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# Impact of female and male obesity on IVF/ICSI: results of 700,000 ART-cycles in Germany

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**Abstract**

To our knowledge, this is the first analysis in which male and female weights have been combined. The registry dataset covering a 12-year period was analysed for all treatment cycles where an embryo transfer was reported. In all, 706,360 cycles were analysed. Treatments include IVF, ICSI, IVF/ICSI and CPE. The highest success rate in IVF cycles was found in couples, with an obese male partner. In the group of obese women, the pregnancy rate decreased to 27.2%. Similar to IVF treatment, the highest success rate in ICSI cycles was found in couples, where either the male or the female partner was obese. The highest success rate in cycles with a cryopreserved embryo transfer was observed in couples where both partner were obese. The lowest success rate was seen where the female partner was obese. Our data analysis suggests that the combination of an obese male and a normal-weight female is positively related to better implantation rates in IVF as well as ICSI-cycles. This combination is more likely to be found in couples with a higher social status. Therefore, the increased pregnancy rate in this group might as well be related to other lifestyle factors associated with higher social status.

**Keywords:** *IVF, ICSI, weight, ART, lifestyle, social status, BMI*

## Introduction

According to the World Health Organization (WHO), excessive weight and obesity are defined as an abnormal accumulation of fat that may represent a health risk [1]. Infertility is one of these health risks.

The body mass index (BMI) forms a simple index of the weight-to-height ratio, and is used to indicate excessive weight and obesity in adult populations. It is defined as weight in kilograms divided by square of the height in metres ($kg/m^2$) [1]. In adults, WHO definitions do not differentiate between either sex or age. The BMI should, however, only be considered as a rough guideline since it may not represent the same level of obesity in different individuals. An individual is defined as being 'overweight' if their BMI is equivalent to or greater than 25, while a BMI equivalent to or greater than 30 represents a state of 'obesity'.

Eurostat, the European Communities Statistical Office, records and analyses national data received from the statistical authorities of EU member nations. Reported obesity rates among men ranged from 5.4% to 22.8%, while among women, these rates ranged between 7.1% and 35.6% [2]. The prevalence of obesity and excess weight (pre-obese and obese) among adults indicated respective ranges between 6 and 27% and 26–68% [2]. Among men, obesity was higher in 14 of 36 countries or regions providing data broken down according to gender, while the rates of pre-obesity were greater among men in all 36 countries or regions. The rates were highest in Albania, Bosnia and Herzegovina and the United

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Kingdom (Scotland) and lowest in Turkmenistan and Uzbekistan [2].

In Germany, the rate for obese men was reported as being 13.6% while the overall rate for women was 12.3%.

With respect to reproduction in general, 13.5% of females and 15.3% of males in the 30–39 year age bracket exhibited a BMI $> 30$ [3]. In the high income group, this percentage decreased to 3.9% (female) and 11.0% (male). In the low-income group, the percentages increased to 22.2% (female) and 15.9% (male) [4].

The correlation between body weight and success rates for assisted reproduction techniques (ART) is discussed controversial.

The German IVF Registry (www.deutsches-ivf-register.de, DIR) was founded in 1982 and has since modified its data collection requirements on several occasions [5]. Nearly, all German IVF units are currently using a standard, computer-based dataset description but employ different software tools. These tools have also undergone numerous developments as well. Since 1997, all ART cycles reported to the system have been entered prospectively (within 7 days from the start of controlled ovarian hyperstimulation). Participation in the registry became mandatory in 1999. Compared to the IVF registries of other nations, the German national registry contains more information about reproductive history such as risk factors and pre-existing conditions. Hypertension, diabetes, smoking, a history of thrombosis, allergic reactions, psychiatric disorders and also obesity (BMI $>= 30$) are included for both partners. Up to four different categories can be selected.

Based on our research, this represents the largest ART dataset to be analysed for any correlation between obesity and pregnancy rates. The cycles had been carried out at 120 IVF units. To our knowledge, this is the first analysis in which male and female weights have been combined.

