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

2 **Running title:** Great expectations of IVF patients

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13 **Key words:** ‘Reproductive techniques, assisted’, ‘IVF’, ‘prognosis’, ‘Live Birth’, optimism

14 Abstract

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

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

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

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

31 **Participants/materials, setting, methods:** Dispositional optimism ('LOT-R' questionnaire) and expectations of
32 IVF success (numerical rating scale) were assessed in eligible couples commencing a 2nd-6th IVF cycle on T1.
33 Expectations of IVF success and anxiety ('Spielberger State-Anxiety Inventory') were (re)assessed on T2. The
34 inter-partner correlation of expectations of IVF success was examined. Linear mixed models examined
35 hypothesized determinants of expectations of IVF success (T1) and explored (determinants of) whether
36 participants reconsidered their expectations after receiving their IVF prognosis (T1-T2) and whether couple's
37 IVF prognosis was associated with anxious reactions (T2).

38 **Main results and role of chance:** The mean of the IVF success rates expected by patients immediately after
 39 oocyte aspiration was 59.1% (± 20.0), irrespective of gender ($p=0.077$). Partners expectations of IVF success
 40 were moderately correlated ($r=0.483$; $p<0.001$). Expectations of IVF success were positively associated with
 41 the participant's dispositional optimism ($p<0.001$), but were not associated with their partner's dispositional
 42 optimism, women's age and their previous (un)successful IVF experiences. Gynaecologists gave couples their
 43 calculated IVF prognosis ranging from 4.8 to 69.2% (mean=30.9%) at the time of embryo transfer. Gender did
 44 not influence whether participants reconsidered their expectations after receiving their prognosis. In contrast
 45 to the subgroup ($n=78$), who received at least an average IVF prognosis and that did not reconsider their
 46 expectations of IVF success, the subgroup ($n=70$) receiving a below average IVF prognosis lowered their
 47 expectations of IVF success (interaction effect: $p<0.001$) from 55% to 46%. A below average IVF prognosis was
 48 associated with anxious reactions in women but not in men (interaction effect: $p=0.011$).

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

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

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 61 to this study.

62 INTRODUCTION:

63 The average success rate of an in vitro fertilisation (IVF) cycle is about one in three (ESHRE-EIM-Consortium,
 64 et al., 2020) and most female fertility patients know that average success rates are below 40% (Birenbaum-
 65 Carmeli and Dirnfeld, 2008, Maheshwari, et al., 2008). When it relates to their own IVF cycle, female patients,
 66 however, expect a success rate of no less than one in two, despite recalling their physician to have given them
 67 a success rate of around one in three (Boivin and Takefman, 1995, Miron-Shatz, et al., 2020). The discordance
 68 between female patient's knowledge of average IVF success rates and their high expectations from their own
 69 cycle seems driven by their desire to achieve success and their decision to continue IVF (Croyle and Cooper,
 70 1983, Festinger, 1957, Harmon-Jones and Mills, 1999). In response to open-ended questions, female patients
 71 shared that they expect an above average performance of their fertility clinic and (family) reproductive
 72 systems (de Groot, et al., 2016, Miron-Shatz, et al., 2020). To the best of our knowledge, expectations of male
 73 patients from their own IVF cycle and the effect of partners on each other's expectations (i.e. inter-partner
 74 correlation) have yet to be studied. Insight into IVF experiences and (personality) characteristics driving patient
 75 expectations of IVF success is limited.

76 This study hypothesized that expectations of IVF success would be negatively associated with the number of
 77 previous unsuccessful embryo transfers and positively associated with having achieved a live birth with IVF
 78 treatment. Given female members of the general public had lower expectations than males (Adashi, et al.,
 79 2000, 79 Stoebel-Richter, et al., 2012), a negative association with expectations of IVF success was
 80 hypothesized for female gender. A negative association with expectations of IVF success was also hypothesized
 81 for female age as female patients know that average IVF success rates depend on age (Maheshwari, et al.,
 82 2008, Swift and Liu, 2014). A positive association was hypothesized between expectations of IVF success and
 83 patient and partner 'dispositional optimism', the relatively stable generalized expectation that positive
 84 outcomes will occur across important life domains (Scheier and Carver, 2018). The personality trait
 85 dispositional optimism proved to be associated with expecting therapeutic benefit in cancer patients (Jansen,
 86 et al., 2016) and with better long term health expectations in patients with acute coronary disease (Bekke-
 87 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.

