

# Women show a higher level of anxiety during IVF treatment than men and hold different concerns: a cohort study

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## Abstract

**Purpose** The aim of the present study was to determine levels of anxiety during the course of IVF treatment and gender differences in treatment anxiety.

**Methods** This was a prospective cohort study set in a university affiliated, tertiary care IVF program. 119 women and 82 men entering the clinic to undergo IVF treatment filled out questionnaires containing the Spielberger state-trait-anxiety-inventory (STAI) as well as further items on specific stress triggers.

**Results** Women and men undergoing IVF have higher levels of anxiety than the average population in Germany. Overall, female patients show significantly higher values (mean  $\pm$  SD) for state and trait anxiety ( $47.4 \pm 11.0$  and  $40.1 \pm 9.85$ ) than their male partners ( $41.4 \pm 9.66$  and  $35.3 \pm 8.57$ ,  $p < 0.01$ ). Over the course of several IVF cycles, average STAI scores increased for both genders. When asked about specific stress factors on a 4-point scale from ‘not at all’ to ‘very much so’, women report as their main anxiety the failure to achieve a successful pregnancy, scoring significantly higher on questions like ‘obtaining a negative pregnancy test’ ( $3.24 \pm 0.82$ ,  $p < 0.01$ ) and ‘disclosure of infertility’ ( $3.02 \pm 1.10$ ,  $p < 0.001$ ). Their male partners are more concerned about the health risks the women have to take such as ‘side effects of ovarian

stimulation’ ( $2.55 \pm 0.77$ ,  $p = 0.002$ ) and ‘bleeding or infection after the oocyte aspiration’ ( $2.58 \pm 0.84$ ,  $p = 0.007$ ). Both genders indicated to be very little worried about multiple pregnancies after IVF.

**Conclusions** Women show a higher level of anxiety during IVF treatment and hold different concerns. Neither of the sexes appears to be familiar with the risks associated with multiple pregnancies, a matter that should better be addressed.

**Keywords** Treatment anxiety · Gender differences · Controlled ovarian stimulation · Cost · Resource utilization · IVF · Stress factors · Patient dropouts

## Introduction

Current evidence suggests that a 56 % of all infertile patients eventually seek medical care [1]. It was reported in the early 1990s already that the psychological symptoms associated with infertility are similar to other serious medical conditions like HIV or chronic pain [2]. A meta-analysis from 2011 summarizing prospective psychosocial studies suggests a lack of association of pretreatment emotional distress and lower pregnancy outcome in women undergoing a cycle of treatment in assisted reproductive technology, a matter couples should be informed about to reduce the stress they might experience during infertility treatment [3, 4]. Nonetheless, psychological distress may cause couples to retreat from IVF treatment prior to the achievement of pregnancy despite relatively good chances to succeed in later attempts. Preventing premature treatment discontinuation would furthermore increase the cumulative pregnancy rate and thereby the efficacy of IVF treatment [5].

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Several studies have shown that IVF treatment is responsible for high levels of emotional and social distress in patients, causing numerous couples to drop out of treatment before the goal of pregnancy is achieved [6]. A significant number of patients seems to be terminating treatment out of own volition and not for financial reasons [7–9]. At least 30 % of couples seem to be dropping out of treatment due to psychological distress before the goal of pregnancy is reached, with some half of the couples dropping out of therapy before the actual IVF treatment has even begun [10–12]. High dropout rates in IVF treatment due to psychological reasons are a well described phenomenon in the literature, and the way they have been tackled has changed over the past decades towards an integrated approach in fertility care, that calls upon all fertility clinic staff to be involved in the provision of psychosocial care [13].

It is clear that the decision of a couple to continue or discontinue treatment will be modulated by numerous factors, which will rank differently depending on economic, social and emotional circumstances. It is also likely that within a given setting, females and males might systematically differ in psychological stress and concerns. To date, still very little is known about gender differences and what specific procedures during IVF therapy trigger most distress. The question of male treatment anxiety has, with some exceptions, not been tackled to full extent in current literature yet [14]. Furthermore, we felt the need to also include psychosocial concerns during IVF therapy, e.g., changes within the couple's social environment, occurrence of relationship problems as well as the fear of being childless into the survey to broaden the frame of possible stressors. Those reasons for IVF treatment termination are to be identified and remedied in order to ensure the patient's continuation of IVF and thus improve treatment success [15].

