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Body mass index and short-term weight change in relation to treatment outcomes in women undergoing assisted reproduction

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Abstract

Objective—To assess the relation between BMI and short-term weight change with ART outcomes.

Design—Prospective cohort study.

Setting—Fertility center at an academic medical center.

Patients—170 women undergoing 233 ART cycles.

Methods—Baseline BMI and short-term weight change were related to ART outcomes. Regression models accounting for repeated observations were used to adjust data for potential confounders.

Results—Overweight and obesity were associated with lower live birth rates. The adjusted live birth rate (95% CI) was 42% (28%–58%) among women with a BMI between 20 and 22.4 kg/m² and 23% (14%–36%) among overweight or obese women (p,trend=0.03). Short-term weight loss was associated with a higher proportion of MII oocytes retrieved. The adjusted proportion of MII eggs was 91% (87%–94%) for women who lost 3kg or more and 86% (81%–89%) for women whose weight remained stable (p,trend=0.002). This association was stronger among women who

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were overweight or obese at baseline. Short-term weight loss was unrelated to positive β hCG, clinical pregnancy or live birth rates.

Conclusions—Overweight and obesity were related to lower live birth rates in women undergoing ART. Short term weight loss was related to higher MII yield, particularly among overweight and obese women, but unrelated to clinical outcomes.

Keywords

body weight; weight loss; obesity; infertility; assisted reproduction

Introduction

Overweight and obesity are well described risk factors for infertility, particularly as it relates to ovulation disorders (1–2). The development and refinement of assisted reproductive technology (ART) over the last decades has coincided with a rapid increase in the prevalence of obesity among women of reproductive age (3–4). Consequently, there is interest in understanding the effects excess body weight may have on assisted reproduction. Many studies have clearly documented that overweight and obese women have significantly lower live birth rates than lean women undergoing assisted reproduction (5–6). However, it is not clear what specific treatment stages are affected by excess body weight. Some studies have described deleterious effects of obesity in a multitude of intermediate endpoints including total and MII oocyte yield (7), fertilization rate (8) and embryo quality (9). However, lack of consistency in the methods used to assess some of these outcomes across studies and of the statistical methods used to analyze them has precluded firm conclusions in this area.

Given the consistency of the association of body weight with natural fertility and with live birth rates in the ART setting, it has become a common clinical practice to advise underweight patients to gain weight and overweight or obese patients to lose weight prior to the initiation of infertility treatments. In fact, there is ongoing debate on whether access to ART should be limited to women who are not overweight or obese (10–13). Nevertheless, the evidence in support of these recommendations is scarce. In this paper, we used data from an ongoing study that enrolls patients at a referral fertility center to examine the associations of body weight and short term weight change with embryological and clinical outcomes of women undergoing assisted reproduction.

Materials and Methods

Study population

Participants were women enrolled in the EARTH Study, an ongoing prospective cohort started in 2004 aimed at identifying environmental and nutritional determinants of fertility among couples presenting for infertility evaluation and treatment at the Massachusetts General Hospital Fertility Center. Women and men between 18 and 45 years using their own gametes for intrauterine insemination (IUI) or in vitro fertilization (IVF) were eligible to enroll in the study. Enrollment as a couple is not required for participation. Upon entry, all subjects completed a nurse-administered brief lifestyle and medical questionnaire and underwent an anthropometric evaluation by a trained research nurse. They were also asked to provide blood and urine samples, to allow the investigators access to their medical records, and to complete a detailed questionnaire addressing lifestyle and medical history at home. Women were then followed during each of their IUI and IVF treatment cycles for clinical outcomes until a live birth was achieved or they discontinued their treatment at MGH. The current report includes women who joined the study between December 2004

and October 2010 and completed at least one IVF treatment cycle by March 31, 2011. The study was approved by the Human Subject Committees of the Harvard School of Public Health and Massachusetts General Hospital.

