Women’s perspectives regarding subcutaneous injections, costs and live birth rates in IVF

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BACKGROUND: The addition of recombinant LH (rLH) to controlled ovarian hyperstimulation (COH) shows a beneficial effect on ongoing pregnancy rates in poor responder women, with an increase of ongoing pregnancy rate. Next to this possible beneficial effect, there are two potential drawbacks of adding rLH to COH; women have to administer extra injections, and daily rLH injections generate additional costs. We therefore investigated women’s perspectives on an additional injection of rLH with respect to live birth rates (LBR) and out-of-pocket costs in a discrete choice experiment.

METHODS: Women eligible for IVF were asked to choose between treatments that differed in LBR after one IVF cycle, the amount of self-administered injections and out-of-pocket costs or reimbursement. The relative weights that women place on these attributes were estimated with a logistic regression model. To test for heterogeneity of preferences among women, patient characteristics were included in the model.

RESULTS: Two-hundred and thirty-four women were asked to participate in the study. In total, 223 women responded (response rate 95%) and 206 questionnaires were analysed. An increase of one daily injection did not alter women’s treatment preference. LBR and costs did have a significant ($P$, 0.001) impact on women’s choice of IVF treatment. Patient characteristics significantly influenced the effect of costs on women’s preferences.

CONCLUSIONS: One extra daily injection will not cause a woman to refrain from a certain IVF treatment. However, to compensate for the out-of-pocket costs of this extra daily injection, the expected LBR should at least be 6%.

Key words: IVF / live birth rate / injections / controlled ovarian stimulation

Introduction

The aim of women embarking on IVF is to have a child, and patient preference studies in reproductive medicine have clearly demonstrated that live birth rates (LBR) are the pivotal factors for women in their decision-making (Nieuwkerk et al., 1998; Bayram et al., 2005; Steures et al., 2005; Twisk et al., 2007; Van Mello et al., 2010). On the other hand, monetary resources in society are not unlimited. As such, healthcare workers are to provide the most cost-effective treatment.

An important part of IVF treatment is ovarian hyperstimulation, and many regimens have been tried and studied in an attempt to optimize IVF results. Recently, it has been suggested that the addition of recombinant LH (rLH) to controlled ovarian hyperstimulation (COH) shows a beneficial effect on ongoing pregnancy rates in poor responder women, with an increase of ongoing pregnancy rate from 20 to 32% with the addition of rLH (Mochtar et al., 2007). Next to this possible beneficial effect, there are two potential drawbacks of adding rLH to COH; women have to administer extra subcutaneous injections and these daily rLH injections generate additional costs.

What women prefer when it comes to injections during IVF has not been substantiated. We do know that IVF is perceived as an invasive and burdensome treatment (Eugster and Vingerhoets, 1999). The mental and psychological distress that accompanies an IVF treatment has been described since the early 1990s (Kopitzke et al., 1991; Edelmann et al., 1994). This burden and distress even causes...
Women to drop out of treatment for the following reasons: psychological burden, poor prognosis, relationship problems and physical burden (Olivius et al., 2004; Verberg et al., 2008; Domar et al., 2010). This physical burden encompasses infection, ovarian hyperstimulation syndrome and administration of subcutaneous injections (Olivius et al., 2004). The cumulative dropout rate after three reimbursed IVF cycles can be as high as 62% (Land et al., 1997).

Studies that compared drop out rates in women during conventional IVF and mild stimulation IVF (i.e. fewer daily injections and shorter duration of the stimulation) state that mild stimulation IVF has a lower drop out rate (Heijnen et al., 2007; Verberg et al., 2008) and suggest that a mild treatment protocol is related to a reduction of anxiety and treatment-related stress (Verberg et al., 2008). Other research goes on to suggest that mild stimulation protocols will be better tolerated by patients (Fauser et al., 1999).

These data suggest that women prefer an IVF treatment with fewer injections rather than more, but the studies generating these data were designed to investigate the reasons why women drop out of treatment and not how women receiving IVF perceive treatment aspects—for example, injections.

One study that investigated patient preferences in conventional IVF versus mild stimulation IVF showed that 60% of the women undergoing conventional IVF find side effects of hormone treatment unacceptable or severe, compared with 5% of the women treated with mild IVF (Haigaard et al., 2001). The side effects of the hormone treatment were not mentioned, and only 49% of respondents had commented on this section of the questionnaire.