Accordingly, the aim of the current study was explore anxiety level differences and concern differences between women and men undergoing IVF therapy. Moreover, to facilitate the possibility of comparability with other studies on IVF anxiety, the Spielberger state–trait–anxiety–inventory (STAI) was embedded in the questionnaire, being a well-known and often used tool to determine and measure anxiety levels during IVF treatment [16, 17].

## Methods

In this prospective cohort study conducted between November 2012 to June 2013 female and male patients entering the university affiliated tertiary IVF program in Luebeck for a first or repeat consultation were asked to participate in a six page survey consisting of the STAI

(state–trait–anxiety–inventory) and a 25-item questionnaire about specific stress factors and possible triggers for treatment anxiety. The primary goal of this study was to determine gender differences in STAI anxiety levels. Secondly, gender differences between the STAI anxiety levels in correlation to education, number of treatment cycles and current stage within IVF treatment were determined. Paired comparison within couples was not implemented nor intended in the study design. The institutional review board of the University of Luebeck reviewed and monitored the study and granted its full approval in September 2012.

## Design of the questionnaire

The survey consisted of six pages breaking down as follows: The first page contained questions about the patients' age, the level of education, current stage in IVF therapy ('first conversation', 'repeat consultation', 'follicular puncture or insemination', 'embryo transfer', 'pregnancy test') and number of previous treatment cycles. Next, two pages of the aforementioned Spielberger state–trait–anxiety–inventory (STAI) had to be filled out. The STAI is a wide-spread instrument for measuring anxiety levels in adults and consists of two pages with questions on a 4-point Likert scale ('not at all' to 'very much so'), concerning the temporary condition of 'state anxiety' and the more long-standing quality of 'trait anxiety'. The overall scores for each value range from 20 to 80 points and can be referenced to norm group. Also, two pages with questions on Visual Analogue Scales (VAS) about the anxiety levels at prior visits in hospitals or at private doctors as well as dentists were included. Lastly, the sixth page comprised of 25 questions about specific stress factors and possible triggers for treatment anxiety on a 4-point Likert scale from 'not at all' to 'very much so'. The questions were assembled on the basis of clinical interest and relevance and had not been validated on a norm group before (Table 1).

## Statistical analyses

Descriptive statistics for continuous variables [mean, SD, median, and 5th and 95th percentiles (P5, P95)] and for discrete variables (number, proportion, percentage) as well as *p* values of differences between the items and sexes were estimated and calculated using either Mann–Whitney *U* test, *T* test or the Kruskal–Wallis test, as appropriate. The 95 %-confidence intervals were calculated using 1000 bootstrap samples and the Hodges–Lehmann-estimator. The dataset has not been statistically adjusted for multiple testing.

**Table 1** Patient cohort with age, education, current treatment cycle of IVF treatment, duration of infertility as well as number of genetic children

	Male		Female	
	Mean	<i>n</i>	Mean	<i>n</i>
Age in years	37.22 ± 7.4	82	34.29 ± 4.7	119
Highest level of education <sup>a</sup>				
None		0		1
5 year high school degree		7		4
6 year high school degree		28		46
College degree		18		29
University degree		33		44
In which treatment cycle are you right now?				
First cycle		39		43
Second cycle		14		17
Third cycle		9		20
Fourth cycle or more		21		41
What is your current stage within the IVF treatment?				
First conversation		13		15
Repeat consultation		27		38
Follicular puncture or insemination		29		37
Embryo transfer		16		25
Pregnancy test <sup>b</sup>		1		5
For how many months have you had the wish to have children?	42.48 ± 40.84		41.76 ± 29.96	
How many children do you already have, including other partnerships?				
None		64		97
One child		16		22
Two children		3		1
More than two children		3		4

<sup>a</sup> German levels of education (Hauptschule, Realschule, Abitur, Studium) originally asked were translated to fit American standard

<sup>b</sup> Number might be biased due to some couples' misunderstanding, selecting the item 'repeat consultation' when actually present for the pregnancy test

## Results

### State–trait–anxiety–inventory

One hundred and nineteen women (average age 34.29 ± 4.7) and 82 men (average age 37.22 ± 7.4) completed the questionnaire at different stages and within different cycles of the IVF treatment whilst waiting for the next procedure or medical consultation. Incomplete surveys were dismissed.