Clinical management and assessment of outcomes

All subjects underwent an evaluation for infertility which included a follicle-stimulating hormone (FSH; Elecsys FSH reagent, Roche Diagnostics) level drawn on the third day of the menstrual cycle to assess ovarian reserve. Subjects underwent one of three IVF treatment protocols: 1) luteal phase GnRH-agonist protocol, 2) follicular phase GnRH-agonist/Flare protocol, or 3) GnRH-antagonist protocol. All treatment cycles were preceded by a cycle of oral contraceptive pills unless contraindicated. On day 3 of induced menses, exogenous gonadotropins [FSH (Gonal-F, Follistim, Bravelle)] and/or Human Menopausal Gonadotropin [hMG (Repronex, Menopur)] were initiated. In the luteal phase GnRH-agonist protocol, Lupron dose was reduced at, or shortly after, the start of ovarian stimulation with FSH/hMG. FSH/hMG and GnRH-agonist or GnRH-antagonist was continued to the day of trigger with Human Chorionic Gonadotropin (hCG), 36 h before oocyte retrieval. Estradiol (E2) levels were measured throughout the monitoring phase of the subject's IVF treatment cycle (Elecsys Estradiol II reagent kit, Roche Diagnostics). Oocyte retrieval was performed when, on transvaginal ultrasound, at least 3 follicles had reached 16 mm greater and the E2 level had reached at least 600 pg/mL. Endometrial thickness and appearance was also monitored by ultrasound during this phase and the thickness reached on the day of hCG trigger was recorded.

Embryologists determined the total number of oocytes retrieved per cycle and evaluated the maturity of the oocytes. In intracytoplasmic sperm injection (ICSI) cycles, outer cells were removed from the oocytes 2 to 3 hours after retrieval. Oocytes were then classified as germinal vesicle, metaphase I, metaphase II (MII) or degenerated. For IVF cycles with insemination, maturity status was determined at the time of the evaluation for successful fertilization (17 to 20 hours after retrieval). The outer cells were removed from all oocytes and all fertilized oocytes were categorized as MII oocytes. The unfertilized oocytes were evaluated according to their morphological characteristics in the same manner as oocytes from ICSI cycles. After ICSI or insemination, oocytes were checked for fertilization and categorized as normally fertilized (two pronuclei) or abnormally fertilized (otherwise). The resulting embryos were then graded for quality according to their morphological characteristics on day 3 and assigned a score between 1 (best) and 5 (worst). For this analysis, grade 3, 4 and 5 embryos were considered poor quality. Cleavage rate was assessed by counting the number of cells in the embryo on day 3. Embryos that had 6–8 cells on day 3 were considered to have cleaved at a normal rate, embryos with 5 cells or fewer were considered to be slow cleavage, and embryos with 9 or more cells were considered to have accelerated cleavage.

Clinical outcomes were assessed among women who underwent an embryo transfer. Positive β -hCG was defined as an elevation in plasma β -hCG levels above 6 IU/L at 17 days after oocyte retrieval. Clinical pregnancy was defined as a positive β -hCG with the confirmation of an intrauterine pregnancy by ultrasound. Live birth was defined as the birth of a neonate on or after 24 weeks gestation.

Anthropometric assessment

Height and weight were measured by trained research nurses at study enrollment (baseline) and on subsequent clinical appointments that took place at least 7 days after the baseline visit. Body mass index (BMI) was calculated from these measurements and divided into five categories: <20 kg/m², 20–22.4 kg/m², 22.5–24.9 kg/m², 25–29.9 kg/m² and 30 kg/m². We

also calculated the change in body weight between baseline and the last clinical appointment prior to an ART cycle. Weight change was categorized into stable body weight for women who maintained their body weight within 1kg of their baseline weight, weight gain (1kg to 3kg, >3kg) or weight loss (−1kg to −3kg, < −3kg).

Statistical analysis

We used regression techniques based on generalized linear mixed models or generalized estimating equations (GEE) to take full advantage of the available data while accounting for correlations in outcomes across cycles within a woman. The specific technique was chosen based on the specific outcome under examination. We used linear mixed models when peak E2 levels and endometrial thickness were the outcome (continuous outcomes). We used GEE Poisson models when oocyte yield and MII yield were the outcomes (counts). We used GEE logistic models when the proportion of MII to total oocytes retrieved, fertilized eggs, poor quality embryos, accelerated embryo cleavage, slow embryo cleavage, positive β -hCG, clinical pregnancy and live birth were the outcomes (proportions). For all the analyses we fitted multivariate models where terms for age, day 3 FSH levels, primary infertility diagnosis and treatment protocol were included. All multivariate models for weight change were also adjusted for baseline BMI. We used linear combinations of the regression parameters to express the results in a clinically relevant scale. Tests for linear trends (14) were conducted using the median values of each category of BMI or weight change as a continuous variable. We formally tested whether the associations of weight change with all the outcomes examined differed according to baseline BMI by fitting regression models with cross-product terms between weight change and baseline BMI and fitting stratified models according to baseline BMI (<25 kg/m² and ≥25 kg/m²). Similarly, we examined whether the associations of clinical outcomes with weight change and baseline BMI were modified by the presence of polycystic ovary syndrome (PCOS). Analyses were conducted using Statistical Analysis Software (SAS) version 9.2 (SAS Institute Inc., Cary, NC).