## Methods

The registry dataset covering a 12-year period (from 1997 through 2008) was analysed for all treatment cycles where an embryo transfer was reported. In all, 706,360 cycles were analysed. In 650,452 cycles information concerning weight was given. Treatments include standard *in vitro* fertilisation (IVF), intracytoplasmatic sperm injection (ICSI), a single cycle combination of IVF and ICSI (IVF/ICSI) and so called cryopreserved embryo transfer (CPE, embryos derived from cryopreserved oocytes in 2-PN-stage). A maximum of three embryos were transferred according to the German Embryo Protection Act of 1991.

The obesity category was assigned to four groups: none, female, male, both.

The outcome was defined as the proportion of embryo transfer which resulted in clinical pregnancies. In turn, a clinical pregnancy was defined as the occurrence of at least one ultrasonically confirmed gestational sac; either with or without positive detection of a heartbeat. Thus, this definition includes ectopic pregnancies and pregnancy losses, but excludes biochemical pregnancies.

For the statistical analysis intervals with a 95% confidence level were used as a binomial dependent variable to indicate a success model (defined as either a clinical pregnancy or a miscarriage).

In models evaluating the impact of the obese individuals (male, female), the reference group was represented by couples where both partner's BMI was $< 30$.

Wald's Chi-Square ($\chi^2$) test was used to test the null hypothesis of no association, while the accuracy of the estimates was evaluated using the 95% confidence interval. Statistical significance was considered to be reached at $P$-values $< 0.05$.

Statistical analysis was performed using Version 9 of the Statistica software package (StatSoft ®, Tulsa, OK, USA).

## Results

Beginning in 1982, the data collection regulations of the German IVF-Registry were modified several times. In 1997, new software utilising a revised dataset description was implemented.

Rules related to the plausibility of the data entered into the system were generated with varying acceptance levels and therefore varying percentages of item records at the entry site. Figure 1 illustrates the percentage rates for male and female obesity (BMI $>$ 30). It was found that data entry for female patients increased between 1997 and 2001. The highest percentage of all treatment cycles was recorded in 2003.

In male patients, an uninterrupted increase up to a level of 8% of all treatment cycles can be seen from 1997 onwards.

IVF cycles represent 28.2% of all employed treatment methods (Table I). The highest success rate was found in couples, with an obese male partner (30.4% clinical pregnancy rate). Compared with not obese couples (0) this was statistically significant for this treatment group (2). In the group of obese women (1), the pregnancy rate decreased to 27.2%.

ICSI cycles represent 48.4% of all treatment methods employed. Similar to IVF treatment, the highest success rate was found in couples, where either the male or the female partner was obese (28.54 vs. 28.75 clinical pregnancy rates). When compared to those couples with a BMI $\leq 30$, this level was statistically significant for this treatment group. The lowest success rate was seen, where none of the patients were obese.