(insert table I about here)

Variables

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

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

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

149 *(insert figure 1 about here)*

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

159 Both partners' anxiety immediately after embryo transfer and receiving their IVF prognosis was assessed with
 160 the 'State-Anxiety Inventory (STAI-state)'. The STAI-state includes twenty questions rated on a 4-point Likert
 161 scale and results in a score between 20 and 80 (the higher the score, the more anxious; cut-off for clinical
 162 cases in female fertility patients: 50.93; in male fertility patients: 45.70)(Hashemi, et al., 2012, Spielberger and
 163 Sydeman, 1994, Zurlo, et al., 2020)

164 Three variables were extracted from couple's medical records: female age, live birth following IVF (yes/no)
 165 and number of unsuccessful embryo transfers.

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

169 ***Analysis***

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

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

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

180 - ***Determinants of expectations of IVF success***

181 Linear mixed models examined the univariable associations between the IVF success expected by participants
 182 immediately after oocyte aspiration (T1; dependent variable) and its hypothesized determinants, whilst taking
 183 account of clustering within couples with random intercepts (Hendriks, et al., 2017, Kenny, et al., 2020). More
 184 specifically, the following six hypothesized determinants were examined: gender, female age, live birth
 185 following IVF, number of previous failed embryo transfers, patient's dispositional optimism and partner's
 186 dispositional optimism. Hypotheses were only accepted if the p-value was smaller or equal to 0.007 ($=0.05/7$,
 187 taking account of a Bonferroni correction for multiple testing). Whether these associations were affected by
 188 gender (i.e. interaction with gender) was also assessed.

- ***IVF prognoses and reconsidering expectations of IVF success***

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.

- ***IVF prognoses and anxious reactions***

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.

(insert table II about here)

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.

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

241 The vast majority of patients (88.5%) expected their IVF success rate to be more than one in three immediately
 242 after oocyte aspiration (T1). On average, patients expected an IVF success rate of 59.1% (SD= 20.0; range= 8-
 243 100%) and this did not depend on gender ($p=0.077$). The scatterplot in figure 2 displays a moderate inter-
 244 partner correlation ($r=0.483$; $p<0.001$).

245 *(insert Figure 2 about here)*

246 ***Determinants of expectations of IVF success***

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

254 *(insert table III about here)*

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

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

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

263 Gender did not appear to influence expectations of IVF success (main effect: $p=0.085$) nor whether
 264 participants reconsidered their expectations after receiving their IVF prognosis (i.e. interaction between
 265 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)

