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Original Article

# Quality of life and pregnancy outcomes among women undergoing *in vitro* fertilization treatment: A longitudinal cohort study

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**KEYWORDS**
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Quality of life;
FertiQoL;
Pregnancy

*Background/purpose:* This study assessed the quality of life (QoL) and pregnancy outcomes among infertile women undergoing *in vitro* fertilization (IVF) treatment to investigate the association between QoL and IVF pregnancy outcomes.
*Methods:* This study included 686 women with 1205 embryo transfers (ETs). QoL was measured using the fertility quality of life (FertiQoL) tool before ET. FertiQoL comprises two modules: a Core module (including mind/body, emotional, relational, and social domains) and a Treatment module (covering treatment environment and tolerability domains). The FertiQol total and subscale scores were computed and scored in the range of 0–100 (higher scores indicate better QoL). Multivariate generalized estimating equation analyses were carried out to assess the association between QoL and IVF pregnancy outcomes, with adjustment for time-varying factors across multiple ETs for a given person.
*Results:* The lowest score in the core module was for the emotional domain (62.0), and that in the Treatment module was for the tolerability domain (59.4). QoL scores were significantly and

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positively associated with pregnancy outcomes (i.e., ongoing pregnancy, live birth); with a one unit increase in the emotional domain score, the probabilities of ongoing pregnancy and live birth significantly increased by 2.4% and 2.6%, respectively ($p < 0.05$).
*Conclusion:* This study evaluated the prospective association between QoL and IVF pregnancy outcomes among infertile women. The results highlight the importance of developing clinical strategies to improve QoL among infertile women undergoing IVF treatment, which may further improve the pregnancy rates of this population.


## Introduction

Having children is an important part of many people's lives. Studies have shown that parents whose basic needs are satisfied enjoy parenthood[1,2] and that women who desired pregnancy reported a sense of happiness and satisfaction.[3] Unfortunately, some couples have fertility problems. Recent studies have shown that the prevalence of infertility is ~15% for Chinese women who are at risk for pregnancy and 25% for those who attempted to become pregnant,[4] 37% for Israeli women aged between 15 and 55 who had enrolled in a health plan for 12 months or more,[5] and 10.9% for Danish women aged between 20 and 29.[6] Moreover, infertility is negatively associated with the relational, sexual, and psychosocial well-being of patients.[7]

The optimal treatment for infertility is still debated, with assisted reproductive technology (ART) being an option. However, undergoing ART, especially *in vitro* fertilization (IVF) treatment, is psychologically and emotionally stressful for most patients, with the possibility of perceived distress, depression, or anxiety before, during, and/or after IVF treatment.[8–10] In addition to the fear of not getting pregnant, IVF treatment stresses women with its treatment cost, daily injections, required procedures, and possibility of failure at any stage of the treatment. As a result, undergoing IVF treatment may be similar to being diagnosed with infertility in that it may result in distress, depression,[11–13] and possibly a negative impact on the patient's quality of life (QoL). Although the mental symptoms that occur during fertility treatment are believed to negatively impact pregnancy outcomes,[10] studies have not explored whether the QoL of infertile women is associated with their pregnancy outcomes with ART.

QoL is recognized as an important outcome measure for many populations, including women receiving IVF treatment. QoL provides healthcare professionals with a holistic view of the self-perceived health status of an individual that can be used to determine whether follow-up action is necessary.[14] In addition, QoL contains multiple dimensions,[15] which can assist healthcare professionals in identifying what needs further attention. Given the importance of QoL for healthcare professionals, Boivin et al. developed the fertility quality of life (FertiQoL) tool to capture the QoL of women undergoing treatment for fertility problems.[16] FertiQoL contains multiple dimensions covering different aspects of health, including specific aspects for women receiving infertility treatments (i.e., a Treatment module with treatment environment and tolerability domains).[16] Healthcare professionals can obtain comprehensive QoL information through FertiQoL.

Against this background, the purpose of this study was to measure the QoL and pregnancy outcomes among infertile women undergoing IVF treatment to investigate the association between the QoL measured before embryo transfer (ET) and the pregnancy outcomes of IVF treatment.