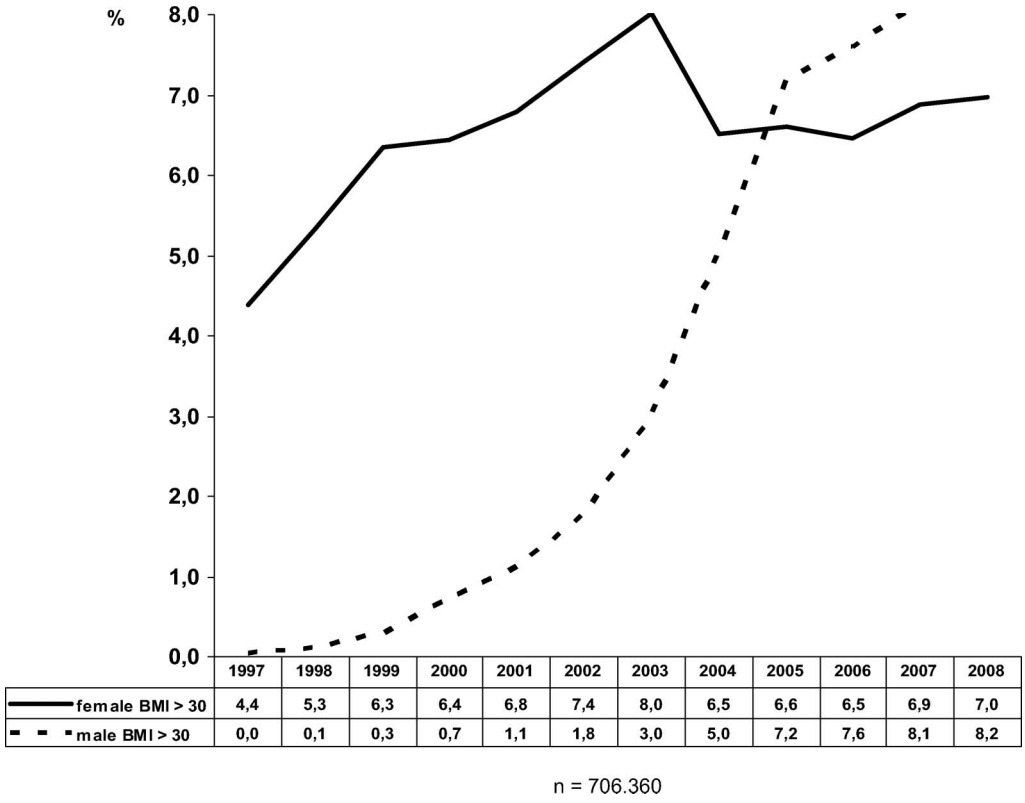


Figure 1. Documentation of BMI > 30 in all treatment cycles, DIR 1997–2008.

Table I. ICSI treatment results for normal and obese individuals, BMI > 30.

| | BMI > 30 | *n* | Confidence interval – 95% | Clinical pregnancy rate | Confidence interval + 95% | *P*-value for Chi-squared |
|---|---|---|---|---|---|---|
| IVF | None | 166,618 | 27.94 | 28.15 | 28.37 | |
| | Female | 11,970 | 26.72 | 27.52 | 28.32 | 0.1361 |
| | Male | 3,782 | 28.91 | 30.38 | 31.85 | 0.0028 |
| | Both | 1,102 | 27.94 | 28.15 | 28.37 | 0.3826 |
| ICSI | None | 282,645 | 27.47 | 27.63 | 27.80 | |
| | Female | 18,866 | 27.89 | 28.54 | 29.18 | 0.0069 |
| | Male | 10,288 | 27.88 | 28.75 | 29.63 | 0.0130 |
| | Both | 3,009 | 26.25 | 27.85 | 29.45 | 0.7797 |
| IVF/ICSI | None | 7,330 | 28.64 | 29.69 | 30.73 | |
| | Female | 383 | 23.18 | 27.68 | 32.18 | 0.4177 |
| | Male | 155 | 23.01 | 30.32 | 37.64 | 0.9614 |
| | Both | 40 | 15.16 | 30.00 | 44.84 | 0.9659 |
| CPE | None | 131,412 | 17.04 | 17.25 | 17.45 | |
| | Female | 6,844 | 15.79 | 16.67 | 17.55 | 0.2073 |
| | Male | 4,911 | 16.35 | 17.41 | 18.47 | 0.7656 |
| | Both | 1,097 | 15.42 | 17.68 | 19.95 | 0.7536 |
| All | | 650,452 | 25.44 | 25.54 | 25.65 | |

Female obesity is correlated with the lowest clinical pregnancy rate (CPR) in stimulation cycles whereas male obesity with the highest CPR.

Where both procedures are carried out in a single cycle, IVF/ICSI represent the smallest group with an overall incidence of only 1.2%. The reasons for performing IVF/ICSI vary. In general, an unexpected reduction in sperm quality could be considered to be the primary reason. Again, akin to both IVF and ICSI treatment, the highest success rate was observed in couples in which the male partner was obese (30.3% clinical pregnancy rate). This was not statistically significant for this treatment group. The lowest success rate was observed where the female partner was obese.

Cycles in which a cryopreserved embryo transfer was performed represent 22.2% of all treatments.

The highest success rate was observed in those in couples where both partner were obese (17.7% clinical pregnancy rate). This was not statistically significant for this treatment group. The lowest success rate was seen where the female partner was obese.

## Discussion

The expression 'obesity' is derived from the Latin term, '*obesus*', which can be translated as: 'one who has become plump through eating' [6].

Several studies had been performed to investigate the correlation between weight and ART outcomes. But findings are inconsistent and the scientific discussion is ongoing.

Some studies found decreased implantation and pregnancy rates in obese and overweight women [3,7–16], whereas others have not found such an effect for ART cycles in relation to obesity [17–24].