Public financing of assisted reproduction treatments (ARTs) ranges from virtually no subsidy in the USA to funding of a limited number of cycles in most European countries and to unrestricted reimbursement with co-payments in Australia (Hughes and Giacomini, 2001; Nachtiegl, 2006; Chambers et al., 2009; Connolly et al., 2010). In the Netherlands, where state funding is available for up to three IVF attempts, the costs of an additional rLH injection are, as yet, not reimbursed. A recent study demonstrated that a price increase in ART associated with the introduction of co-payment for ART reduced the utilization of IVF (Connolly et al., 2009). This suggests that when treatment access is dependent on user fees, costs are restrictive for many patients (Connolly et al., 2010).

So, in view of the existing data, it would seem that both the addition of daily injections of rLH and the costs may affect patients’ preferences for an IVF treatment. We therefore investigated patients’ perspectives by performing a discrete choice experiment (DCE), in which we examined the relative weight women place on an additional subcutaneous injection of rLH with respect to LBRs and out-of-pocket costs.

Materials and Methods

Setting

This patient preference study was conducted alongside an RCT (the L-AGE trial), comparing the effect of COH with rFSH and rLH versus rFSH alone in 244 women with poor ovarian response undergoing their first IVF cycle, in the Academic Medical Centre or the Onze Lieve Vrouwe Gasthuis in Amsterdam, the Netherlands. Women with poor ovarian response were defined as all women aged 35–41 years or women aged less than 35 years with poor ovarian reserve, defined as FSH > 12 IU/ml accompanied with an antral follicle count ≤ 5. Women in the trial were randomly allocated to rLH plus rFSH (1:2 ratio) or rFSH alone after down-regulation with a GnRH agonist in a long protocol with a mid-luteal start. The study was registered with EudraCT (EudraCT number 2007–007487–22) and the Dutch National Trial Register (Trial ID: NTR1457).

Participants

All women who attended an IVF information session in the period from July 2009 to May 2010 before commencing their first IVF cycle were asked to participate in the DCE. In total, 234 women were asked to participate. The IVF information sessions were held every 3 months in the period from July 2009 to May 2010 in the Academic Medical Centre in Amsterdam, the Netherlands. After these sessions, a questionnaire was handed out and women were asked to fill it in and hand it back when they returned to the outpatient clinic 1 month later for cycle scheduling. All women started treatment within 3 months after the cycle scheduling appointment. The women who forgot to bring their questionnaire were given a new one upon arrival at the clinic. They were asked to complete the questionnaire on the spot before their scheduling appointment to ensure that all questionnaires were filled in before the start of the treatment. In the L-AGE trial, women were included if they were poor responders; in the DCE, we decided to include women of all subfertility indications to get a broad view of the women’s preferences.

Questionnaire

The questionnaire included a letter explaining the purpose of the study and information on COH and rLH, focusing on the extra subcutaneous injection, costs of rLH and LBRs (The Supplementary Data contain a translated version of the information provided).

The questionnaire consisted of two parts. In the first part, general data on the women were collected. This included their age, education, income, duration of subfertility, cause of subfertility, prior fertility treatment and obstetric history. In the second part of the questionnaire, preferences for LBR, an additional injection and costs were studied by means of a DCE. Institutional review board approval was not needed because a questionnaire study is not subject to the Dutch ‘Medical Research Involving Human Subjects Act’.

Discrete choice experiment

The DCE assumes that a given healthcare treatment can be described by its characteristics. These characteristics are called ‘attributes’. The patients’ preference for a treatment is determined by the variants of these attributes, called ‘levels’. In this case, the treatment was an IVF cycle, and its attributes were LBR, daily subcutaneous injections and out-of-pocket costs. The relative importance of the attributes and trade-offs that patients make between them can be assessed by offering a series of choices between two or more (hypothetical) treatment alternatives with different combinations of attribute levels (Louviere et al., 2007).

In comparison with other preference techniques (e.g. visual analogue scale and the time-trade-off method), a DCE presents a reasonably straightforward task and resembles more closely a real-world decision, i.e. trading-off health and non-health outcomes (Bijlenga et al., 2009).

