Great expectations of IVF patients: the role of gender, dispositional optimism and shared IVF prognoses

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Abstract

Study question: What success rates do male and female IVF patients expect? What determines patients’ expectations? Might patients reconsider their expectations after receiving their individual IVF prognosis and does receiving their prognosis trigger anxious reactions?

Summary answer: Female and male IVF patients have unrealistic high expectations which are positively associated with their dispositional optimism, and which are only reconsidered by patients receiving a less than average IVF prognosis, the latter leading to more anxious reactions in females.

What is known already: Female patients undergoing IVF are known to have unrealistic expectations of the success of their own IVF cycle. The available evidence suggests women expect above average performance of their fertility clinic and (family) reproductive systems. The association of gender and personality trait dispositional optimism, with expectations of IVF success and the impact of providing couples with their IVF prognosis has not been studied previously.

Study design, size, duration: A total of 148 partnered individuals participated in this prospective survey at two separate points in treatment: following oocyte aspiration (T1) and embryo transfer (T2) (2019-2020, participation rate=85%). At the time of embryo transfer, gynaecologists provided couples with their IVF prognosis, calculated with the Adapted van Loendersloot model. Women and their male partners completed questionnaires independently and immediately following oocyte aspiration and embryo transfer.

Participants/materials, setting, methods: Dispositional optimism (‘LOT-R’ questionnaire) and expectations of IVF success (numerical rating scale) were assessed in eligible couples commencing a 2nd-6th IVF cycle on T1. Expectations of IVF success and anxiety (‘Spielberger State-Anxiety Inventory’) were (re)assessed on T2. The inter-partner correlation of expectations of IVF success was examined. Linear mixed models examined hypothesized determinants of expectations of IVF success (T1) and explored (determinants of) whether participants reconsidered their expectations after receiving their IVF prognosis (T1-T2) and whether couple’s IVF prognosis was associated with anxious reactions (T2).
Main results and role of chance: The mean of the IVF success rates expected by patients immediately after oocyte aspiration was 59.1% (±20.0), irrespective of gender (p=0.077). Partners expectations of IVF success were moderately correlated (r=0.483; p<0.001). Expectations of IVF success were positively associated with the participant’s dispositional optimism (p<0.001), but were not associated with their partner’s dispositional optimism, women’s age and their previous (un)successful IVF experiences. Gynaecologists gave couples their calculated IVF prognosis ranging from 4.8 to 69.2% (mean=30.9%) at the time of embryo transfer. Gender did not influence whether participants reconsidered their expectations after receiving their prognosis. In contrast to the subgroup (n=78), who received at least an average IVF prognosis and that did not reconsider their expectations of IVF success, the subgroup (n=70) receiving a below average IVF prognosis lowered their expectations of IVF success (interaction effect: p<0.001) from 55% to 46%. A below average IVF prognosis was associated with anxious reactions in women but not in men (interaction effect: p=0.011).

Limitations, reasons for caution: The study design and sample size were more optimal for examining hypothesised determinants of patient’s expectations of IVF success than for studying the impact of sharing prognoses with patients. Whether (reconsidering) expectations influences IVF discontinuation rates and achieved live birth rates has yet to be followed-up.

Wider implications of the findings: Clinics are advised to offer patients the opportunity of receiving their IVF prognosis. Providing prognoses is in line with patient preferences and tempers the unrealistic high expectations of (fe)males with a less than average prognosis. A sensitive communication style is indicated, as lower prognoses are associated to anxious reactions in women, which do not exceed previous observations.

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INTRODUCTION:

The average success rate of an in vitro fertilisation (IVF) cycle is about one in three (ESHRE-EIM-Consortium, et al., 2020) and most female fertility patients know that average success rates are below 40% (Birenbaum-Carmeli and Dirnfeld, 2008, Maheshwari, et al., 2008). When it relates to their own IVF cycle, female patients, however, expect a success rate of no less than one in two, despite recalling their physician to have given them a success rate of around one in three (Boivin and Takefman, 1995, Miron-Shatz, et al., 2020). The discordance between female patient’s knowledge of average IVF success rates and their high expectations from their own cycle seems driven by their desire to achieve success and their decision to continue IVF (Croyle and Cooper, 1983, Festinger, 1957, Harmon-Jones and Mills, 1999). In response to open-ended questions, female patients shared that they expect an above average performance of their fertility clinic and (family) reproductive systems (de Groot, et al., 2016, Miron-Shatz, et al., 2020). To the best of our knowledge, expectations of male patients from their own IVF cycle and the effect of partners on each other’s expectations (i.e. inter-partner correlation) have yet to be studied. Insight into IVF experiences and (personality) characteristics driving patient expectations of IVF success is limited.