The UK team of Maheshwari et al. summarised 21 articles focused on ART and weight [3]. They carried out a statistical analysis comparing different weight groups. They were able to demonstrate that, for example, a female BMI > 30 provided a slight advantage within the obese group when compared with one of < = 30. This was found in six papers covering 7,848 cycles.

Esinler et al. from Turkey were only able to analyse ICSI treatments [19]. They employed a ranking based on three BMI groups for 775 couples (18.5–24.9, 25.0–29.9, ≥30). There was a slight increase in pregnancy rates (44.6%, 45.4%, 48.1%) with no statistically significance.

Our findings are the first based on a data set of about 700,000 ART-cycles and the first differentiating between both male and female obesity. It is also the first study to separately compare IVF, ICSI, IVF/ICSI and CPE within such a large dataset. But our results are somewhat conflicting.

The ICSI group exhibited an increased pregnancy rate for obese women and men (Figure 3). These findings are statistically significant and partly similar to those of Esinler.

The correlation between male obesity and ART success rates was analysed in literature reviewed by Hammoud et al. from Salt Lake City [25]. Their observational findings indicate that obesity at a population level results in reduced male fertility among infertile couples. However, the effect of obesity on male infertility seems to be modest.

Stewart et al. from Melbourne analysed semen specimens from 225 pregnant women who conceived naturally [26]. Abstinence, total testicular volume, varicocele grade and obesity (BMI > 30) were independently significantly related to total sperm count. Compared to those with a BMI < 30 ($n = 188$), obese subjects ($n = 35$) had significantly lower total sperm counts. They concluded that obese fertile men appear to have reduced testicular function.

In contrast, findings from our study were able to demonstrate an increased pregnancy rate in all treatment groups for obese men. For IVF and ICSI, this was statistically significant.

In the German IVF registry, the percentage of obese men with a BMI > 30 increased continuously between 1997 and 2008. This apparently does not relate to a general change in the German lifestyle, but rather to an increased awareness of this risk factor based on increased documentation in the registry records. Therefore, the indicated percentage demonstrates an underestimation of male obesity. Also prevalence of female obesity seem to be underestimated.

In a review study from Turkey, Erel illustrated that a controversy extends throughout currently ongoing discussions [27].

While some studies indicate decreased implantation and pregnancy rates in obese and overweight women,– others are unable to determine any such effects.

As an example, this seems to be related to the secondary analysis of obese women to determine whether or not they exhibit a PCO syndrome [18].

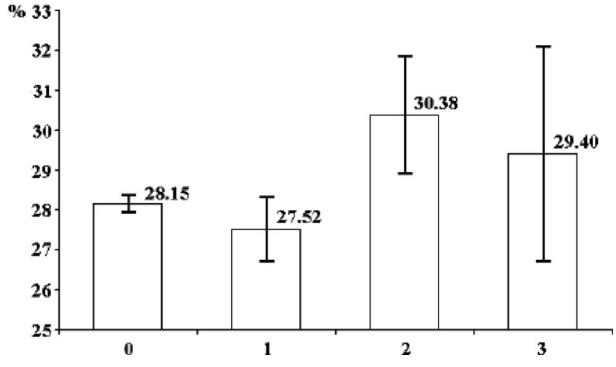


Figure 2. IVF clinical pregnancy rate, 1997–2008. 0 = Female + male BMI ≤ 30 ($n = 166,618$), 1 = Female > 30 ($n = 11,940$), 2 = Male > 30 ($n = 3,782$), 3 = Female + male > 30 ($n = 1,102$).

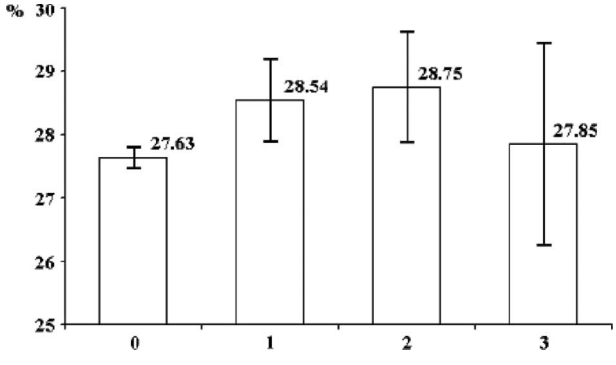


Figure 3. ICSI clinical pregnancy rate, 1997–2008. 0 = Female + male BMI ≤ 30 ($n = 282,645$), 1 = Female > 30 ($n = 18,866$), 2 = Male > 30 ($n = 10,288$), 3 = Female + male > 30 ($n = 3,009$).