Attributes and attribute levels

The selection of the most relevant attributes of an IVF cycle and their levels was based on the data from the literature on LBR per cycle (Templeton et al., 1996; Lintsen et al., 2007; HFEA, 2008; SART, 2008; Nyboe Andersen et al., 2009), and monetary information was acquired.
from a pharmaceutical company that produces the rLH injections (Merck Serono). After consensus (by A.M.M. and N.M.M.) on the attributes and levels and development of the choice sets, the questionnaire was presented to an expert panel (consisting of two gynaecologists, one resident and one PhD student, all specialized in reproductive medicine) that offered the final adjustments. The final decisions were made by A.M.M and N.V.M.

The attributes and their levels are presented in Table I. The attribute levels of LBR per cycle ranged from 5 to 30%. These percentages are based on literature (Templeton et al., 1996), a large Dutch study (Lintsen et al., 2007) and LBRs per fresh cycle from national databases; the USA (SART, 2008), the UK (HFEA, 2008) and the European Society of Human Reproduction and Embryology (ESHRE) consortium (Nyboe Andersen et al., 2009). Women aged below 35 years have a higher average LBR fresh per cycle than women aged 40 year, therefore, we used a LBR ranging from 30 to 5%. The attribute levels of daily injections were two or three daily subcutaneous injections. In our IVF stimulation protocol, women receive a daily GnRH agonist injection and a daily rFSH injection (in total, two injections); therefore, if we were to add rLH, this would result in three daily injections.

In the Netherlands, where state funding is available for up to three IVF attempts, the costs of an additional rLH injection are not reimbursed. The out-of-pocket cost of rLH injections for one IVF treatment cycle is roughly €1000 (Merck Serono). The attribute levels of costs were reimbursement (zero cost) or out-of-pocket costs of €1000.

**Development of the choice sets**

The combination of the three IVF attributes, with two attributes at two levels and one attribute at six levels, provided 24 (2^2 × 6^1) hypothetical alternatives for an IVF treatment. We used a fractional factorial design to generate a functional sample of 14 alternatives. The fractional factorial method systematically selects this sample according to an orthogonal design. Orthogonality guarantees an optimal balance of the levels and attributes with a minimal correlation (Louviere et al., 2007). The orthogonal design was generated by Orthoplan (Statistical Package for Social Sciences (SPSS) version 14.0, SPSS Inc., USA) and a set of 14 alternatives were selected and formed treatment option A. To ensure minimal overlap of attribute levels, we created a set of alternatives to form treatment option B by means of a syntactical fold over technique, based on the profiles of treatment option A (Ryan et al., 2001). As a result, each choice set consisted of two options representing hypothetical alternatives for an IVF treatment. An example of a choice set is shown in Fig. 1. The 14 choice sets for treatment options A and B were considered sufficient to estimate all main effects representing the relative importance of each attribute.

Women had to choose their most preferable option in each choice set, without an opt out alternative (e.g. ‘no treatment’ option) as these women would all be undergoing IVF treatment in the future and ‘no treatment’ would not have been a realistic option.

**Table I** Attributes with corresponding levels per IVF cycle.

<table>
<thead>
<tr>
<th>Attributes</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live birth rate (%)</td>
<td>5, 10, 15, 20, 25, 30</td>
</tr>
<tr>
<td>Daily injections</td>
<td>2, 3</td>
</tr>
<tr>
<td>Costs (€)</td>
<td>0*, 1000</td>
</tr>
</tbody>
</table>

*Insurance company reimbursement.

**Figure 1** An example of a choice set, representing hypothetical alternatives for an IVF treatment, as presented in the questionnaire.
To assess the understanding of the attributes (LBR, number of injections and out-of-pocket costs), the questionnaire contained two dominant choices (rationality tests). In these sets, one of the two IVF alternatives was characterized by equal or logically preferable levels on all attributes.

Statistical significance was set at $P < 0.05$.

Pilot study

The questionnaire was tested for interpretation and face validity among 14 fertility doctors and nurses at the Academic Medical Centre in Amsterdam, the Netherlands, and 10 subfertile women without previous IVF experience. The information letter was clear, and the DCE itself was well understood by all participants in the pilot study and therefore only minor modifications were made to the final version of the questionnaire.