This study hypothesized that expectations of IVF success would be negatively associated with the number of previous unsuccessful embryo transfers and positively associated with having achieved a live birth with IVF treatment. Given female members of the general public had lower expectations than males (Adashi, et al., 2000, 79 Stoebel-Richter, et al., 2012), a negative association with expectations of IVF success was hypothesized for female gender. A negative association with expectations of IVF success was also hypothesized for female age as female patients know that average IVF success rates depend on age (Maheshwari, et al., 2008, Swift and Liu, 2014). A positive association was hypothesized between expectations of IVF success and patient and partner ‘dispositional optimism’, the relatively stable generalized expectation that positive outcomes will occur across important life domains (Scheier and Carver, 2018). The personality trait dispositional optimism proved to be associated with expecting therapeutic benefit in cancer patients (Jansen, et al., 2016) and with better long term health expectations in patients with acute coronary disease (Bekke-Hansen, et al., 2014).
Fertility clinic staff reported complexity in treating patients with unrealistic expectations despite being informed about average success rates (Boivin, et al., 2017, van den Boogaard, et al., 2011). University student’s knowledge about average IVF success rates could be improved by providing an information brochure (Wojcieszek and Thompson, 2013) but strategies for improving patient expectations of their own cycle had yet to be developed. Patients and professionals have both advocated the value of informing patients of their IVF prognosis (i.e. chance of IVF success calculated for a specific couple)(Dancet, et al., 2011, van Loendersloot, et al., 2013). Several performant prognostic models have recently been published but their impact on clinical practice has yet to be studied (Ratna, et al., 2020). It would be interesting to explore the impact of providing a less than average IVF prognosis on expectations of IVF success in male and female patients. In addition, finding out whether receiving a less than average IVF prognosis causes psychological reactions in male and female patients would be of interest as IVF patients had higher levels of distress on days on which they received negative medical feedback (e.g. quantity or quality of oocytes or embryos) (Boivin, 2000, Boivin, 2019).

The aim of this study was to examine both male and female expectations of IVF success, its inter-partner correlation, and potential determinants (e.g. dispositional optimism). In addition, this study explored the impact of providing women and men with a less than average IVF prognosis on their expectations of IVF success and on their psychological reactions.

**MATERIAL & METHODS**

**Design, setting**

A prospective cohort study was conducted between March 2019 and September 2020 at the tertiary fertility clinic of the University hospital of Leuven (Belgium).

**Ethical approval**

Approval was obtained from the medical ethics committee of the Leuven University and the Leuven University Hospital (s61837).

**Sample**
Eligible heterosexual couples starting a 2nd-6th IVF cycle (with or without ICSI, with own fresh gametes, without Pre-implantation Genetic testing) after at least one previous IVF cycle with the same partner at the recruiting clinic. Couples starting their first IVF cycle were not eligible as this study relied on a prognostic model taking account of whether fertilisation occurred in the previous IVF cycle (Devroe, et al., 2020). Couples initially recruited but not having an embryo transfer (i.e. due to failed fertilisation, no suitable embryo or the last-minute decision to freeze all embryos due to the risk of ovarian hyper stimulation syndrome) or completing <50% of the questionnaires were excluded. The a priori defined sample size of 70 female and 70 male partners was calculated to have more than 10 participants of each gender for each of the six factors for which we wanted to examine the association with expectations of IVF success (Kleinbaum, et al., 1988).

Recruitment, data-collection and study procedures

Table I displays the study procedures and their timing. On the day of their oocyte aspiration, eligible couples were invited to participate in the study by their reproductive medicine midwife. Interested couples were thoroughly informed by the researcher and were asked to confirm informed consent in writing. Coded paper pencil questionnaires were disseminated among women and their partners to be completed immediately following oocyte aspiration (T1) and again following fresh embryo transfer (T2). Partners were asked to complete their questionnaire separately, each taking approximately five minutes. In contrast to the mean clinic success rate of one in three given prior to IVF, gynaecologists provided participants with their IVF prognosis (i.e. chance of IVF Live birth per oocyte aspiration calculated for a specific couple) in written format and discussed it with them at the time of embryo transfer. In line with patient preference, this written individualized information included an image of the transferred embryo(s) (Bladh Blomquis, et al., 2017). In line with standard clinical practice, it also included the (mean) 1-4 star quality rating of the transferred embryo(s) (i.e. based on the number of cells, their symmetry in size and degree of fragmentation) and number of cryopreserved embryos.

Variables
Of the cycles studied, several variables were assessed immediately after oocyte aspiration (T1) and/or immediately after embryo transfer (T2) of the studied IVF cycles, as displayed in table I.