## Methods

### Study participants

This is a longitudinal cohort study of infertile couples undergoing IVF treatment at the Assisted Reproductive Technology Center at National Cheng Kung University Hospital, Taiwan. Permission for this study was obtained from the Institutional Review Board of National Cheng Kung University Hospital, Tainan, Taiwan (B-ER-105-114). All women with infertility problems undergoing ETs from 2012 to 2017 were included in this study; those with poor quality of embryo, cancelled IVF cycles, thin endometrium (i.e., less than 7 mm) or lost at follow-up were excluded from analysis. The definition of poor quality of embryo included severe fragmentation (>25%), non-stage-specific cell size, presence of multi-nucleation in cleavage-stage embryos, undistinguishable inner cell mass with few cells, and poor or uneven appearance of the trophectoderm with very few cells in blastocysts. We also excluded those with mental disorders and those who had suffered a major traumatic event such as the death of someone close at least 6 months prior to QoL data collection. The latter group was excluded because people who have experienced such life events are likely to have negative emotions (e.g., depression, sadness, anxiety), which may negatively affect their psychological well-being or QoL. A total of 686 women with 1205 cycles of ET were included in this study. Since all procedures and treatments were routine care and the patients' data were analyzed and reported anonymously, the requirement for informed consent by participants was waived by the IRB committee.

### IVF treatment protocol

For all IVF cycles, controlled ovarian hyperstimulation, either via a gonadotropin-releasing hormone (GnRH) agonist or a GnRH antagonist protocol, was used. When the leading follicles reached 18–20 mm, recombinant human chorionic gonadotropin (rhCG) was administered, followed

by transvaginal oocyte retrieval 34–36 h later. *In vitro* embryo culture with or without intracytoplasmic sperm injection was then conducted. ET was performed on Day 2–5 with good-quality embryos (based on a morphological study). For frozen ET cycles, previous cryopreserved good-quality embryos were thawed for transfer per standard protocol.

Study participants had the choice of using atosiban, which is a mixed oxytocin/vasopressin V1A receptor antagonist primarily used for the delay of imminent premature labor with minimal side effects.[17] Some evidence has suggested that atosiban may improve the pregnancy outcomes of IVF treatment for women who are at risk of frequent uterine contractions or poor endometrial receptivity (e.g., women with repeated implantation failure[18–20] and those with endometriosis[21]). For cycles with infusion of atosiban (Tractocile; Ferring Pharmaceuticals), a single bolus dose (6.75 mg, 0.9 mL) was administered intravenously before ET, followed by continuous infusion of the remaining dose (30.75 mg, 4.1 mL) in 500 mL of normal saline for 1.5 h.

## QoL assessment

The assessment of QoL was conducted before ET. The study participants self-reported their QoL based on the questions specified in FertiQoL. FertiQoL is the gold standard for the assessment of the infertility-related QoL of patients undergoing ART. FertiQoL comprises two modules: Core FertiQoL and an optional Treatment module. The Core FertiQoL module contains 24 items.[22] Two items are general and 22 items are specific to infertility, covering four domains (i.e., Mind/body, Emotional, Relational, and Social) derived from the item-generation phase and exploratory factor analyses. The Treatment module assesses QoL related to the fertility treatment itself (i.e., treatment environment and tolerability). Although various response formats are used, they are all based on a five-point Likert scale: (i) from very poor to very good (one item); (ii) from very dissatisfied to very satisfied (seven items); (iii) from completely to not at all (four items); (iv) from always to never (eight items); and (v) from an extreme amount to not at all (six items) (see detailed information at www.fertiqol.org). The FertiQol total and subscale scores are computed and scored in the range of 0–100.[22] A higher score on a given subscale indicates better QoL. The English version of FertiQoL has been professionally translated into Chinese.[23] In the present study, the Taiwanese version of FertiQoL was utilized with satisfactory internal consistency ($\alpha = 0.79–0.83$).

## Pregnancy outcomes

A test for β-human chorionic gonadotropin hormone (β-HCG) was given 14 days after ET. The primary outcomes of this study include chemical (biochemical) pregnancy, ongoing pregnancy, and live birth rate. Biochemical pregnancy was confirmed by a blood sample β-HCG level of above 30 IU/L, which is typically found in the blood of pregnant women as early as 10 days after conception. Ongoing pregnancy was confirmed by the presence of gestational sacs with a heartbeat at the 10th week of gestational age. Live birth was based on the documentation of a live fetus (or fetuses) after the 24th gestational week.