Analyses

The DCE was analysed by taking each choice between the two treatment alternatives as an observation and then analysed by a logistic regression model. Assuming that all attributes have an independent effect on a women’s preference, the following model was estimated (Hahn and Shapiro, 1966; Ryan et al., 2001; Louviere et al., 2007):

$$V = \beta_0 + \beta_1 \times \text{livebirthrate} + \beta_2 \times \text{numberofinjections} + \beta_3 \times \text{costs}$$

(i) $V$ is the observable relative utility (i.e. satisfaction or happiness) that is composed of the preference scores for the individual $\beta$-coefficients of the model.

(ii) $\beta_0$ is the constant term reflecting the preference option A relative to option B.

(iii) $\beta_1$ to $\beta_3$ are the coefficients of the attributes indicating the relative weight individuals place on a certain attribute.

The absolute value of $V$ has no direct interpretation, but an alternative with a higher $V$ is preferred over an alternative with a lower $V$ (Louviere et al., 2007). The sign of a coefficient reflects whether the attribute has a positive or negative effect on the overall utility. The value of each coefficient represents the importance that respondents assign to an attribute.

To take heterogeneity of preferences into account among women, we included age, parity, duration of subfertility, income, previous treatment with subcutaneous injections and diagnosis of the subfertility as interaction terms in the model. The statistically insignificant variables were excluded from the model by backward stepwise elimination. Results are presented for the final reduced model, which includes the main effects and significant interactions effects only.

To investigate the willingness of women to trade-off €1000 to achieve a certain LBR, we calculated the ratio between the coefficient of the cost attribute and the attribute LBR. Thus, $\beta_3/\beta_1$ represents an estimate of what the minimum preferred LBR for women is in order to be willing to pay €1000 of out-of-pocket costs.

Results

Two-hundred and twenty-three women completed the questionnaire. The response rate was 95% (223/234), which is comparable with other DCE studies (Bijlenga et al., 2009; Bekker-Grob de et al., 2010). Sixteen questionnaires were excluded because the women did not complete all the 14 choice sets. Of the 207 women, 206 passed the rationality test, which indicates that the women understood the DCE task well.

Baseline characteristics

In total, 206 data sets were analysed. Baseline characteristics of the women are shown in Table II.

Discrete choice experiment

The results of the reduced logistic regression model, which contains the main effects of the attributes and the significant interaction effects, are shown in Table III. Both LBR ($\beta_1$) and costs ($\beta_2$) had a significant impact on women’s preference for IVF treatment ($P < 0.001$). The positive sign on LBR indicates that women’s preference for IVF treatment increased with the increase of LBR. The negative sign on costs indicates that women’s preference decreased in case of ‘out-of-pocket’ cost of €1000. An increase of one daily subcutaneous injection, from two to three injections, did not affect women’s preference for IVF treatment ($P = 0.54$).

As for the interaction terms, the costs attribute was found to be significantly more important for women: (i) 35 years or younger, (ii) with one or more children, (iii) with subfertility for 2.5 years or longer and (iv) with a very low and low/moderate household income. The negative signs on these interaction terms indicate that women with these characteristics have additional negative attitudes towards out-of-pocket cost of €1000.

The minimum preferred LBRs for the specific patient profiles are shown in Table IV. The LBRs were calculated from the beta coefficients of the attributes and the interaction effects. In general, women participating in this study were willing to pay €1000 when the LBR is 6% or more. Women found that a LBR of $<6\%$ is not worth €1000 of out-of-pocket costs. Depending on age, parity, duration of subfertility and income, women were willing to pay €1000 of out-of-pocket costs if compensated by at least a LBR ranging from 5 to 14% per IVF cycle. For example, a secondary subfertile 35-year-old woman with a very low income who has been trying to conceive for less than 2.5 years is willing to pay out-of-pocket costs of €1000 if it coincides with at least a LBR of 13% per IVF cycle. On the other hand, a primary subfertile 40-year-old woman with a high income who has been trying to conceive for more than 2.5 years is willing to pay out-of-pocket costs of €1000 if it coincides with at least a LBR of 6% per IVF cycle.