Both partner’s dispositional optimism was assessed using the reliable Live Orientation Test (LOT-R) (Scheier et al. 1994). This questionnaire included 10 questions to be rated on a 5-point-Likert scale and results in a score between 0 and 24 (the higher, the more optimistic, no cut-off value) (Scheier, et al., 1994).

Both partners’ expectations of IVF success, i.e. the live birth rate expected per completed IVF cycle including all fresh and frozen embryo transfers from the same episode of ovarian stimulation, was assessed with a single question. This question was to be rated on a numerical rating scale, based on the ‘Factors Affecting Fertility Scale’ (Bunting and Boivin, 2008), which ranges from 0 to 100 (intervals of 10) and has three explanatory text balloons (Figure 1). If patients did not tick a whole number (e.g. 40 or 50), the distance was measured and registered in more detail (e.g. 43).

Each couple’s IVF prognosis, i.e. the live birth rate predicted per completed IVF cycle including all fresh and frozen embryo transfers from the same episode of ovarian stimulation, was generated on the day of embryo transfer with the ‘Adapted van Loendersloot model’ (Devroe, et al., 2020, van Loendersloot, et al., 2013). This model includes eight clinical variables (i.e. female age, duration of infertility, previous delivery, male infertility, diminished ovarian reserve, endometriosis, basal FSH, number of failed IVF cycles) and five IVF laboratory variables of the previous IVF cycle (i.e. fertilisation) or of the studied IVF cycle (i.e. number of embryos and mean morphological score, presence of 8 cell embryos and morulae on day 3). The Adapted van Loendersloot model proved to be performant for the studied clinic with a c-statistic of 0.74 (0.71 after cross-validation) and a calibration plot practically coinciding with the diagonal (Devroe, et al., 2020).

Both partners’ anxiety immediately after embryo transfer and receiving their IVF prognosis was assessed with the ‘State-Anxiety Inventory (STAI-state)’. The STAI-state includes twenty questions rated on a 4-point Likert scale and results in a score between 20 and 80 (the higher the score, the more anxious; cut-off for clinical cases in female fertility patients: 50.93; in male fertility patients: 45.70) (Hashemi, et al., 2012, Spielberger and Sydeman, 1994, Zurlo, et al., 2020)
Three variables were extracted from couple’s medical records: female age, live birth following IVF (yes/no) and number of unsuccessful embryo transfers.

Finally, both partners assessed the novel individualized information by indicating whether they would recommend it to family and friends having an embryo transfer on a 4-point Likert scale (i.e. definitely not, probably not, probably yes, definitely).

**Analysis**

Data were imported and analysed in the Statistical Package for Social Science (SPSS version 27.0). Missing data were managed with mean imputation. The clinical, IVF laboratory and other examined characteristics of the sample were described. The previously proven reliability of the LOT-R and STAI-state was re-evaluated for our sample of Belgian fertility patients with Cronbach’s alpha statistics (cut-offs: >0.70 reliable; 0.60-0.70 moderately reliable) and Item Total Correlations (ITC; cut-offs: >0.40) (Sixma, et al., 1998).

- **Expectations of IVF success and inter-partner correlations**

  A scatterplot was computed to display (the ranges of) the expectations of IVF success of women and their male partner immediately after oocyte aspiration (T1) and their inter-partner correlation (i.e. Pearson correlation coefficient, r). In addition, whether expectations of IVF success (T1) depended on gender was examined with linear mixed models, taking account of clustering within couples with random intercepts.

- **Determinants of expectations of IVF success**

  Linear mixed models examined the univariable associations between the IVF success expected by participants immediately after oocyte aspiration (T1; dependent variable) and its hypothesized determinants, whilst taking account of clustering within couples with random intercepts (Hendriks, et al., 2017, Kenny, et al., 2020). More specifically, the following six hypothesized determinants were examined: gender, female age, live birth following IVF, number of previous failed embryo transfers, patient’s dispositional optimism and partner’s dispositional optimism. Hypotheses were only accepted if the p-value was smaller or equal to 0.007 (=0.05/7, taking account of a Bonferroni correction for multiple testing). Whether these associations were affected by gender (i.e. interaction with gender) was also assessed.
A linear mixed model including a random intercept for couple-ID explored the association between the appreciation of the individualized information (dependent variable) and receiving a below average IVF prognosis (yes/no) and gender and the interaction between the latter two variables.

Couple’s mean IVF prognosis and participant’s mean expectation of IVF success immediately after embryo transfer and being informed of their IVF prognosis (T2) were described.