In our study, we demonstrated different outcomes for IVF and ICSI cycles. In the latter group, we found a statistically significant increase in those couples were the woman was obese.

The opposite but statistically not significant result was determined in the IVF cycle group.

Wass et al. distinguished between an android and gynaecoid fat distribution [28]. Their findings suggest an increased significance for android fat distribution, rather than for obesity per se.

Sneed et al. analysed the correlation between BMI, age and ART success [29]. They concluded that in younger patients, BMI has a significant negative impact on IVF outcomes. This affect disappears after the age of 36. Our analysis only broke down treatment by type, not by age groups.

Martinuzzi et al. from New York analysed 417 patients under the age of 36 who underwent an initial, fresh, non-donor *in vitro* fertilisation (IVF) [22]. They defined four BMI groups ($<18.5$, 18.5–24.9, 25–29.9, $\geq 30$). Cancellation rates, peak estradiol levels and the mean number of recovered oocytes were similar in all groups. Clinical and ongoing pregnancy rates were similar among groups.

We were only able to determine a slight and insignificant decrease of pregnancy rates among females in the IVF group (Figure 2). This finding is probably due to obese women with cycle disorders because of PCO-like syndromes and therefore treated with IVF. All other overweight groups demonstrated increased pregnancy rates.

Recently, Awartani et al. from Saudi Arabia demonstrated that IVF and ICSI treatments differed in a group of 406 patients with an average BMI of 32.1 when compared with 141 women with an average BMI of 37.7 [30]. The clinical pregnancy rates per initiated cycle varied between 19.9% and 28.6%.

Bellver et al. from Spain compared IVF and ICSI treatment in 4,227 couples broken down into four different female weight groups [31]. Statistically, the pregnancy rates differ significantly ($<20$ BMI: 45.0%, 20–24.9 BMI: 44.8%, 25–29.9 BMI: 42.3% and $>30$ BMI: 37.9%).

Dechaud et al. from France analysed 573 patients who underwent *in vitro* fertilisation (IVF) or ICSI [20]. They defined four BMI groups ($<20$, 20–24, 25–29, $\geq 30$). With the exception of the totally required r-FSH dosage, all other parameters of ovarian response were comparable. In the group with a BMI $\geq 30$, this dose was statistically higher when compared to the other groups. All parameters related to the IVF outcome were comparable, including cancellation rates, implantation rates and pregnancy rates.

One limitation of the presented study lays in the fact that documentation of lifestyle factors such as a BMI $> 30$ increased for women between 1997 and 2003, while in men the increase occured between 1997 and 2008 (Figure 1). Therefore, the prevalence of obesity in the German registry dataset in the early years of item recording may represent an underestimation.

On the other hand and based on our observations, no other dataset comprising 700,000 cycles has ever been previously analysed which accounts for the validity of our results.

We only focused on clinical pregnancy rates and did not separately analyse subjects such as PCO syndromes, number of oocytes, embryo quality, miscarriage rates and stimulation protocols. This was due to raw data limitations in the long-term collection of the national registry and the design of this preliminary study.

On the other hand, this population-based analysis is based not merely on a single centre, but covers on average 120 centres, giving it a coverage range of practically 100% of all cycles in a single country over a 12-year period.

Most surprisingly, our data analysis suggests that the combination of an obese male and a normal-weight female is positively related to better implantation rates in IVF as well as ICSI-cycles. According to the study of Robert Koch-Institute [4], this combination is more likely to be found in couples with a higher social status. Therefore, the increased pregnancy rate in this group might as well be related to other lifestyle factors associated with higher social status.

## Acknowledgements

All participating IVF-units in Germany cooperated in the German IVF Registry. Only this cooperation enables such an analysis with numerous cycles. The authors thank all units for this support. A list of all units is available on www.deutsches-ivf-register.de

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