Discussion

The basic concept investigated in this study was: does the addition of an extra daily subcutaneous injection change women’s preferences for an IVF treatment? Mild stimulation IVF protocols, for example, have been called patient-friendly IVF in the literature without any studies to determine what ‘patient-friendliness’ really means (Verberg et al., 2009). If we indeed want to offer IVF that is patient-friendly, we should start by inquiring what patients prefer during IVF. In this study, we addressed a part of this issue, and further research should investigate patient preferences in IVF in more detail.

Here, we assessed the preferences of women regarding the addition of an injection of rLH to rFSH relative to LBRs and out-of-pocket costs. LBR and costs did have a significant impact on women’s preference. An increase of the daily subcutaneous injections, from two to three injections, did not affect women’s preference. The costs attribute was more important for women 35 years or younger, with one or more children,
Table II Baseline characteristics of subfertile women awaiting IVF treatment.

<table>
<thead>
<tr>
<th>Age women n (%)</th>
<th>99 (48)</th>
<th>107 (52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35 years old</td>
<td>99 (48)</td>
<td>107 (52)</td>
</tr>
<tr>
<td>≥35 years old</td>
<td>107 (52)</td>
<td></td>
</tr>
<tr>
<td>Women with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 pregnancies n (%)</td>
<td>74 (36)</td>
<td></td>
</tr>
<tr>
<td>≥1 children</td>
<td>38 (18)</td>
<td></td>
</tr>
<tr>
<td>≥1 miscarriages</td>
<td>37 (18)</td>
<td></td>
</tr>
<tr>
<td>≥1 TOP</td>
<td>13 (6)</td>
<td></td>
</tr>
<tr>
<td>≥1 ectopic pregnancy</td>
<td>3 (1)</td>
<td></td>
</tr>
<tr>
<td>≥1 preterm delivery</td>
<td>3 (1)</td>
<td></td>
</tr>
<tr>
<td>≥1 neonatal death</td>
<td>1 (0.5)</td>
<td></td>
</tr>
<tr>
<td>Duration of subfertility (months ± SD)</td>
<td>37.7 ± 26.5</td>
<td></td>
</tr>
<tr>
<td>Previous fertility treatment n (%)a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 clomiphene citrate cycles</td>
<td>4 (2)</td>
<td></td>
</tr>
<tr>
<td>≥1 IUI cycles</td>
<td>57 (28)</td>
<td></td>
</tr>
<tr>
<td>≥1 IVF cycles</td>
<td>33 (16)</td>
<td></td>
</tr>
<tr>
<td>Primary diagnosis of subfertility n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male factor</td>
<td>90 (44)</td>
<td></td>
</tr>
<tr>
<td>Unexplained subfertility</td>
<td>62 (30)</td>
<td></td>
</tr>
<tr>
<td>Imminent ovarian failure</td>
<td>25 (12)</td>
<td></td>
</tr>
<tr>
<td>Tubal factor</td>
<td>18 (9)</td>
<td></td>
</tr>
<tr>
<td>Oocyte vitrification</td>
<td>4 (2)</td>
<td></td>
</tr>
<tr>
<td>Anovulation (PCOS)</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td>Endometriosis</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td>Not reported</td>
<td>3 (1)</td>
<td></td>
</tr>
<tr>
<td>Education level n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowb</td>
<td>19 (9)</td>
<td></td>
</tr>
<tr>
<td>Moderatec</td>
<td>63 (31)</td>
<td></td>
</tr>
<tr>
<td>Highd</td>
<td>121 (59)</td>
<td></td>
</tr>
<tr>
<td>Not reported</td>
<td>3 (1)</td>
<td></td>
</tr>
<tr>
<td>Household income per year n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very low</td>
<td>26 (13)</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>60 (29)</td>
<td></td>
</tr>
<tr>
<td>Moderatef</td>
<td>47 (23)</td>
<td></td>
</tr>
<tr>
<td>Highg</td>
<td>57 (28)</td>
<td></td>
</tr>
<tr>
<td>Not reported</td>
<td>16 (8)</td>
<td></td>
</tr>
</tbody>
</table>

(n = 206)

TOP, termination of pregnancy; IUI, intra uterine insemination; PCOS, polycystic ovary syndrome.
aSome women had received both IUI and IVF.
bPrimary school/intermediate vocational education.
cHigher general secondary education/pre-university secondary education.
dHigher vocational education/university.
e≥€10 000–€25 000.
f€25 000–€50 000.
g€50 000–€75 000.
h≥€75 000.