Results

There were 170 women who collectively underwent 233 IVF/ICSI cycles with complete anthropometric and clinical data available for analyses. Women were primarily Caucasian (86%), had never smoked (72%) and had a mean (SD) age of 35.4 (3.9) years. The mean (SD) BMI at study enrollment was 24.5 (4.7) kg/m² with 35% of women being overweight (BMI 25–29.9 kg/m²) or obese (BMI ≥30 kg/m²). The average time between study enrollment and the anthropometric evaluation preceding their first ART cycle was 140 days and the median [25th–75th percentile] change in body weight during this period was 0.3 [−0.1, 1.8] kg. However, among women who lost weight (N=45 women), the median weight loss was 3.1 kg (range: 1.1 – 26.5 kg) and among women who gained weight (N=64 women), median weight gain was 2.2 kg (range: 1.1 – 13.3 kg). Weight change was unrelated to the time between enrollment and first IVF cycle ($p = 0.56$).

Table 1 presents the clinical and demographic characteristics of the study participants in relation to baseline BMI. Weight change was inversely related to baseline BMI. Women who were overweight or obese at baseline were more likely to lose 1kg or more than lean women (41% vs. 19%; $p=0.002$). Yet, gaining 1kg or more was not strongly related to being overweight or obese at baseline ($p = 0.46$). Baseline BMI was also significantly related to initial treatment protocol. Luteal phase agonist protocols were most commonly used in lean women and flare protocols were most commonly used in obese women. Day 3 FSH levels and total gonadotropin dose in the first cycle appeared to increase with increasing baseline BMI but the relations failed to reach statistical significance.

Table 2 presents the relations of BMI and weight change with endometrial thickness and controlled ovarian hyperstimulation outcomes. Baseline BMI was inversely related to peak E2 levels. Being overweight or obese at baseline was related to a 332 (102–561) ng/dL lower peak E2 level ($p=0.004$). BMI was unrelated to endometrial thickness, total oocyte yield and yield of MII oocytes. Short term weight loss was associated with a higher yield of MII oocytes, particularly when expressed as the percentage of total oocytes retrieved. This association was more evident among women who were overweight or obese at baseline. The proportion of MII oocytes retrieved (95% CI) for overweight or obese women who subsequently lost 3kg or more was 87% (80%, 92%) compared to 76% (66%, 84%) among overweight or obese women whose weight remained stable ($p = 0.002$) after adjusting for age, day 3 FSH levels, infertility diagnosis and treatment protocol. The corresponding proportions among women who were lean at baseline were 93% (87%, 96%) for those who subsequently lost 3kg or more and 88% (83%, 92%) for women with stable body weight. Nevertheless, this interaction was not statistically significant (p , interaction=0.32). Since oocyte maturity is evaluated under different conditions in IVF insemination and ICSI cycles we also evaluated whether the relation between weight change and oocyte yield differed according to cycle type. The association between short term weight change and MII yield was also slightly stronger in IVF insemination cycles (p , trend = 0.003) than in ICSI cycles (p , trend = 0.06). However, formal testing for heterogeneity of the association according to cycle type suggested no statistically significant differences by insemination procedure (p , interaction=0.11).

Baseline BMI was unrelated to fertilization rate overall and in IVF cycles (Table 3). Interestingly, in ICSI cycles, weight loss was associated with lower fertilization rates (p , trend=0.03). There was no differential association of weight change with fertilization rate in ICSI cycles by levels of baseline BMI (p , interaction = 0.12). BMI and weight change were also unrelated to the proportion of poor quality embryos or embryo cleavage rate (data not shown).