A linear mixed model with expectations of IVF success (two time points) as dependent continuous variable, with the main effect of time point, gender and below average prognosis and their four potential interactions and with random intercepts for couple-ID and subject-ID was fitted. This model allowed exploring whether participants reconsidered their expectations of IVF success (i.e. main effect of time point) and which participants had higher expectations (i.e. main effect of the determinants gender and below average prognosis) and/or reconsidered their expectations (i.e. interaction effect of time point and a determinant).

Backward elimination from this model, ensured that only significant main and interaction effects remained in the final model. The direction of the significant main effects on expectations of IVF success were to be appraised by describing the mean expectation of IVF success of the subgroups differing in dichotomous determinant. Significant interaction effects on expectations of IVF success were to be appraised with linear mixed models per subgroup.

A linear mixed model explored whether anxiety (i.e. dependent variable) was associated with gender and with receiving a below average IVF prognosis (i.e. main effects), and whether gender (m/f) influenced the association between anxiety and the received prognosis (i.e. interaction effect), whilst including a random intercept for couple-ID. The potential interaction effect was to be appraised with linear regressions per subgroup.

RESULTS

Participants
A total of 87 of the 102 invited eligible couples agreed to participate (participation rate = 85%). Reasons for declining study participation were: not willing to participate in any study (n=9) and not interested in receiving their IVF prognosis (n=6). Thirteen couples were excluded for the following reasons: failed fertilisation (n=6), no suitable embryo for transfer (n=2), freeze all due to risk over ovarian hyper stimulation syndrome (n=1) and <50% completion of questionnaires (n=4). The following missing data was imputed (i.e. replaced by the mean) for a very small minority of couples: (i) male partner’s questionnaires from the day of embryo transfer (T2; n=3) and both partner’s expectations of IVF success immediately after the embryo transfer (T2; n=1). The characteristics of the 74 finally included couples are summarized in Table II.

Regarding the clinical variables of this cohort, the mean female and male age were respectively 33.8 (±4.4) and 36.1 (±5.0) years of age. About a third of the couples had a previous delivery (31.1%). The mean duration of infertility was 3.2 (±1.6) years and participating couples previously experienced on average 1.57 (±1.0) failed IVF cycles. About half of the couples had a male infertility diagnosis (52.7%). A minority of the couples had a diagnosis of diminished ovarian reserve (4.1%) and one in five had a laparoscopic diagnosis of stage III or IV endometriosis (20.3%). The mean basal FSH (IU/ml) was 8.5 (±6.4). Regarding the IVF laboratory variables, for the vast majority fertilization had occurred in the previous cycle (94.6%). The mean number of embryos after oocyte retrieval was 5.6 (±3.0) and the mean morphological score on day three was 2.6 (on a scale of 1 to 4; the lower, the better). On day three a majority had at least one eight-cell embryo (70.3%). Having a morula on day three was very uncommon (1.4%). Regarding the additional variables for which the association with expectations of IVF success (T1) was examined, about one in five couples previously delivered an IVF child (18.9%) and the mean number of previous failed embryo transfers was 2.39 (±2.0). The mean level of dispositional optimism of women and men was, respectively: 14.52 (±4.6) and 15.3 (±3.3)(p=0.21).

Reliability of the questionnaires

The reliability of both questionnaires was confirmed in our sample of Belgian fertility patients. More specifically, the Cronbach’s Alpha coefficients of the LOT-R and STAI-state questionnaires were 0.81 and 0.94 respectively and all item total correlations were larger than 0.4.
**Expectations of IVF success and inter-partner correlations**

The vast majority of patients (88.5%) expected their IVF success rate to be more than one in three immediately after oocyte aspiration (T1). On average, patients expected an IVF success rate of 59.1% (SD= 20.0; range= 8-100%) and this did not depend on gender (p=0.077). The scatterplot in figure 2 displays a moderate inter-partner correlation (r=0.483; p<0.001).

*(insert Figure 2 about here)*

**Determinants of expectations of IVF success**

Table III summarizes the findings of the linear mixed model analyses examining the associations between expectations of IVF success immediately after oocyte aspiration (T1) and each of its six hypothesized determinants. None of the hypothesized determinants of expectations of IVF success interacted with gender (p ≥ 0.50). Only one of the six hypotheses was accepted: patient’s own level of dispositional optimism was significantly associated with their expectations of IVF success immediately after oocyte aspiration (p<0.001). Participant’s expectations of IVF success was not associated with their gender, female age, (un)successful IVF experiences and their partner’s dispositional optimism.

*(insert table III about here)*

**IVF prognoses and reconsideration of expectations of IVF success**

The vast majority of participants (92%) would recommend the individualised information including the IVF prognosis to family and friends. The appreciation of the individualised information was not associated with gender (p=0.412), with receiving a below average IVF prognosis (p=0.063) and these two factors did not interact (p=0.879).