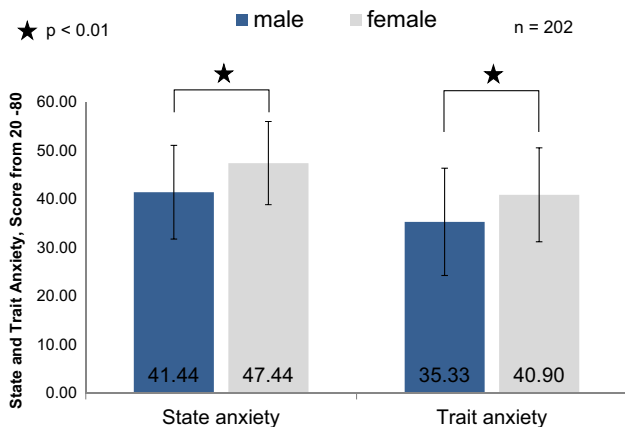
Women and men undergoing IVF score higher on the STAI than the average population in Germany, for whom an average score for the women of 38.08 ± 10.29/37.01 ± 9.95 and for the men of 36.83 ± 9.82/34.45 ± 8.83 for state–anxiety and trait–anxiety, respectively, have been determined [18]. Overall, female patients show significantly higher values for state and trait anxiety

(47.4 ± 11.0; 40.1 ± 9.85) than their male partners (41.4 ± 9.66; 35.3 ± 8.57,  $p < 0.01$ ) (Fig. 1).

No significant differences could be found in our study in levels of STAI-state or STAI-trait anxiety concerning different levels of education. Furthermore, when focussing on five different time points during the IVF treatment, patients of both genders did not show significant differences in anxiety levels per time point ( $p = 0.56$  for STAI-S;  $p = 0.09$  for STAI-T).

With increasing numbers of previous IVF cycles, couples were scoring significantly higher on STAI–state ( $p < 0.01$ ) as well as STAI–trait ( $p < 0.05$ ) scores, Fig. 2. No gender differences were to be found in this regard.

Moreover, splitting up the sample group into quartiles and comparing the first quartile of patients, scoring under the 25 % rank (<P25) in STAI-state or STAI-trait, with the rest of the patient group (>P25), similar findings could be



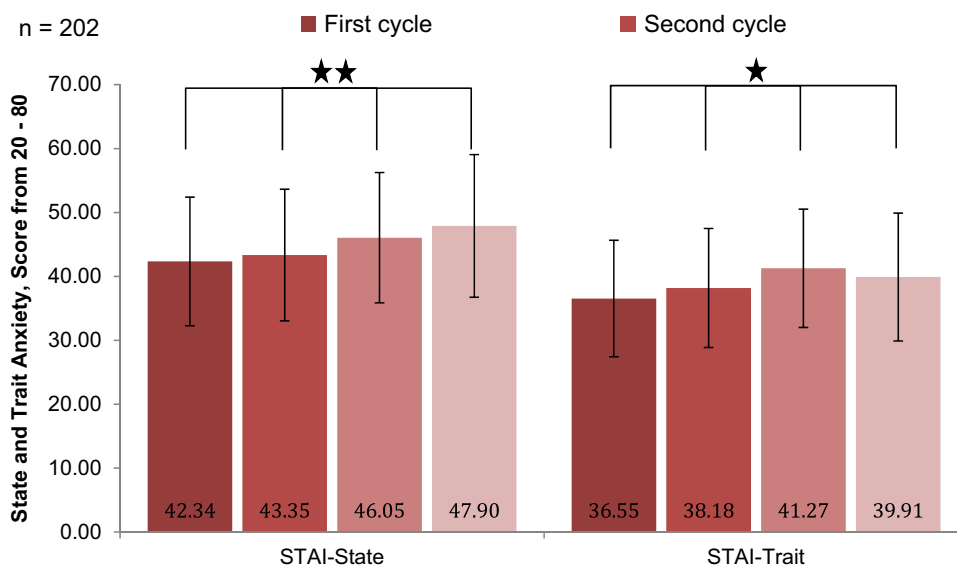
**Fig. 1** Female and male STAI–state and STAI–trait values, reaching from 20 to 80 points