We examined the associations of BMI and weight change with clinical outcomes among women who underwent an embryo transfer (Table 4). Being overweight or obese at baseline was associated with lower live birth rates (adjusted live birth rate = 23% (14–36%)). In addition, being obese at baseline was associated with a lower frequency of positive β -hCG. The highest positive β -hCG, pregnancy and live birth rates were observed among women with a BMI between 20 and 22.4 kg/m². Weight change was unrelated to these outcomes.

Lastly, we evaluated the possibility of interactions between BMI, weight change and PCOS on clinical outcomes. There was no evidence that the relation of weight change with positive β -hCG, clinical pregnancy or live birth rates differed according to baseline BMI (p , interaction = 0.93 for positive β -hCG, 0.07 for clinical pregnancy and 0.32 for live birth). PCOS did not modify the association of baseline BMI with positive β -hCG (p , interaction = 0.50), clinical pregnancy (p , interaction = 0.41) or live birth (p , interaction = 0.57) rates. Likewise, it did not modify the association between weight change and positive β -hCG rate (p , interaction = 0.56). However, the relation of weight change with clinical pregnancy and live birth rates appeared to differ between women with and without PCOS (p , interaction = 0.04 in both cases). In women without PCOS, weight loss appeared to have no influence on clinical pregnancy ($p = 0.12$) or live birth ($p = 0.11$) rates. However, among women with PCOS, weight loss was associated with significantly lower clinical pregnancy ($p = 0.05$) and live birth ($p = 0.04$) rates. Nevertheless, these results were entirely dependent on data from the only 2 women with PCOS who lost weight in this study.

Discussion

We examined the associations of BMI and short term weight change with embryological and clinical outcomes in a contemporary cohort of women undergoing infertility treatment with ART. As expected, BMI was associated with reduced peak E2 levels and live birth rates. Losing weight prior to initiation of ART was related to higher yield of MII oocytes, particularly among women who were overweight or obese at baseline. Short term weight change, however, was not related to clinical outcomes among women who underwent an embryo transfer.

An understanding of the strengths and limitations of our study is necessary to properly interpret the results. Assessing the relation between short-term weight change is both the most innovative aspect of our study and an important limitation. We assessed weight change as the difference in weight on the last clinical appointment preceding an ART cycle and weight upon study entry. Since we used data across multiple ART cycles whenever these data was available and a substantial proportion of participants had undergone IUI and/or ART cycles prior to joining the study, follow-up body weight will represent both real pre-treatment changes in body weight during the specified period as well as any residual effects that treatment may have on body weight during and after the completion of the previous treatment cycle. However, since ovarian stimulation does not result in lasting weight gain despite statistically significant weight gain during an ovarian stimulation cycle (15), this potential limitation is unlikely to affect our results. A second limitation with our approach is that we did not assess whether short-term weight change was voluntary or not. Unintentional weight loss could be present in women with undetected chronic wasting conditions. However, the demographic profile of these women along with the fact that the majority of women who lost weight were overweight or obese at baseline strongly suggests that weight loss in this study was most likely intentional. Conversely, weight gain in this study is most likely unintentional and, as discussed above, unrelated to treatment. A related problem was that the magnitude of weight loss among women who lost weight was modest. The median weight change among all women who lost weight was -3.1 kg and the median in among women in the group of women who lost at least 3kg was -4.6 kg. Therefore our data may not be generalizable to women with a greater amount of weight change.

Our findings regarding the association of BMI with ART outcomes are consistent with the existing literature on this topic. Peak E2 levels decreased linearly with increasing baseline BMI. This finding is in agreement with 5 previous studies (7–8, 16–18), collectively representing 4,175 ART cycles, where a statistically significant inverse relation between BMI and peak E2 levels was documented and consistent with an additional 8 studies (16,778 ART cycles) (6, 19–26) documenting an inverse relation that failed to reach statistical significance. Equally consistent with the literature is the lack of association of BMI with fertilization rate and embryo quality. Although, three previous studies have reported an association between BMI and decreased fertilization rate (8, 27–28), another eleven studies, collectively representing more than 25,000 ART cycles, have found no association between BMI and fertilization rate (6–7, 9, 16–18, 23–24, 29–31). Likewise, the majority of studies that have so far assessed the relation between BMI and morphology-based embryo quality scores have reported no association between them (6, 21, 23, 26, 31–32) with only two studies suggesting an adverse association of obesity with embryo quality (9, 20). Our findings are also consistent with the preponderance of data on the association of BMI with clinical outcomes. Of the twelve studies that have examined the association between BMI and live birth rate, only the two smallest ones (30, 33) did not document linear decrease in live births with increasing BMI. In all the remaining studies (5–6, 17, 24, 26, 28, 31–32, 34–35) there was an absolute reduction in live birth rates of approximately 5% to 10% when the leanest and heaviest women within each study are compared. The largest study conducted to