291 DISCUSSION

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

300 *Reflection on the findings*

301 Interestingly, this study shows that male patients have equally high expectations of IVF as previously shown
 302 in females (Boivin and Takefman, 1995, Miron-Shatz, et al., 2020) and that expectations of women and men
 303 depend on their dispositional optimism. Males and females do not differ either in the limited extent in which
 304 they reconsider their expectations after having received a below average IVF prognosis. Females did have
 305 higher state anxiety scores than males, as previously reported (Edelmann and Connolly, 2000, Schaller, et al.,
 306 2016, Zurlo, et al., 2020), but equally small proportions of males and females (15-16%) scored above the
 307 clinical thresholds for state anxiety in fertility patients, as these thresholds are gender specific (Zurlo, et al.,
 308 2020). The interesting observation that a below average prognosis was only associated to the anxiety of
 309 females and not of males is in line with females being mainly concerned about not achieving pregnancy whilst
 310 males are mainly concerned about the health risks for their female partners (Schaller, et al., 2016) and with
 311 the fertility specific distress dimension 'need for parenthood' being associated to the state anxiety of females
 312 but not of males (Zurlo, et al., 2020). The observed anxious reactions of women with a below average
 313 prognosis were in line with those previously reported in women in the active phase of treatment (45.3 vs 40
 314 – 53 on average) (Gabnai-Nagy, et al., 2020, Gürhan, et al., 2009, Karlidere, et al., 2008, Turner, et al., 2013)
 315 and more implicit medical feedback (e.g. number of oocytes and embryos) also causes distress (Boivin, 2000,
 316 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 (Scheier, 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 interpreted 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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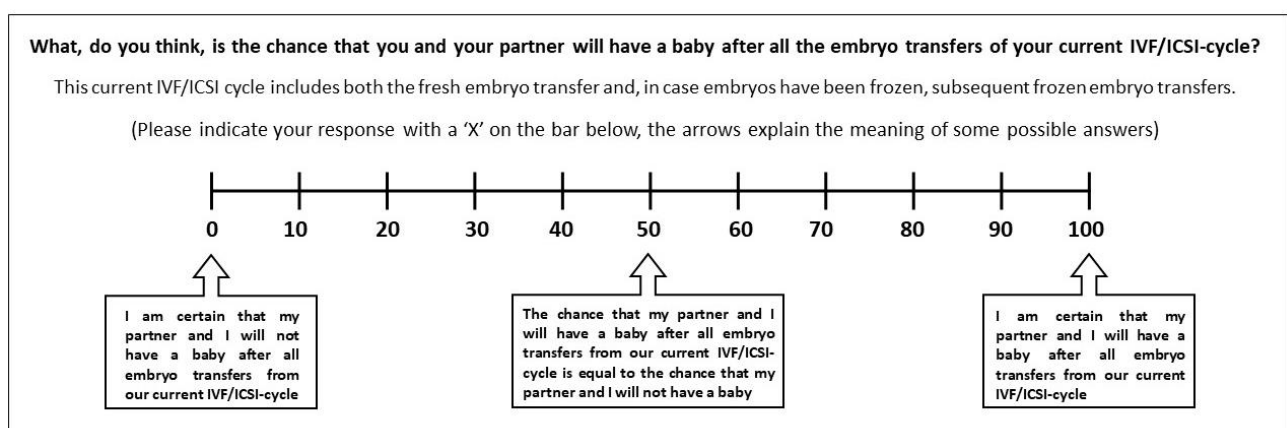


Figure 1: Question used to assess the expectations of IVF success

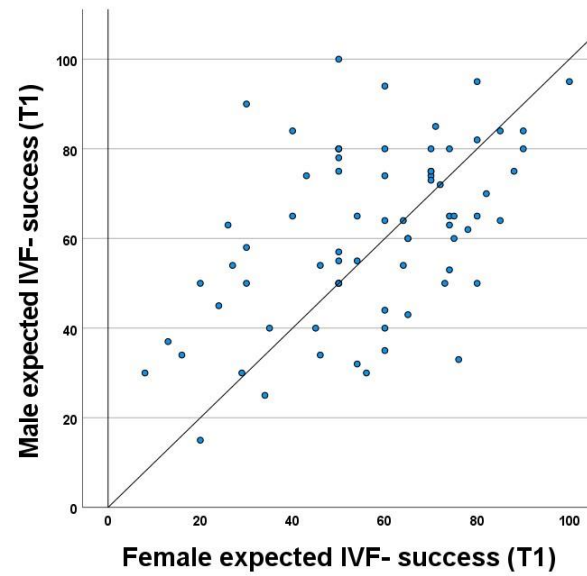


Figure 2: Scatterplot of female vs. male partner's expectations of IVF success (T1)