with subfertility for 2.5 years or longer and with a very low and low/moderate household income. All the earlier-mentioned patient characteristics that give an additional negative attitude towards out-of-pocket cost are easily understood except for women with subfertility of 2.5 years or longer. Before an attempt is made to explain this finding, the variable outcome should be put in context. This variable was marginally significant (P-value 0.05) and had a low β-coefficient (−0.2). We hypothesize the following explanations: women with a longer subfertility have lost hope of achieving a live birth after all these years and feel that investing €1000 is throwing their money away. However, if they have lost hope of a live birth, it is counterintuitive that they would continue with their treatment. Another explanation could be that women who have a longer subfertility have already invested in previous fertility treatments and have a better insight into what the costs are; therefore they make a more informed decision, resulting in a negative attitude towards paying 1000 euro.

The strength of this study is that it has high external validity. The population is a good representation of women eligible for IVF, owing to the large number of participants, various indications of subfertility and large range of duration of subfertility. This study also includes women in all walks of life, and considers the differences of income and education level between the women. When comparing the demographic characteristics of our participants to the demographic characteristics of Dutch women undergoing IVF; the indications for IVF are similar to data from a large Dutch cohort study comprising almost 5000 patients undergoing IVF, representing 11 of the 13 IVF clinics in the Netherlands (Lintsen et al., 2010). The only difference is that the participants of our study are older (52% ≥ 35 years old) than the IVF population in the Lintsen et al. (2010) study (38% ≥ 35 years old). This may well be explained by the fact that the Dutch cohort study was performed on data from 2002 to 2004, and our study was from 2009 to 2010. Over those years, the average maternal age for undergoing a first IVF has increased (de Mouzon et al., 2010).

Still, a DCE has its limitations. Attributes and attribute levels were designed with the help of an expert panel and data from literature, but
this careful procedure does not guarantee that other attributes are irrelevant. An example of other attributes that are also a part of an IVF treatment are time on a waiting list, continuity of staff and attitudes of staff. We refrained from including these attributes because we wanted to make clean cut, easy to follow trade-offs for women comparing the preference for two or three injections and we did not want to dilute this effect by adding more attributes. Another limitation is that 44% of the women participating in this study had previous intrauterine insemination (28%) and/or IVF (16%) treatment elsewhere and thus had used subcutaneous injections before, which could have influenced their preference. On the other hand, this does mimic real life and therefore increases the generalizability of the data. To check for this confounder, we included previous treatment as an interaction term into the model and it did not influence women’s preferences.

Economic evaluations of IVF have implicitly assumed that leaving the facility with a child is the most important factor for women (Bartels, 1987; Batman, 1988; Page, 1989; Wagner and St Clair, 1989; Webb and Holman, 1990; Haan, 1991; Neumann et al., 1994). Our findings confirm this but also indicate that out-of-pocket costs do start to matter when the LBR falls <5–14% per IVF cycle, depending on specific patient characteristics. The only DCE published to date on patient preferences in IVF did not investigate the effect of an additional daily injection on the preferences of women but focused on more general aspects of an IVF treatment (Ryan, 1999). Ryan (1999) found that good staff attitudes were more important than a 6% increase in the chances of taking home a baby and concluded that women care about more issues than purely leaving the service with a child.

As patient preference studies in IVF and other fertility treatments are overdue, the DCE model presented in this study could be used to answer more patient preference questions.

In summary, daily subcutaneous injections do not influence the preferences for an IVF treatment, in contrast to LBR and costs. Therefore, it is important for doctors to know that an extra daily injection will not cause a woman to refrain from a certain IVF treatment. Also, the results of this study have important implications for future economic evaluations of IVF, as the willingness to pay of out-of-pocket costs is strongly related to LBR and specific patient characteristics.

**Supplementary data**

Supplementary data are available at http://humrep.oxfordjournals.org/.

**Authors’ roles**

A.M.M. contributed to the study design, data acquisition, data analysis and manuscript drafting. E.W.B-G. took part in data analysis, interpretation of the data and critical revision of manuscript. M.H.M. and F.V. played a role in study design, data interpretation and revisions of manuscript. N.M.M. was involved in study design and data analysis. She also participated in interpretation of the data and revised the manuscript critically.

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**References**


