and 3 months for fertile couples. For example, a woman who reported taking >12 months to conceive whose pregnancy ended 24 months before enrollment would have been excluded because her attempt would have been estimated to start before the 4-year window (24 months + 9 months for the pregnancy + 18 months for the attempt time = 51 months before enrollment). This criterion resulted in 3415 exclusions because these couples had no attempt starting in the 4-year window). Thus, our final study population consisted of 2111 couples.

Data for BMI (kg/m^2) were based on self-reported weight and height at time of enrollment. This information was missing for 644 men and for 316 women.

Statistical Analysis

Data on infertility were analyzed by logistic regression. The outcome parameter is the infertility odds ratio (OR), and ORs above unity reflect increased infertility, ie, reduced fertility. We first analyzed men's BMI as a continuous variable excluding couples with missing BMI data (analysis sample = 1329). We then categorized BMI to examine dose–response relationships and included those missing BMI as a separate category (analysis sample = 2111). The BMI category of 20 to 22 kg/m^2 was used as the referent. Potential confounders considered were wives' BMI and the following characteristics for both the man and woman: age, smoking status, use of alcohol, and exposure to solvents and to pesticides. Information on male BMI and potential confounders was obtained for the time of enrollment, but we assume they had not changed substantially from the time of pregnancy attempt, which could have happened at any time during the 4 years before enrollment. Age was the exception; we calculated the age that the applicator and spouse were at the estimated time they started trying to conceive and used that in all analyses.

RESULTS

Characteristics of the couples are shown in Table 1; 28% were infertile. Infertility is higher among older couples, for men and women with increased BMI, for men and women who smoke, and among those exposed to solvents. Adjusting for both male and female age and female BMI, a 3-unit increase in male BMI relative to a reference group of men with BMI of 20 to 22 kg/m^2 is associated with infertility (adjusted OR = 1.10; 95% confidence interval [CI] = 0.99–1.22). Further adjustment for male and female smoking, alcohol, solvent and pesticide exposure as well as state of residence marginally increases the male BMI effect (1.12; 1.01–1.25). There is a dose–response relationship between increasing male BMI and infertility, except for the blunted effect in the highest category (Fig. 2). The adjusted ORs were 2.13 (CI = 1.18–3.85) and 1.83 (0.84–3.97) for the 2 highest male BMI categories 32–34 kg/m^2 and 35+ kg/m^2, respectively.

We conducted several sensitivity analyses to evaluate potential bias. First, to limit differential misclassification of BMI, we excluded couples who had started trying to conceive less than 1 year before enrollment because no infertile couple could be so classified. Next, we limited analyses to couples with female BMI of less than 26 kg/m^2 to evaluate the importance of residual confounding by female BMI. Third, to see if the effect was seen predominantly among older men, we divided the group at age 32, the median male age. Finally, we limited analyses to the highest quality infertility data by

TABLE 1. Characteristics of 2111 Farmers and Their Wives in the Analysis Sample and the Associated Prevalence of Infertility, Agricultural Health Study, United States, 1993–1997

	Men		Women	
Characteristic	No.	Percent Infertile	No.	Percent Infertile
Age (years)				
<25	123	28	305	21
25–29	586	19	787	20
30–34	802	26	765	31
35–39	468	38	254	52
40–54	132	46	0*	
Body mass index (kg/m^2)				
<20	32	22	223	25
20–22	160	21	568	26
23–25	503	25	461	27
26–28	390	30	224	25
29–31	228	34	169	32
32–34	105	37	85	41
35+	50	38	65	43
Missing	644	27	316	29
Smoking				
Never smoked	1484	26	1583	26
Exsmoker	329	29	297	30
Current smoker	252	35	163	44
Missing	46	37	68	34
Use of alcohol (drinks per month during the past 12 mo)				
Nonuser	417	34	696	30
<3	346	30	733	25
3–8	605	25	477	27
9–26	358	23	121	28
≥27	307	28	46	37
Missing	78	33	38	45
Solvent exposure				
No	523	26	1321	26
Monthly	761	29	757†	31
Daily or weekly	208	33		
Missing	619	26	33	39
State				
Iowa	1650	27		
North Carolina	461	33		

*Excluded in defining the sample.
†Solvent exposure for women was simply a yes/no variable; 757 are exposed.