## Clinical characteristics

The patients' characteristics and several laboratory measurements of interest were collected, including maternal age at ET (years), body mass index (BMI, calculated as weight/height squared [$kg/m^2$]), gravidity, parity, history of pregnancy loss, history of ET failure, infertility factors (i.e., from wife, husband, both, or unknown), infertility duration, anti-Müllerian hormone (AMH) (ng/mL), fresh or frozen embryos transferred, number of embryos transferred, and ET dates. The endometriosis stage of individuals was recorded, which was determined according to the classification of the American Society of Reproductive Medicine (ASRM) and confirmed by the findings of histopathological examination. We also reviewed medical records to identify potential psychological symptoms or disorders during IVF treatment. No significant psychological symptoms/illnesses were found in our study population at the start of or during IVF treatment.

## Statistical analyses

The characteristics of the study participants are presented as descriptive and inferential statistics. Descriptive statistics, including mean and standard deviation (SD), for continuous variables, as well as percentages and frequencies for dichotomous and categorical variables, were tabulated. Because QoL assessment and pregnancy outcomes (i.e., biochemical pregnancy, ongoing pregnancy, live birth rate) of multiple ETs from a given patient were likely to be correlated (e.g., for each ET, QoL and pregnancy outcomes were measured; if a person had several ETs, then QoL and pregnancy outcomes were repeatedly measured), generalized estimating equation (GEE) analysis[24] was applied to assess the association between QoL and IVF pregnancy outcomes. GEE is a specific statistic that can account for the correlation of repeated measures (e.g., QoL, pregnancy outcomes) across multiple ETs within a subject to control for confounding by time-invariant factors from the unmeasured underlying characteristics of individuals. GEE analysis has been recognized as the most appropriate analytic procedure for IVF data collected from multiple cycles.[25] Multivariate GEE analysis was conducted with adjustment for significant factors associated with the outcome of interest (e.g., QoL, pregnancy outcomes), which were determined based on univariate analyses. In particular, we adjusted for time-varying factors as covariates in multivariate analysis because some factors (e.g., maternal age, type of embryo transferred [i.e., fresh or frozen], number of embryos transferred) could vary over time across multiple ETs for a given person. A logistic GEE model with an exchangeable working correlation matrix specified was used for dichotomous data of pregnancy outcomes. Odds ratios (ORs) and 95% confidence intervals (CIs) are also presented. All statistics were prepared with the use of R software (version 3.4.0). All statistical tests were 2-sided, with a $p$-value of less than 0.05 considered to indicate statistical significance.

## Results

Table 1 shows the patients' characteristics. Specifically, the mean (SD) maternal age at ET was 35.69 (4.62) years, the mean BMI was 22.35 (3.48) kg/m$^2$, and the average infertility duration was 4.88 (3.33) years.

Table 2 shows the QoL scores measured by FertiQoL for the study participants. Of note, the lowest score in the core module was for the emotional domain (62.0), and that in the Treatment module was for the tolerability domain (59.4).

Fig. 1 shows the results of univariate analyses of the association between QoL and IVF pregnancy outcomes. It shows that pregnancy rates (i.e., chemical pregnancy, ongoing pregnancy, live birth) increased with increasing patients' QoL as measured by total core, total treatment, and total FertiQoL scores. Details of the univariate analysis models are provided in Supplementary Table 1.

Table 3 shows the results of univariate analyses to assess the association of individual patients' clinical characteristics (measured at the date of ET) with IVF pregnancy outcomes. Maternal age at ET, AMH, infertility duration, number of oocytes retrieved, number of embryos transferred, and type of embryo transferred (i.e., fresh or frozen) were significantly associated with pregnancy outcomes ($p < 0.05$). These variables were further adjusted in multivariate analyses for the association between patients' QoL measured before ET and IVF pregnancy outcomes (i.e., presented in Table 4). We found that emotional QoL scores were significantly associated with IVF pregnancy outcomes; this can be interpreted as follows: with a one unit increase in the QoL score, the probabilities of ongoing pregnancy and live birth rate significantly increased by 2.4% and 2.6% ($p < 0.05$), respectively.