The mean IVF prognosis of couples was 30.9% (±16.8; range=4.8-69.2%). The mean expectation of IVF success of participants immediately after embryo transfer and receiving their IVF prognosis (T2) of 54.5% (SD= 23.6; range= 0-100%) was almost twice as high.

Gender did not appear to influence expectations of IVF success (main effect: p=0.085) nor whether participants reconsidered their expectations after receiving their IVF prognosis (i.e. interaction between gender and time point; p=0.237). ‘Below average IVF prognosis’ (<30.9%) affected expectations of IVF success
(p<0.001) and whether participants reconsidered their expectations after receiving their IVF prognosis (p<0.001). The full model, including all three potential determinants and their interactions, and backward elimination did not identify additional significant main or interaction effects. The final model included below average IVF prognosis (p<0.001), time point (p<0.001) and the interaction between time point and below average IVF prognosis (p<0.001). Expectations of IVF success (T1&T2) was lower in participants with a below average IVF prognosis compared to participants with at least an average IVF prognosis (50.6 vs. 63.8, on average). The subgroup of 78 participants with at least an average IVF prognosis did not reconsider their expectations of IVF success after receiving their prognosis (p=0.480) whilst those with an below average IVF prognosis (n=70) changed their expectations of IVF success (p<0.001) from a mean of 55% to a mean of 46%.

Figure 3 displays the following for the participants with and without a below average IVF prognosis: expectations of IVF success immediately after oocyte aspiration, received IVF prognosis and expectations of IVF success immediately after the embryo transfer and receiving their IVF prognosis.

(insert figure 3 about here)

**IVF prognoses and anxious reactions**

The model included the main effects of gender (p<0.001) and of below average IVF prognoses (p=0.003) and the interaction effect between below average IVF prognoses and gender (p=0.043). More specifically, females were more anxious than males but only about 15% of both female and male participants scored above the fertility patient and gender specific clinical threshold for state anxiety (Table IV). Women who received a less than average IVF prognosis had more anxious reactions than women with at least an average IVF prognosis (45.3 vs. 37.2; p<0.001) whilst a below average IVF prognosis was not associated with anxious reactions in men (p=0.126). Of note, state anxiety (male, female) immediately after the embryo transfer and receiving individual IVF prognosis was not associated with clinical pregnancy rate (i.e. presence of fetal heart pulsation; n=15/74) from this fresh embryo transfer (p=0.443; p=0.521).

(insert table IV about here)
Female and male IVF patients both expect a live birth rate from their completed IVF cycle of around 60%, with partner expectations moderately correlated. Of six hypothesized determinants, only patient’s own level of dispositional optimism determined expectations of IVF success. To our knowledge, no previous study explored a strategy to offset patient’s unrealistic expectations from their own IVF cycles. This study exploring the impact of sharing personalized IVF prognoses with patients, suggests that only patients who received a less than average IVF prognosis (<31%) lowered their expectations from 55% to 46% (irrespective of gender). Receiving a less than average prognosis was associated with anxious reactions in female participants, but not in their male partners. Males and females, however, rarely scored above the clinical threshold for state-anxiety.

**Reflection on the findings**

Interestingly, this study shows that male patients have equally high expectations of IVF as previously shown in females (Boivin and Takefman, 1995, Miron-Shatz, et al., 2020) and that expectations of women and men depend on their dispositional optimism. Males and females do not differ either in the limited extent in which they reconsider their expectations after having received a below average IVF prognosis. Females did have higher state anxiety scores than males, as previously reported (Edelmann and Connolly, 2000, Schaller, et al., 2016, Zurlo, et al., 2020), but equally small proportions of males and females (15-16%) scored above the clinical thresholds for state anxiety in fertility patients, as these thresholds are gender specific (Zurlo, et al., 2020). The interesting observation that a below average prognosis was only associated to the anxiety of females and not of males is in line with females being mainly concerned about not achieving pregnancy whilst males are mainly concerned about the health risks for their female partners (Schaller, et al., 2016) and with the fertility specific distress dimension ‘need for parenthood’ being associated to the state anxiety of females but not of males (Zurlo, et al., 2020). The observed anxious reactions of women with a below average prognosis were in line with those previously reported in women in the active phase of treatment (45.3 vs 40 – 53 on average) (Gabnai-Nagy, et al., 2020, Gürhan, et al., 2009, Karlidere, et al., 2008, Turner, et al., 2013) and more implicit medical feedback (e.g. number of oocytes and embryos) also causes distress (Boivin, 2000, Boivin, 2019). Moreover, no association between anxiety immediately after the embryo transfer and IVF
success was observed in this cohort and compelling evidence on an association between (changes in) state-

anxiety during treatment and actual IVF success is missing as prospective studies and meta-analyses thereof

are equivocal (Boivin, 2019, Nicoloro-SantaBarbara, et al., 2018, Purewal, et al., 2018).