observed: The number of patients of both genders within the first quartile (<P25) of the STAI–state (STAI-S) score dropped significantly, when correlated to increasing number of treatment cycles, see Table 2 ( $n = 196$ ;  $p < 0.01$ ).

There was no significant difference between the sexes to be found comparing quartile groups.

Furthermore, the scores for STAI-S and STAI-T were decreasing with increasing number of own children before IVF therapy. In our sample, mean STAI scores did not differ significantly between patients with children and patients without children, on neither STAI–state ( $p = 0.17$ ) nor STAI–trait ( $p = 0.10$ ) levels. In exception, if looking merely at male patients, the more children the male patients had prior to treatment, the lower they scored on the general personality attribute of being anxious, the STAI–trait ( $p < 0.05$ ).

**Fig. 2** Mean values of male and female anxiety scores of STAI-S and STAI-T per IVF cycle rank. \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$



**Table 2** The number of patients of both genders within the first quartile (<P25) of the STAI–state (STAI-S) score correlated to increasing number of treatment cycles drops significantly ( $n = 196$ ;  $p < 0.01$ )

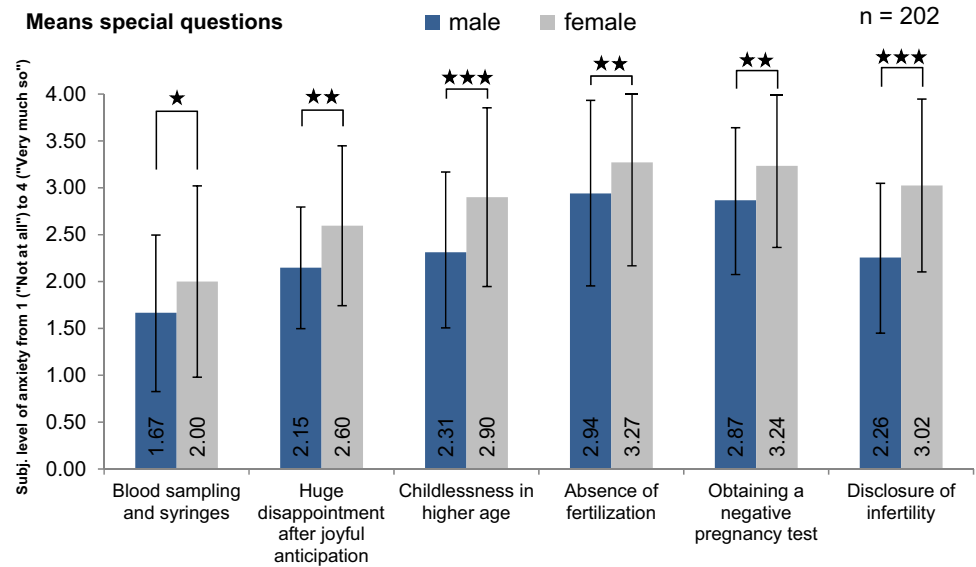
	Quartile of STAI-S score		Combined
	<P25	>P25	
In which cycle of IVF treatment are you at the moment?			
First	48	31	79
Second	18	10	28
Third	23	5	28
Fourth and more	52	9	61
Overall	141	55	196

There was no difference between the sexes. Information was missing or inconclusive on five patients