**Table 1** Characteristics of 686 patients with a total of 1205 repeated measures.

| Characteristics | N | Mean (SD) or % |
|---|---|---|
| Maternal age at ET (years) | 1104 | 35.69 (4.62) |
| BMI (kg/m$^2$) | 1200 | 22.35 (3.48) |
| AMH (ng/mL) | 414 | 3.19 (3.08) |
| Gravida | | |
| None | 693 | 58% |
| At least one | 502 | 42% |
| Parity | | |
| None | 1005 | 84% |
| At least one | 190 | 16% |
| Infertility duration (years) | 1202 | 4.88 (3.33) |
| Number of oocytes retrieved | 656 | 9.15 (6.22) |
| Number of embryos transferred | 1173 | 2.55 (0.95) |
| Number of IVF cycles | 421 | 1.93 (1.79) |
| Day of ET | | |
| Day 1—3 | 635 | 68% |
| Day 4—5 | 296 | 32% |
| ET failure history | | |
| None | 317 | 47% |
| At least one | 360 | 53% |
| Pregnancy loss history | | |
| None | 295 | 70% |
| At least one | 129 | 30% |
| Infertility factor | | |
| Male | 432 | 36% |
| Female | 476 | 40% |
| Both | 135 | 11% |
| Unknown | 157 | 13% |
| Type of embryo transferred | | |
| Fresh | 687 | 58% |
| Frozen-thawed | 505 | 42% |
| Atosiban administration | | |
| Yes | 373 | 31% |
| No | 829 | 69% |

Abbreviations: SD: standard deviation, BMI: body mass index, AMH: anti-Müllerian hormone, ET: embryo transfer, IVF: *in vitro* fertilization.
Notes: "N" refers to the number of repeated embryo transfers (ETs) (e.g., the total of ETs was 1205); for every ET, the QoL and pregnancy outcomes were measured.

## Discussion

Given the growing interest in the QoL of women with infertility, we used a large cohort of infertile women who were undergoing IVF treatment to examine this issue. To the best of our knowledge, this is the first study to use a longitudinal design to investigate the prospective association between QoL and pregnancy outcomes with ART. Our results demonstrate that the emotional QoL measured before ET is a significant predictor for positive pregnancy outcomes of IVF treatment, while other domains of QoL had insignificant associations.

The importance of the psychological state in the health of individuals has been described in other populations. For example, a recent study showed that mental health has direct and indirect effects on physical health.[26] Hence, it is possible that poor emotional QoL lowers the physical condition of infertile women, and consequently affects their

**Table 2** QoL scores measured using FertiQoL for all study participants (i.e., 686) with a total of 1205 embryo transfers.

| QoL | N | Mean (SD) |
|---|---|---|
| Core subdomains | | |
| Emotional | 756 | 62.0 (16.6) |
| Mind/body | 753 | 62.9 (20.5) |
| Relational | 734 | 70.9 (13.2) |
| Social | 745 | 70.7 (15.9) |
| **Total Core score** | 707 | 66.7 (13.7) |
| Treatment subdomains | | |
| Environment | 731 | 67.4 (13.5) |
| Tolerability | 751 | 59.4 (13.8) |
| **Total Treatment score** | 729 | 67.5 (12.9) |
| **Total FertiQoL score** | 686 | 67.0 (12.2) |

Abbreviations: N; number of repeated measures, QoL: quality of life, SD: standard deviation.
Notes: Range of QoL scores is 0—100, with higher scores indicating better QoL. "N" refers to the number of repeated embryo transfers (ETs); for every ET, the QoL was measured.