**Strengths & limitations**

This prospective cohort study has five important strengths. First, male and female participants both completed

questionnaires independently as opposed to only studying female expectations of IVF success (Boivin and

Takefman, 1995, Miron-Shatz, et al., 2020). Including men and studying partner-correlations is relevant as men

and women have similar psychological reactions to the uncertainty of IVF procedures (Boivin, et al., 1998) and

as men contribute to women’s treatment decisions (Sol Olafsdottir, et al., 2013). Secondly, our sample is

representative of the average fertility population, with an 85% participation rate and with an average

predicted prognosis of live birth per completed IVF cycle of 31%, ranging from 5 to 69% (ESHRE-EIM-

Consortium, et al., 2020). Thirdly, dispositional optimism (Scheirer, et al., 1994) and state-anxiety (Spielberger

and Sydeman, 1994) were assessed with reliable standardized questionnaires. In the absence of a standardized

tool for assessing expectations of IVF success, we based our novel tool on the reliable Factors Affecting Fertility

Scale of Bunting and Boivin (2008). Furthermore, the expectations of IVF success and the IVF prognosis were

both clearly defined as the chance of live birth per completed IVF cycle and the provided IVF prognosis was

generated by a prognostic model with proven performance for the recruiting clinic (c-statistic= 0.74; (Devroe,

et al., 2020). Finally, the holistic scope of our study is demonstrated by the examined determinants ranging

from previous IVF experiences to personality characteristics and by exploring the impact of sharing prognoses

with patients on both expectations and psychological reactions. This prospective cohort study has limitations

too. The restricted sample size and design were appropriate for examining the six hypothesized determinants

of expectations of IVF success but only allowed exploring the impact of sharing calculated IVF prognoses with

patients. A larger sample size would have allowed examining the impact of more potential determinants on

expectations and reconsiderations thereof. A randomized controlled trial (RCT) design rather than a pre-test-

post-test design would have disentangled the impact of providing IVF prognoses from the effect of treatment

stage and implicit medical feedback on expectations and anxiety. Our complex mixed models that took

account of dyadic measurements of expectations and anxiety and of repeated measurements of expectations
were valuable for exploring the impact of gender and of a below average IVF prognosis. Our complex models did not correct for a difference in state anxiety at T1, as we did not assess anxiety at T1 and as oocyte aspiration (T1) and embryo transfer (T2) might affect anxiety differently.

**Implications for research**

The effect of sharing IVF prognoses suggested by this longitudinal study triggers the design of a randomized controlled trial disentangling the effect of sharing IVF prognoses from the effect of treatment stage (oocyte aspiration vs. embryo transfer) and of more implicit medical feedback (e.g. number of supernumerary embryos for cryopreservation) on the expectations of IVF success and on anxious reactions (Boivin, et al., 1998, Svanberg, et al., 2001).

Another suggestion for further research is to follow up the current or preferably a larger cohort to elicit whether the dispositional optimism of females and males is associated with actual (besides expected) cumulative IVF success rates. Older small-scale studies and several large-scale epidemiological studies from other fields make a strong case that optimism translates into health outcomes, such as coronary heart disease and even mortality (Kim, et al., 2017, Rasmussen, et al., 2009, Scheier and Carver, 2018, Tindle, et al., 2009).

In IVF women dispositional optimism, which seemed part of a broader personality constellation, was found to be positively associated with ovarian response (Lancastle and Boivin, 2005), and it was negatively associated with clinical depressive symptoms following IVF failure (Litt, et al., 1992). It seems important for follow-up studies to monitor IVF discontinuation as a behavioural pathway explaining the potential association between dispositional optimism and physical health (Scheier & Carver, 2018) as IVF discontinuation impacts cumulative IVF success rates (Gameiro, et al., 2013). Moreover, examining the hypothesis that receiving a below average IVF prognosis increases IVF discontinuation seems interesting. The currently observed decrease in expectations of IVF success among men and women receiving a less than average IVF prognosis might translate into an increased IVF discontinuation rate, as previous surveys showed that women’s low expectations of IVF success were associated with high IVF discontinuation rates (Boivin, et al., ESHRE 2020, Callan, et al., 1988). Surprisingly though, patients shared in interviews that repeated unsuccessful embryo transfers whilst having high (rather than low) expectations led to distress and ultimately to IVF discontinuation (Peddie, et al., 2005).
Furthermore, it would also be interesting to interview couples in-depth on how they process a provided personal IVF prognosis, depending on their health literacy, mathematical skills and beliefs. Interestingly, the expectations of patients with an above average prognosis were not affected and patients with a below average prognosis only slightly reconsidered their expectations after receiving their prognosis (i.e. from 55% to 46%). A small minority of couples (6% of addressed couples) even explicitly opted for denial by choosing not to receive their personal IVF prognosis.