date found that, compared to normal weight women (BMI 18.5–24.9 kg/m²), the odds of failing to achieve a live birth was 18% higher in overweight (BMI 25–29.9 kg/m²) women, 36% higher among class I (BMI 30–34.9 kg/m²) and class II (BMI 35–39.9 kg/m²) obese women and 48% higher among class III (BMI 40 kg/m²) obese women using their own eggs (5).

We found that short-term weight loss was associated with a higher yield of MII oocytes, particularly among women who were overweight or obese at baseline, but it was unrelated to embryo development or clinical outcomes among women who reached embryo transfer. Results of a recent animal experiment suggest that the observed association may reflect a true biological effect of short term weight change. Adult female mice reared on chronic caloric restriction that are put on an *ad libitum* diet for 1 month (resulting in weight gain) produce fewer MII oocytes and a lower number of embryos reaching blastocyst stage than female mice that are kept on caloric restriction (36). In addition, despite the effects on MII oocyte yield, there were no statistically significant differences in pre-implantation embryonic development following IVF between the mice kept under caloric restriction and the mice allowed to feed *ad libitum* (36). Embryo transfer and evaluation of pregnancy outcomes was not performed in this animal study and thus there is no animal data to compare with our results. However, it is not entirely surprising that, despite the observed positive effect on oocyte quality, weight change was unrelated to clinical outcomes among women who underwent an embryo transfer given that the best embryos available are usually selected for transfer which may, to some extent, minimize any effects short term weight gain may have on clinical ART outcomes.

We also found that short-term weight loss was related to a lower fertilization rate in ICSI cycles. There is not, to our knowledge, previously published data to compare these results with. We do not have a satisfactory explanation for this finding and believe it may be a chance finding. Similarly, we believe that our finding that weight loss may be detrimental for clinical outcomes among women with PCOS is also likely a chance finding since only 2 women with PCOS lost weight in this study. While interesting, this finding is at odds with previous literature showing a beneficial effect of weight loss on reproductive performance of women with PCOS (37–38). Nevertheless, given the paucity of data in this area it is important that other studies examine these associations.

Contrary to our expectation, we did not observe any beneficial effect of short term weight loss in relation to clinical outcomes. To our knowledge, two previous studies examined the relation between short term weight change and clinical outcomes of women undergoing infertility treatment with ART. Clark and colleagues compared the pregnancy rates between obese women who underwent a lifestyle program with women who dropped out of this program. Among the women who failed to conceive spontaneously during the program and went on to receive infertility treatment, 26 of the 47 women who completed the program and underwent IVF became pregnant compare to none of the 35 women who dropped out of the program and underwent IVF (39). More recently, Moran and collaborators completed a pilot randomized trial of weight loss among obese women undergoing ART. There were no differences in pregnancy or live births between women randomized to lifestyle intervention (n=18) and women randomized to control (n=20) (40). Clearly, the data available to date does not clarify whether losing weight prior to initiating ART has any beneficial effects on clinical outcomes.

In summary, we found an association of BMI with lower peak E2 levels and live birth rates. This is consistent with the current literature. In addition, we found that short term weight loss has a beneficial effect on MII oocyte yield (particularly among overweight or obese women) but was unrelated to clinical ART outcomes. Thus, our results are not consistent

with recommendations to either limit access of obese women to ART or to delay their treatment until weight loss is achieved. However, given the limitations of this study and the paucity of data on the relation between short term weight change and ART outcomes it is important that this question is addressed further, ideally in randomized trials.