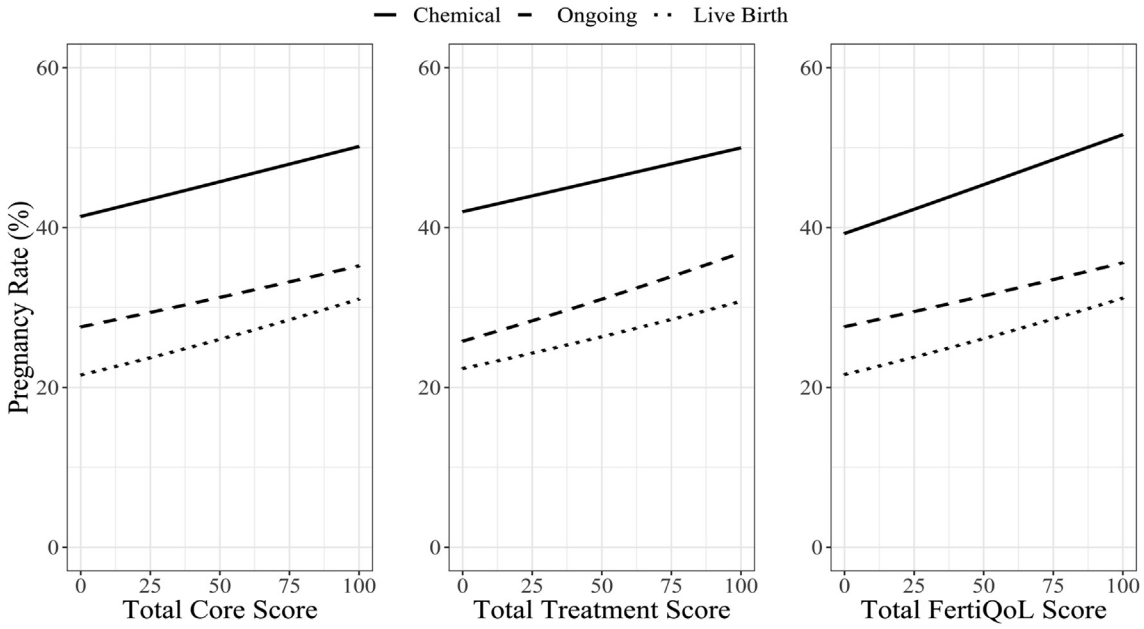


**Figure 1** Results of univariate analyses of the association between quality of life (measured by FertiQoL at the date before embryo transfer) and subsequent pregnancy outcomes of *in vitro* fertilization treatment (i.e., chemical pregnancy, ongoing pregnancy, live birth).

pregnancy outcomes. Additionally, a longitudinal study on fertility and the environment found prospective associations between stress and time-to-pregnancy and infertility among a cohort of women from the United States.[27] That is, the pregnancy outcomes were significantly influenced by the psychological state of the women. Considering this result, one could assume that impaired emotional QoL may have a negative effect on pregnancy outcomes among women receiving fertility treatments. Specifically, the results of the present study support a prospective relationship between emotional QoL and pregnancy outcomes among women receiving IVF treatment. This implies that psychological consultation and support, which can improve the emotional state of infertile women during IVF treatment, may increase the possibility of successful pregnancy and highlights an opportunity to improve IVF pregnancy rates by decreasing the impact of infertility and fertility treatments on the emotional health of patients.

Our results confirm that FertiQoL is a sensitive instrument for capturing the differences between infertile women with positive and negative pregnancy outcomes. These results show that FertiQoL, especially its emotional domain, can be used in clinical practice to predict pregnancy outcomes among women undergoing IVF treatment. Based on such predictions, clinicians may use different strategies to improve pregnancy rates. For example, if a clinician finds that an infertile woman has a poor emotional domain score on FertiQoL, they may want to address the emotional problems of the patient before fertility treatments are administered to increase the chance of successful pregnancy. On the other hand, if a clinician finds that an infertile woman has a satisfactory emotional QoL score, they may want to provide fertility treatments in a timely manner. In addition, with growing evidence showing that the use of atosiban during ET might improve subsequent pregnancy outcomes of IVF treatment,[18–21] atosiban might be suggested to patients with poor emotional QoL.

Several strengths of this study are acknowledged. First, this is the first longitudinal cohort study to evaluate the prospective association between QoL measured before ET and subsequent pregnancy outcomes of IVF treatment based on considerable numbers of infertile women (686) and ETs (1,205). Second, the QoL was measured using FertiQoL, which allows a global and comprehensive evaluation of health-related QoL for women undergoing IVF treatment. FertiQoL has supplanted other QoL measures designed for specific subpopulations with infertility problems. Third, we applied GEE analyses with adjustment for the correlation among repeated measures on study outcomes (e.g., QoL, pregnancy) for a given person to control for confounding by time-invariant factors from the unmeasured underlying characteristics of individuals (i.e., a patient who had poor pregnancy outcomes may have had a tendency to not get pregnant in the following ET cycles; a correlation exists between repeated measures on pregnancy outcomes over multiple ETs for a given person). In addition, we used multivariate analyses to adjust for time-varying variables (e.g., maternal age, type of embryo transferred [i.e., fresh or frozen]) across multiple ETs over time as covariates in the GEE models. These methodological efforts are expected to minimize the potential biases commonly seen in longitudinal cohort studies to provide reliable estimates.