Finally, examining the experience of gynaecologists who communicate IVF prognoses would be interesting as professionals are known to struggle with communicating natural conception prognoses (van den Boogaard, et al., 2011) and bad news (Boivin, et al., 2017). The availability of performant prognostic models (Ratna, et al., 2020) and the written individualized information tested in this study might facilitate communicating IVF prognoses (van den Boogaard, et al., 2011). In this study, prognoses were provided at the time of embryo transfer, when patients are known to request personalized feedback (Bladh Blomquis, et al., 2017, Dancet, et al., 2010, Tuil, et al., 2006) and when the performant Adapted van Loendersloot model, taking account of laboratory variables from that IVF cycle, can be used (Devroe et al, 2020). The model of McLernon and colleagues is complementary to the currently used model and can be used prior to the start of IVF or in between cycles for providing prognoses for entire multiple cycle IVF trajectories (McLernon, et al., 2016).

**Implications for clinical practice**

Clinics are advised to offer patients the opportunity of receiving their personal IVF prognosis from the very first to their very last contact with patients, as it tempers the unrealistic expectations of patients with a below average prognosis. Offering patients their prognosis is patient-centred as it gives voice to patient’s request for personalized information (Bladh Blomquis, et al., 2017, Dancet, et al., 2010, Tuil, et al., 2006) and as practically all currently studied patients would advise family and friends to ask for their personal IVF prognosis. The observed association between having received a below average prognosis and state anxiety should not hold clinics back from sharing IVF prognoses but importantly should encourage clinics to adopt a sensitive communication style whilst providing prognoses.
**Data availability statement:** The data underlying this article will be shared on reasonable request to the corresponding author.

**Contributors:** JD, KP, TMD, JV and EAFD contributed substantially to the conception and design of this study. JD and KP made an essential effort for the acquisition of the data. JD, AL and EAFD analysed the data and involved JB in the interpretation of the data. JD and EAFD prepared this manuscript and KP, TD, JB, AL and JV revised the intellectual content critically, approved the final manuscript and agreed to be accountable for all aspects of the work.

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**Figure 1:** Question used to assess the expectations of IVF success

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What, do you think, is the chance that you and your partner will have a baby after all the embryo transfers of your current IVF/ICSI-cycle?

This current IVF/ICSI cycle includes both the fresh embryo transfer and, in case embryos have been frozen, subsequent frozen embryo transfers.

(Please indicate your response with a 'x' on the bar below; the arrows explain the meaning of some possible answers)

- I am certain that my partner and I will not have a baby after all embryo transfers from our current IVF/ICSI-cycle
- The chance that my partner and I will have a baby after all embryo transfers from our current IVF/ICSI-cycle is equal to the chance that my partner and I will not have a baby
- I am certain that my partner and I will have a baby after all embryo transfers from our current IVF/ICSI-cycle
Figure 2: Scatterplot of female vs. male partner’s expectations of IVF success (T1)

Figure 3: Individual’s reconsideration of expectations of IVF success prior to and after receiving their IVF prognosis at the time of embryo transfer

Legend: *31% is the mean IVF prognosis of this cohort
Table I: Study procedures, variables and tools according to their timing

<table>
<thead>
<tr>
<th>Immediately after oocyte aspiration (T1)</th>
<th>At the time of fresh embryo transfer</th>
<th>Immediately after fresh embryo transfer (T2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Study information</td>
<td>Gynaecologist gives couple their IVF prognosis</td>
<td>Each partner independently fills out a questionnaire assessing:</td>
</tr>
<tr>
<td>• Each partner signs informed consent form</td>
<td></td>
<td>• Expectation of IVF success (numerical rating scale with three explanatory text balloons)</td>
</tr>
<tr>
<td>Each partner independently fills out a questionnaire assessing:</td>
<td></td>
<td>• Anxiety (STAI-state)</td>
</tr>
<tr>
<td>• Dispositional optimism (LOT-R)</td>
<td></td>
<td>• Likelihood of advising the novel feedback sheet (4-point Likert scale)</td>
</tr>
<tr>
<td>• Expectation of IVF success (numerical rating scale with three explanatory text balloons)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table II: Characteristics of the 74 participating couples