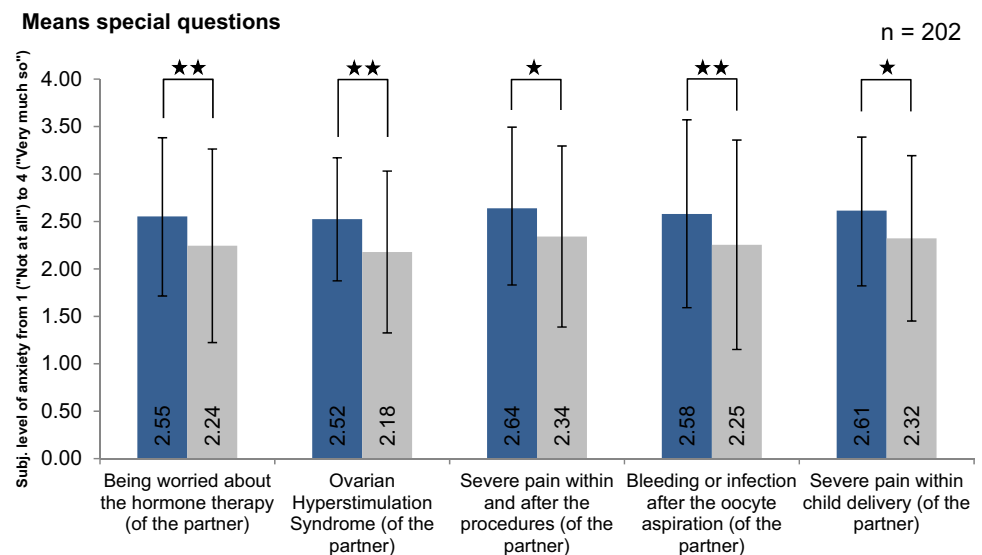
**Specific questionnaire concerning IVF treatment**

When asked about the specific stress factors on a 4-point Likert scale from ‘not at all’ to ‘very much so’, women reported as their main anxiety the idea of failing to achieve a successful pregnancy, scoring significantly higher on the questions ‘obtaining a negative pregnancy test’ ( $3.24 \pm 0.82$ ,  $p < 0.01$ ), ‘huge disappointment after joyful anticipation’ ( $2.60 \pm 0.95$ ,  $p < 0.01$ ), ‘childlessness in higher age’ ( $2.90 \pm 1.10$ ,  $p < 0.01$ ), ‘absence of fertilization’ ( $3.27 \pm 0.81$ ,  $p < 0.001$ ) and ‘disclosure of infertility’ ( $3.02 \pm 1.10$ ,  $p < 0.001$ ) (Fig. 3). Besides, women stated to be more concerned and stressed by the procedures of ‘blood sampling and syringes’ than men ( $2.00 \pm 1.02$ ,  $p < 0.05$ ).

**Fig. 3** Womens' and mens' significant differences on specific anxiety triggers within IVF therapy. \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$



**Fig. 4** Womens' and mens' significant differences on specific anxiety triggers within IVF therapy. \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$



Their male partners, however, were significantly more concerned about the health risks women have to take during IVF treatment, such as 'side effects of ovarian stimulation' ( $2.55 \pm 0.77$ ,  $p = 0.002$ ), 'ovarian hyperstimulation syndrome' ( $2.52 \pm 0.79$ ,  $p < 0.01$ ), 'severe pain within and after the procedures' ( $2.64 \pm 0.82$ ,  $p < 0.01$ ), 'severe pain at child delivery' ( $2.61 \pm 0.82$ ,  $p < 0.05$ ) and 'bleeding or infection after the oocyte aspiration' ( $2.58 \pm 0.84$ ,  $p = 0.007$ ) (Fig. 4).

Less than 15 % of subjects in both sexes were moderately or severely worried about the risks associated with multiple pregnancies and there was no sex difference in that regard ( $p = 0.56$ ) (Fig. 5). No significant differences in anxiety levels between sexes could be determined in the other items of the specific 25-question survey.