This study had the following limitations. First, it was conducted in a medical center that specializes in infertility problems, so the women coming to this center may have particularly severe forms of infertility problems or present severe endometriosis. Second, there are several confounders that could influence the pregnancy outcomes of IVF treatment, such as the inclusion of embryos subjected

**Table 3** Results of univariate generalized estimating equation analyses of association between individual clinical characteristics (measured at the date of embryo transfer) and IVF pregnancy outcomes.

| Characteristics | Biochemical pregnancy | | Ongoing pregnancy | | Live birth | |
|---|---|---|---|---|---|---|
| | N | OR (95% CI) | N | OR (95% CI) | N | OR (95% CI) |
| Maternal age (years)[a] | 1122 | 0.915 (0.889—0.941)*** | 1111 | 0.921 (0.893—0.950)*** | 1093 | 0.918 (0.890—0.948)*** |
| Body mass index | 1197 | 0.995 (0.959—1.032) | 1179 | 0.973 (0.936—1.012) | 1144 | 0.964 (0.924—1.005) |
| Anti-Mullerian Hormone (ng/mL)[b] | 397 | 1.093 (1.005—1.188)* | 392 | 1.117 (1.026—1.216)* | 385 | 1.110 (1.023—1.204)* |
| Gravida: at least one vs. none (ref.) | 1193 | 1.031 (0.806—1.319) | 1176 | 1.050 (0.798—1.381) | 1142 | 1.015 (0.760—1.355) |
| Parity: at least one vs. none (ref.) | 1193 | 0.923 (0.654—1.303) | 1176 | 0.864 (0.577—1.293) | 1142 | 0.735 (0.476—1.134) |
| Infertility duration (years)[a] | 1199 | 0.952 (0.917—0.989)* | 1181 | 0.956 (0.918—0.995)* | 1146 | 0.946 (0.907—0.986)** |
| Number of oocytes retrieved[b] | 654 | 1.062 (1.035—1.091)*** | 642 | 1.038 (1.010—1.067)** | 627 | 1.040 (1.010—1.067)** |
| Number of embryos transferred[a] | 1197 | 1.132 (1.002—1.277)* | 1179 | 1.134 (1.002—1.284)* | 1144 | 1.143 (1.005—1.299)* |
| Number of *in vitro* fertilization cycles | 410 | 1.071 (0.964—1.190) | 409 | 0.978 (0.881—1.086) | 407 | 0.943 (0.844—1.053) |
| Day of embryo transfer: Day 4—6 vs. Day 1—3 (ref.)[a] | 941 | 2.749 (2.045—3.695)*** | 930 | 2.389 (1.730—3.300)*** | 914 | 2.470 (1.761—3.455)*** |
| History of embryo transfer failure: at least one vs. none (ref.) | 664 | 1.027 (0.750—1.406) | 653 | 1.072 (0.791—1.452) | 626 | 0.947 (0.679—1.320) |
| Pregnancy loss history: at least one vs. none (ref.) | 412 | 0.871 (0.558—1.360) | 411 | 0.797 (0.493—1.289) | 409 | 0.752 (0.463—1.221) |
| Infertility factor (ref.: unknown) | 1195 | | 1177 | | 1142 | |
| Male | | 0.962 (0.662—1.398) | | 0.925 (0.610—1.402) | | 0.929 (0.600—1.438) |
| Female | | 0.828 (0.573—1.198) | | 0.891 (0.594—1.335) | | 0.864 (0.563—1.327) |
| Both | | 1.049 (0.645—1.708) | | 1.266 (0.762—2.104) | | 1.273 (0.752—2.156) |
| Type of embryo transferred: frozen-thawed vs. fresh (ref.)[a] | 1201 | 1.288 (1.011—1.641)* | 1183 | 1.370 (1.070—1.755)* | 1148 | 1.284 (0.982—1.678) |
| Atosiban: use vs. none (ref.) | 1201 | 0.971 (0.756—1.247) | 1183 | 1.043 (0.801—1.359) | 1148 | 1.036 (0.785—1.369) |

Abbreviations: IVF: *in vitro* fertilization, OR: odds ratio, CI: confidence interval, ref.: reference group.