| Variables presented purely to describe the sample | | |
| Age men (years; mean, SD) | 36.1 (±5.0) | |
| Female infertility (n/N; %) | 46 (62.2%) | |

| Clinical variables taken into account in the IVF prognosis | | |
| Age women (years; mean, SD) | 33.8 (±4.4) | |
| Previous delivery (n/N; %) | 23/74 (31.1%) | |
| Failed IVF cycles (N; mean, SD) | 1.57 (±1.0) | |
| Duration of infertility (years; mean, SD) | 3.2 (±1.6) | |
| Male infertility (n/N; %) | 39/74 (52.7%) | |
| Diminished ovarian reserve (n/N; %) | 3/74 (4.1%) | |
| Endometriosis (n/N; %) | 15/74 (20.3%) | |
| Basal FSH (IU/ml; mean, SD) | 8.5 (±6.4) | |

| IVF Laboratory variables taken into account in the IVF prognosis | | |
| Fertilization in previous cycle (n/N; %) | 70/74 (94.6%) | |
| Embryos in current cycle (N; mean, SD) | 5.6 (±3.0) | |
| Mean morphological score of all embryos on day 3 in the current cycle (1-4; mean, SD) | 2.6 (±0.8) | |
| Presence of 8-cell embryos on day 3 in current cycle (n/N; %) | 52/74 (70.3%) | |
| Presence of Morulae on day 3 in current cycle (n/N; %) | 1/74 (1.4%) | |

| Additional variables for which the association with expected IVF success-T1 was examined | | |
| Previous IVF child (n/N; %) | 14/74 (18.9%) | |
| Number of previous failed ET (mean, SD) | 2.39 (±2.0) | |
| Dispositional optimism women* (mean; SD) | 14.52 (±4.6) | |
| Dispositional optimism men* (mean; SD) | 15.3 (±3.3) | |

Legend:

*Men and their female partner did not differ significantly in their level of dispositional optimism (p=0.21)

Abbreviations:

IVF: in vitro fertilisation
LBR: live birth rate

Table III: Findings on the hypothesized determinants of individual’s expectations of IVF success immediately after oocyte aspiration

<table>
<thead>
<tr>
<th>Hypothesized determinants</th>
<th>Univariable association</th>
<th>Interaction with gender</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate (95% confidence interval)</td>
<td>p-value</td>
</tr>
<tr>
<td>Female gender</td>
<td>-4.203 (-8.875; 0.470)</td>
<td>0.077</td>
</tr>
<tr>
<td>Female age</td>
<td>-0.674 (-1.568; 0.221)</td>
<td>0.138</td>
</tr>
<tr>
<td>Having an IVF child</td>
<td>7.919 (-1.993; 17.837)</td>
<td>0.116</td>
</tr>
<tr>
<td>Number of unsuccessful ETs</td>
<td>0.845 (-1.105; 2.795)</td>
<td>0.391</td>
</tr>
<tr>
<td>Dispositional optimism</td>
<td>1.491 (0.778; 2.205)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Dispositional optimism partner</td>
<td>-0.298 (-1.046; 0.449)</td>
<td>0.431</td>
</tr>
</tbody>
</table>

*Significant compared to the Bonferroni corrected threshold of 0.007

Table IV: State anxiety immediately after receiving their IVF prognosis at the time of embryo transfer

<table>
<thead>
<tr>
<th></th>
<th>Proportion scoring higher than gender specific cut-offs* (%)</th>
<th>Mean anxiety (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women (entire group)</td>
<td>12/74 (16.2%)</td>
<td>41.5 (±10.6)</td>
</tr>
<tr>
<td>- Having received a below average prognosis</td>
<td>9/35 (25.7%)</td>
<td>45.3 (±10.4)</td>
</tr>
<tr>
<td>- Having received at least an average prognosis</td>
<td>3/39 (7.7%)</td>
<td>37.2 (±9.3)</td>
</tr>
<tr>
<td>Men (entire group)</td>
<td>11/74 (15.0%)</td>
<td>37.0 (±8.9)</td>
</tr>
<tr>
<td>- Having received a below average prognosis</td>
<td>7/35 (20.0%)</td>
<td>38.5 (±10.1)</td>
</tr>
<tr>
<td>- Having received at least an average prognosis</td>
<td>4/39 (10.3%)</td>
<td>35.3 (±7.0)</td>
</tr>
</tbody>
</table>

* Gender specific cut-off for State anxiety scores to define clinical cases in fertility patients: female 50.93; males 45.70 (Zurlo et al, 2020)
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