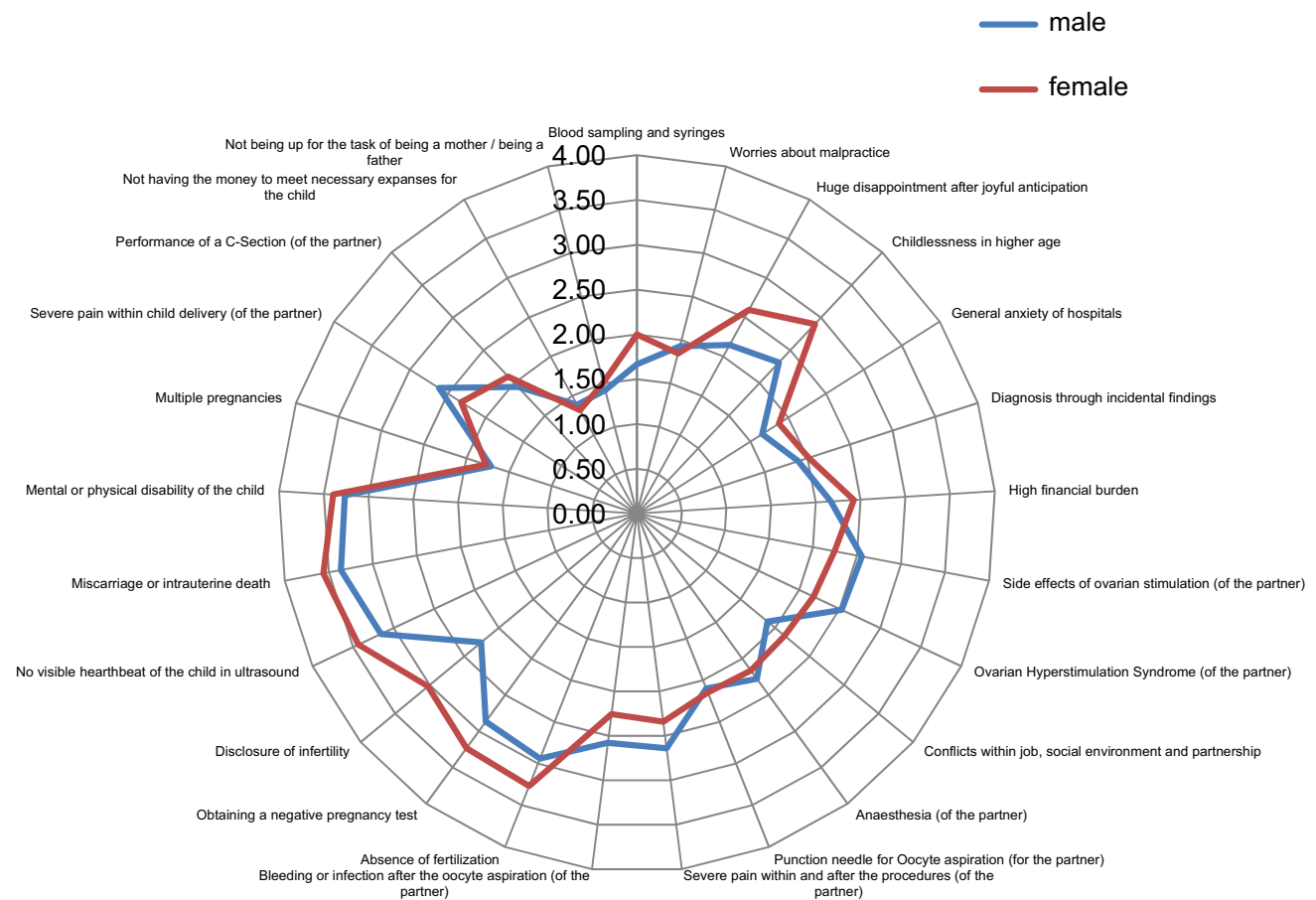
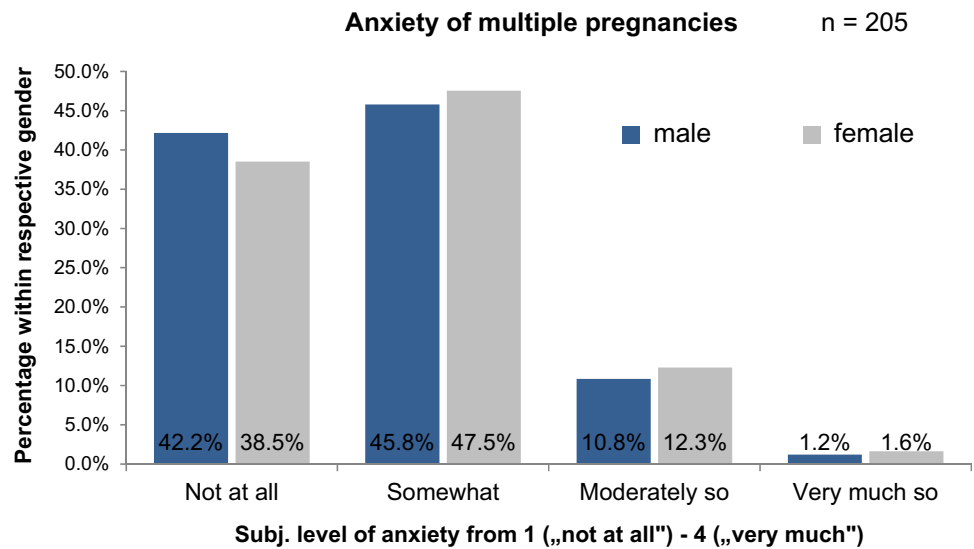
## Discussion