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Table 1

Subject characteristics by baseline body mass index (N=170 women)

	Baseline Body Mass Index (BMI), kg/m ²					p ^a
	<20	20 – 22.4	22.5 – 24.9	25 – 29.9	30	
N	22	47	42	35	24	
<i>Personal Characteristics</i>						
Age, years	34.2 (3.2)	34.8 (3.8)	36.2 (4.3)	35.4 (3.8)	36.1 (4.1)	0.22
Weight change, kg	2.5 (4.2)	1.0 (2.0)	-0.6 (2.9)	0.1 (3.5)	-2.6 (7.9)	<0.001
Time between study entry and follow-up anthropometry, days	140 (146)	150 (141)	100 (88)	141 (132)	191 (176)	0.12
Height, cm	166 (7)	166 (7)	164 (7)	165 (8)	165 (8)	0.89
Smoking status, %						0.27
Never	72	81	62	83	58	
Past	23	19	36	14	38	
Current	5	0	2	3	4	
Race/ethnicity, %						0.18
White/Caucasian	86	91	88	74	88	
Black/African American	0	0	0	6	8	
Asian	9	9	7	9	0	
Other	5	0	5	11	4	
<i>Reproductive characteristics</i>						
Previous IVF cycle, %	27	11	24	17	29	0.27
Previous IUI cycle, %	36	34	36	34	50	0.72
Primary infertility diagnosis, %						0.23
Female factor	46	43	50	37	42	
Male factor	27	19	26	40	46	
Unexplained	27	38	24	23	12	
Initial treatment protocol, %						0.04
Luteal phase agonist	86	72	62	78	46	
Flare	9	11	28	11	29	

	Baseline Body Mass Index (BMI), kg/m ²					p ^a
	5	17	10	11	25	
Antagonist						
Total gonadotropin dose, IU/L	1519 (968)	1676 (965)	1825 (1031)	1867 (913)	2163 (860)	0.19
Day 3 FSH, IU/L	6.4 (2.5)	6.6 (1.7)	7.5 (2.7)	7.0 (1.7)	7.5 (2.6)	0.25

^aFrom ANOVA for continuous variables and the Chi-square test for categorical variables.

Table 2

Body mass index and weight change in relation to endometrial thickness and controlled ovarian hyper-stimulation outcomes, (n = 168 women, 233 cycles).

	N	Endometrial thickness, mm	Peak E2 level, ng/dL	Oocyte yield, n	MII oocyte yield, n	MIH oocytes, % of oocytes retrieved
		Adjusted ^a Mean (95% CI)	Adjusted ^a Mean (95% CI)	Adjusted ^a Yield (95% CI)	Adjusted ^a Yield (95% CI)	Adjusted ^a Rate (95% CI)
Baseline BMI, kg/m ²						
<20	32	10.2 (9.3, 11.1)	2309 (1985, 2633)	9.1 (8.0, 10.2)	7.3 (6.3, 8.4)	82 (75, 88) ^c
20 – 22.4	63	10.3 (9.7, 10.9)	2100 (1875, 2325)	9.2 (8.0, 10.6)	8.2 (7.1, 9.4)	89 (85, 92)
22.5 – 24.9	53	9.9 (9.2, 10.6)	1891 (1632, 2150)	9.9 (8.6, 11.2)	8.7 (7.6, 9.9)	89 (84, 92)
25 – 29.9	47	10.0 (9.3, 10.7)	1692 (1428, 1956) ^c	8.5 (7.3, 9.9)	7.6 (6.6, 8.9)	91 (86, 94)
30	38	10.4 (9.6, 11.2)	1777 (1480, 2072)	10.8 (9.0, 12.9)	9.0 (7.6, 10.7)	85 (80, 89)
P, trend ^b		0.90	0.001	0.36	0.23	0.57
Weight change, kg						
<-3	38	10.2 (9.3, 11.1)	2024 (1706, 2341)	9.9 (8.3, 11.9)	9.1 (7.6, 10.7)	91 (87, 94) ^d
-1 to -3	32	10.2 (9.3, 11.0)	2234 (1910, 2558)	11.2 (9.4, 13.2) ^d	10.1 (8.5, 11.9) ^d	91 (86, 94) ^d
-1 to 1	80	10.2 (9.6, 10.8)	2021 (1803, 2239)	9.2 (8.2, 10.4)	7.8 (6.9, 8.8)	86 (80, 89)
1 to 3	51	10.1 (9.4, 10.8)	2042 (1787, 2296)	9.3 (8.0, 10.7)	8.2 (7.1, 9.6)	89 (84, 92)
>3	31	10.3 (9.3, 11.2)	2198 (1851, 2544)	9.3 (7.6, 11.4)	7.4 (6.1, 8.9)	81 (74, 87)
P, trend ^b		0.98	0.79	0.26	0.03	0.003

^a Adjusted for age, day 3 FSH levels, infertility diagnosis and treatment protocol. Models for weight change are further adjusted for baseline BMI

^b From a separate regression model where categories of BMI or weight change were modeled as a continuous variable.