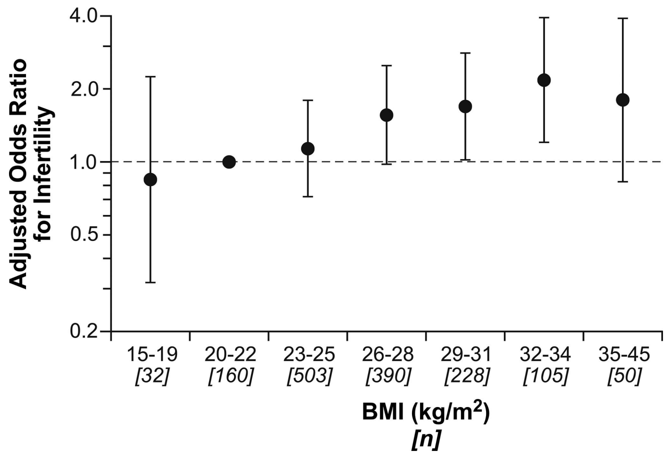

FIGURE 2. Adjusted odds ratios (circles) for infertility among men in the Agricultural Health Study categorized by BMI with BMI of 20 to 22 kg/m^2 as the reference category. The vertical lines show 95% confidence intervals. Adjusted for male and female age, smoking, alcohol, solvent and pesticide exposure as well as state of residence.

excluding couples who reported 12 months or more of trying but for whom we could not be certain that this occurred with their last attempt. In none of these situations was the association between male BMI and infertility substantially attenuated. In the first 3 sensitivity analyses, a 3-unit change in BMI was associated with adjusted ORs of 1.11 to 1.12, and in the analysis limited to the highest quality data, the effect was strengthened (adjusted OR = 1.21; CI = 1.07–1.38).

DISCUSSION

It is well documented that women who are overweight or obese are at higher risk of reproductive problems, including reduced fertility.[8–12] We know of no published literature on male BMI and couple fertility, but we found male BMI to be an independent risk factor for infertility among the couples in the Agricultural Health Study. Our results suggest that a 10-kg increase in male weight may reduce fertility by approximately 10%. Because this may be the first report examining this relationship, our findings should be viewed as a first step in assessing an association.

There are 4 major limitations of our data. First, BMI was collected at the time of enrollment, but we included couples who started trying to conceive at any time during the prior 4 years. Infertile couples could not have started trying within the year before enrollment and still be identified as infertile, so the misclassification might be worse in the infertile group. To evaluate this possibility, we excluded those who started trying to conceive within the year before enrollment and found nearly identical results indicating that this misclassification did not appear to bias our results. A second major limitation is that we did not have data on exact attempt times. Instead, data were collected so that couples who tried for more than 12 months could be identified. Therefore, we had to estimate a "start time" for the attempt to identify couples who began an attempt within the 4-year window. Some of the fertile and infertile couples will actually have begun their attempts before start of that window, but it is difficult to evaluate to what extent that might bias our results.

The third limitation was the difficulty in defining fertility status in the case of multiple pregnancies because infertility history was not pregnancy-specific. However, the findings were even stronger when the analysis was restricted to those couples with the higher-quality data. The fourth limitation is the large subset of men for whom we are missing BMI data. BMI was asked on a takehome questionnaire that was not returned by 30% of the men in our sample. However, those who did not return the questionnaire were very similar to those who did,[13] including having similar infertility status (27% vs 29% infertile).

The study's major strengths are its large sample size and detailed data to control for potential confounders, especially female BMI which, as expected, was correlated with male BMI (r = 0.24). We also conducted a sensitivity analysis to further assess residual confounding with female BMI by limiting the sample to women with relatively low BMI. Our findings remained stable in this subset (female BMI less than 26 kg/m^2).

The study sample had a relatively high rate of infertility. This is not surprising given that unsuccessful attempts were included and the majority of couples were older than age 30 years. Infertility rates depend on the definition used. Marchbanks et al[14] reported the prevalence of a history of infertility to range from 6% (diagnosed by physician) to 33% (unprotected intercourse for 12 months or more) in a U.S. study, this latter figure being even higher than the 28% in our sample.

It is biologically plausible for high male BMI to increase the risk of infertility. Jensen et al[1] recently studied over 1558 young men having premilitary physicals and found that overweight men had reduced sperm count and sperm concentration compared with men of normal weight. Overweight men in Jensen's study also had higher estradiol levels. Three very recent studies also report adverse changes in semen quality associated with BMI.[2–4] Increased BMI may also be associated with low testosterone and sex hormone-binding globulin or alterations in luteinizing hormone.[4,5,15–17] Other studies have found that weight loss in men can change hormone levels.[16,18] It is also possible that high BMI is associated with higher scrotal temperatures, and this can have adverse effects on spermatogenesis.[19] Laboratory studies in mice provide plausibility: disruption of insulin signaling causes both obesity and impaired spermatogenesis.[20]

We did not have data on frequency of sexual intercourse. It is possible that overweight men have less sexual intercourse than their normal-weight counterparts and this could influence fertility. Obesity is a risk factor for erectile dysfunction,[5] but severe erectile dysfunction appears to be rare among men under 50,[21] and all but 3 men in our sample were under 50. Furthermore, when we evaluated the effect of BMI separately for the younger and older men, the effect was very similar in both groups, supporting the idea that erectile dysfunction is not a major cause of higher infertility rates in overweight and obese men in these data.

These findings must be viewed as supportive but not confirmatory of an association given the limitations of the study data. If substantiated, they suggest that personal and societal costs of male infertility and its treatment is an additional price associated with the obesity epidemic.

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