### Findings on anxiety levels in IVF therapy

Women and men in IVF treatment were scoring higher on the STAI than German reference populations and were thus in more psychological distress than the average. This finding goes in strong agreement with the literature and suggests the comparability of our cohort with other studies on this topic. Our findings thereby confirm that infertility treatment is associated with a significant psychological burden for the couples (Fig. 6).

The women in this study scored significantly higher in the STAI than men and were thus not only feeling more anxious than their male counterparts within the therapeutic

**Fig. 5** Percental distribution of female and male patients on an ordinal 4-point Likert scale concerning anxiety of multiple pregnancies.  $p = 0.56$ ;  $n = 205$



**Fig. 6** All 25 items of the specific questionnaire concerning anxiety triggers in IVF therapy in numerical order

situation, but also had generally a more anxious personality. While this is an important fact for the physicians and nurses to know, it does not come as a surprise, since women are known to have higher anxiety levels than men

in psychological tests like the STAI, even under normal circumstances [18]. While the reasons for that are manifold and too diverse to be pinned down in this context, the consequences for the psychological support are of the

utmost importance: Women in infertility treatment, even more so than men, are in dire need of a progressive approach in psychological support in order to guide them through the course of multiple cycles in IVF therapy, preventing them from dropping out prior to achieving pregnancy.

This study should encourage efforts to tackle psychological obstacles during IVF, so that couples, who would otherwise consider dropping out of IVF, are granted necessary psychological support and guidance in time to ensure that they stay in treatment until a third or fourth cycle for an improved therapy outcome.

### **In what aspects do women undergoing IVF differ from men?**

Our study concludes in agreement with current literature that women undergoing infertility treatment are more than anything worried about failing to achieve their ultimate goal of successful pregnancy. Contrary to other studies looking at the factors for female distress in IVF, women in our cohort were not nearly as much worried about physical pain or discomfort as they feared the thought of a childless future. It has to be taken into consideration, that female patients undergoing IVF procedure in their ultimate wish of achieving pregnancy blind out the reality of treatment matters and are less susceptible to informative talks concerning their health risks. It is also important to keep in mind, that even though their mindset focuses on the desire to achieve pregnancy and they do not seem worried in that very moment of invasive procedures like the follicular puncture, pains and psychological discomfort are nonetheless to be experienced.

However, the male partners of our study group were mostly worried about the possible complications of IVF therapy itself, and were not as much worried about failure of achieving pregnancy. Men in IVF therapy seem to not have the desire to have a child of their own as strong as their female partners. The reasons for that remain unclear, though it can be speculated that the idea of having children doesn't depict such an important role within the male patients' life. It is thinkable that men have prepared better coping mechanisms in case of failing IVF therapy, like enforcing a so called life-goal-shift towards other meaningful purposes or simply taking other measures into consideration as adopting a child. Also, females might define themselves and the purpose of being a woman more so than their partners in the role of parenthood as a mother, a matter likely to be strongly influenced by sociocultural circumstances. Other than their female partners, who seem to have a more fixed goal of achieving pregnancy, the men seem to be worrying more about their partners' health and

wellbeing, possibly to compensate for their female partner's lack of health concerns for the time of IVF. Men might value the importance of their partnership more than the goal of being a parent. In further studies it may be worth investigating to what extent men and women in IVF therapy cope differently in regard to the various different causes of infertility.