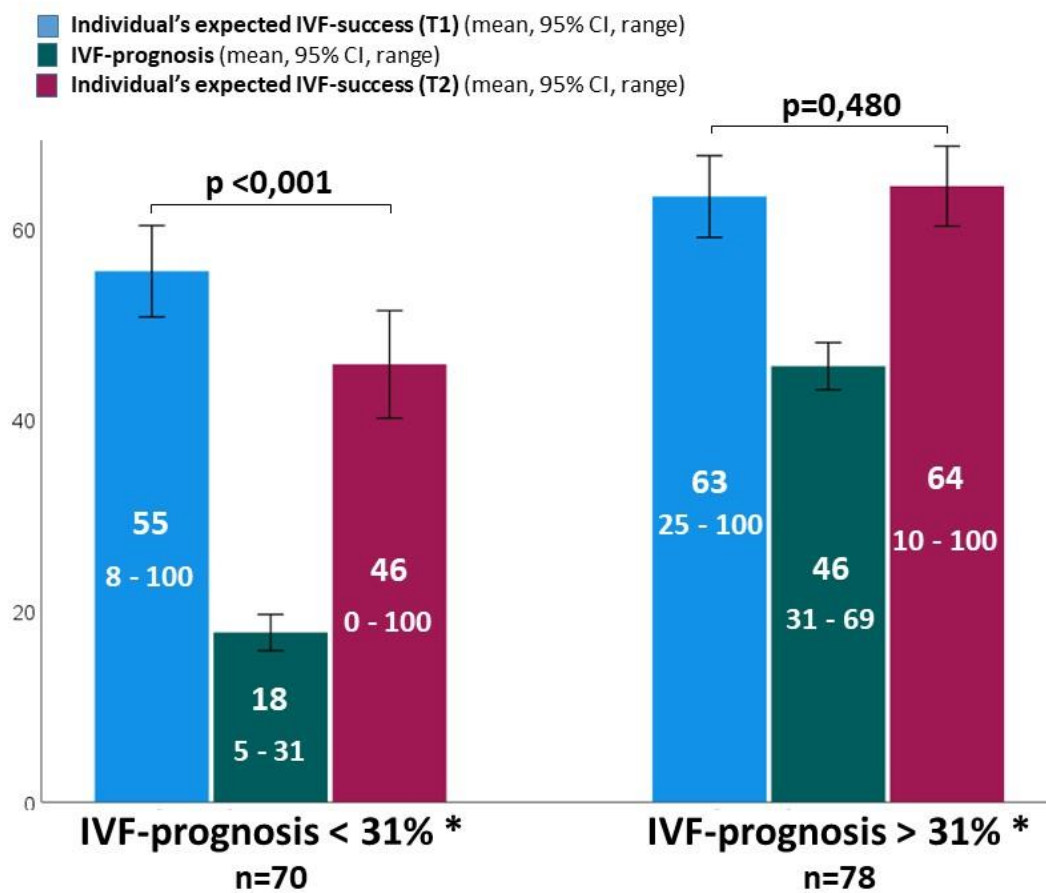


Figure 3: Individual's reconsideration of expectations of IVF success prior to and after receiving their IVF prognosis at the time of embryo transfer

Legend: *31% is the mean IVF prognosis of this cohort

Table I: Study procedures, variables and tools according to their timing

Immediately after oocyte aspiration (T1)	At the time of fresh embryo transfer	Immediately after fresh embryo transfer (T2)
<ul style="list-style-type: none"> • Study information • Each partner signs informed consent form 	Gynaecologist gives couple their IVF prognosis	Each partner independently fills out a questionnaire assessing: <ul style="list-style-type: none"> • Expectation of IVF success (numerical rating scale with three explanatory text balloons) • Anxiety (STAI-state) • Likelihood of advising the novel feedback sheet (4-point Likert scale)
Each partner independently fills out a questionnaire assessing: <ul style="list-style-type: none"> • Dispositional optimism (LOT-R) • Expectation of IVF success (numerical rating scale with three explanatory text balloons) 		

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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 (Nº; 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 (Nº; 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	

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

Hypothesized determinants	Univariable association		Interaction with gender
	Estimate (95% confidence interval)	p-value	p-value
Female gender	-4.203 (-8.875; 0.470)	0.077	Not applicable
Female age	-0.674 (-1.568; 0.221)	0.138	0.738
Having an IVF child	7.919 (-1.993; 17.837)	0.116	0.679
Number of unsuccessful ETs	0.845 (-1.105; 2.795)	0.391	0.891
Dispositional optimism	1.491 (0.778; 2.205)	<0.001*	0.500
Dispositional optimism partner	-0.298 (-1.046; 0.449)	0.431	0.858
*Significant compared to the Bonferroni corrected threshold of 0.007			

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

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