^c Significantly different from women with a BMI between 20 and 22.4 kg/m² (p<0.05)

^d Significantly different from women with stable body weight (p<0.05)

Table 3

Body mass index and weight change in relation to fertilization rate, (n = 168 women, 232 cycles).

	Fertilization Rate, all cycles		Fertilization Rate, IVF cycles		Fertilization Rate, ICSI cycles	
	N	Adjusted ^a Rate (95% CI)	N	Adjusted ^a Rate (95% CI)	N	Adjusted ^a Rate (95% CI)
Baseline BMI, kg/m ²						
<20	31	74 (68, 81)	15	72 (62, 81)	16	77 (66, 86)
20 – 22.4	63	72 (67, 77)	30	70 (60, 79)	33	73 (66, 79)
22.5 – 24.9	53	70 (61, 78)	26	71 (56, 83)	27	70 (59, 80)
25 – 29.9	47	75 (66, 82)	22	79 (64, 89)	25	69 (57, 80)
≥30	38	64 (53, 74)	11	61 (43, 77)	26	64 (51, 76)
P, trend ^b		0.23		0.87		0.08
Weight change, kg						
<-3	39	68 (57, 77)	20	76 (57, 88)	19	59 (46, 71) ^c
-1 to -3	32	69 (59, 77)	15	71 (56, 83)	17	62 (48, 75) ^c
-1 to 1	80	74 (69, 79)	25	71 (60, 79)	54	75 (69, 81)
1 to 3	50	73 (66, 79)	26	69 (55, 81)	24	74 (65, 82)
>3	31	64 (52, 74)	18	60 (46, 73)	13	70 (56, 81)
P, trend ^b		0.98		0.12		0.03

^a Adjusted for age, day 3 FSH levels, infertility diagnosis and treatment protocol. Models for weight change are further adjusted for baseline BMI

^b From a separate regression model where categories of BMI or weight change were modeled as a continuous variable.

^c Significantly different from women with stable body weight (p<0.05)

Table 4

Body mass index and weight change in relation to positive β -hCG, clinical pregnancy and live birth rates, (n = 170 women, 226 cycles).

		Positive β -hCG	Clinical Pregnancy	Live birth
	N	Adjusted ^a Rate (95% CI)	Adjusted ^a Rate (95% CI)	Adjusted ^a Rate (95% CI)
Baseline BMI, kg/m ²				
<20	30	57 (36, 75)	41 (23, 62)	39 (20, 62)
20 – 22.4	62	66 (50, 78)	50 (35, 65)	42 (28, 58)
22.5 – 24.9	51	44 (28, 61) ^c	33 (20, 48)	30 (17, 47)
25 – 29.9	46	56 (39, 72)	34 (22, 48)	23 (12, 40) ^c
30	37	41 (24, 61) ^c	29 (15, 49)	22 (11, 41)
P, trend ^b		0.13	0.09	0.03
Weight change, kg				
<-3	39	57 (33, 78)	23 (10, 43)	16 (5, 38)
-1 to -3	32	48 (29, 69)	37 (21, 57)	28 (12, 54)
-1 to 1	77	52 (39, 66)	43 (30, 57)	37 (24, 53)
1 to 3	49	65 (48, 79)	49 (37, 64)	44 (30, 60)
>3	30	56 (33, 76)	38 (17, 64)	26 (11, 50)
P, trend ^b		0.58	0.09	0.12

^a Adjusted for age, day 3 FSH levels, infertility diagnosis and treatment protocol. Models for weight change are further adjusted for baseline BMI

^b From a separate regression model where categories of BMI or weight change were modeled as a continuous variable.

^c Significantly different from women with a BMI between 20 and 22.4 kg/m² (p<0.05)