### **The role of increasing number of IVF cycles**

As described in earlier studies, in our cohort the psychological distress in couples undergoing IVF treatment increased with every cycle. This circumstance seems to be logical from a patient's point of view, because for a couple with every unsuccessful cycle passed through, the possible failure of the infertility treatment in its finality becomes more and more apparent. It is vital in this situation for the treating physician and his or her team, to encourage the couples after every failed IVF cycle and throughout the whole process of in vitro fertilization to stay in therapy and to explain, that it is normal for the therapy to last more than one cycle until pregnancy is achieved. This again affirmed knowledge of couples' rising psychological and social strain throughout the progression of IVF should lead to the implementation of more targeted psychological guidance efforts in order to prevent early dropouts and thereby improve overall therapy outcome.

### **Insouciance of multiple pregnancies**

In this study a majority of both genders indicated to be very little worried about multiple pregnancies as a result of infertility treatment. Even though this is not a new finding, it should be alarming therapists nonetheless. The health risks of multiple pregnancies are known to be vast, and seemingly not all couples seem to be informed about this matter properly. With the practice of shared-decision-making it lies in the hand of the treating physician to clarify early on in his consultations the dangers of transferring multiple embryos in one therapy cycle. The couples in strong desire for a child might not be as aware as necessary about the possible consequences multiple child birth carries for their own health, the wellbeing of their future children and the possible financial aftermath. Also, the effect of multiple pregnancies on relationships should not be underestimated, as they may lead towards increased marital strain, maternal depression and parental psychosocial distress [19–21]. Couples should thus receive adequate explanation and information early enough in time to be able to make a responsible decision on how many embryos they want to have transferred. The data from this study should encourage doctors' efforts in this regard.

## Comparison to current literature

The main findings of this study go in agreement with current literature on this topic. The recent ESHRE guidelines on routine psychological care in infertility and medically assisted reproduction underline the importance of research on psychological distress in in-vitro-fertilization [22]. The generalizability of this study sample to other populations remains to be proven, but the literature suggests that at least for western civilizations the results are likely to be comparable. New insights have been made in terms of significant gender differences of treatment anxiety and specific stress factors within the treatment, opening new perspectives and possibilities for varying psychological support of men and women during infertility treatment, thus leading towards more pregnancies and an overall better therapy outcome.

## Bias

The questionnaire was completed by the patients on a voluntarily basis, leaving the possibility of a selection bias by including only certain couples, that were open minded to participation. Moreover, the data sample has not been independent with a number of men and women being in a mutual partnership and thus possibly sharing opinions and sorrows concerning IVF. Due to the anonymous design of the study and the nature of the setting it was not feasible to match questionnaires within the couples to account for this, a possible confounder that should be taken into consideration interpreting the results and improved in future studies on this topic.

Additionally, it was not taken into account that many couples of the study sample might have undergone pre-IVF treatment, e.g., low dose stimulation or clomiphene, a thinkable confounder that follow-up studies should include. Furthermore the sample and findings might not be representative in a worldwide context due to strong variations in social, economical and psychological traits between populations. The main bias of this study is the lack of prior statistical analysis concerning validity and reliability of the 25 questions concerning specific stress factors and triggers for treatment anxiety. Future studies in this field of research with expanded financial resources should be taking this into consideration.

## Compliance with ethical standards

Full compliance with ethical standards was confirmed by the ethical institutional review board of the University of Luebeck, who reviewed and monitored the study through its course and granted its full approval in September 2012.

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**Conflict of interest** G. Griesinger has received consultant/honorarium fees from MSD, Ferring, GlycoTope, Serono, Finox, Vitrolife, and IBSA and has served on speaker bureaus for MSD, Ferring, Serono, Vitrolife, and IBSA. C. Banz-Jansen, declares that she has no conflict of interest. M. A. Schaller declares that he has no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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