Notes: "N" refers to the number of repeated embryo transfers (ETs) (e.g., the total of ETs was 1205); for every ET, relevant clinical information (i.e., the variables listed in this table) were measured and subsequent pregnancy outcomes were followed.

*significant at $p$-value $<0.05$; **significant at $p$-value $<0.01$; ***significant at $p$-value $<0.001$.

[a] The variables were significantly associated with pregnancy outcomes in univariate analyses so they were further adjusted in multivariate analyses of the association between quality of life and pregnancy outcomes.

[b] Although these variables were significantly associated with pregnancy outcomes in univariate analyses, the information was not sufficient; about half of ET cycles (i.e., ~600) were missing these variables. Therefore, we did not include these two variables in multivariate analyses of the association between quality of life and pregnancy outcomes.

**Table 4** Odds ratios and 95% confidence intervals for generalized estimating equation analyses for association between the QoL scores measured using FertiQoL and IVF pregnancy outcomes.

| Pregnancy outcomes Variables | Biochemical pregnancy | Ongoing pregnancy | Live birth | Biochemical pregnancy | Ongoing pregnancy | Live birth | Biochemical pregnancy | Ongoing pregnancy | Live birth |
|---|---|---|---|---|---|---|---|---|---|
| | N = 601, n = 433 | N = 593, n = 427 | N = 578, n = 418 | N = 601, n = 433 | N = 593, n = 427 | N = 578, n = 418 | N = 601, n = 433 | N = 593, n = 427 | N = 578, n = 418 |
| | OR (CI) | OR (CI) | OR (CI) | OR (CI) | OR (CI) | OR (CI) | OR (CI) | OR (CI) | OR (CI) |
| **QoL scores** | | | | | | | | | |
| Emotional | 1.011 (0.992 −1.030) | 1.024* (1.002 −1.046) | 1.026* (1.003 −1.049) | | | | | | |
| Mind/body | 0.999 (0.983 −1.015) | 0.990 (0.974 −1.007) | 0.988 (0.971 −1.006) | | | | | | |
| Relational | 1.009 (0.993 −1.025) | 0.997 (0.980 −1.014) | 0.991 (0.974 −1.009) | | | | | | |
| Social | 0.991 (0.976 −1.006) | 0.995 (0.979 −1.012) | 1.001 (0.984 −1.019) | | | | | | |
| Treatment environment | 1.000 (0.986 −1.015) | 1.005 (0.989 −1.021) | 1.000 (0.983 −1.017) | | | | | | |
| Treatment tolerability | 0.993 (0.982 −1.004) | 0.991 (0.979 −1.003) | 0.998 (0.985 −1.012) | | | | | | |
| Total Core score | | | | 1.005 (0.990 −1.021) | 1.003 (0.987 −1.020) | 1.008 (0.991 −1.025) | | | |
| Total Treatment score | | | | 0.993 (0.978 −1.009) | 0.995 (0.977 −1.012) | 0.997 (0.979 −1.015) | | | |
| Total FertiQoL score | | | | | | | 1.000 (0.986 −1.015) | 0.999 (0.984 −1.014) | 1.005 (0.990 −1.021) |
| **Adjusted covariates** | | | | | | | | | |
| Endometriosis | 0.582 (0.323 −1.049) | 0.640 (0.35 −1.172) | 0.722 (0.388 −1.343) | 0.577 (0.322 −1.034) | 0.631 (0.350 −1.140) | 0.728 (0.395 −1.343) | 0.588 (0.329 −1.052) | 0.641 (0.354 −1.158) | 0.738 (0.400 −1.362) |
| Maternal age at ET | 0.920*** (0.882 −0.960) | 0.916*** (0.876 −0.958) | 0.920*** (0.879 −0.962) | 0.923*** (0.885 −0.963) | 0.923*** (0.883 −0.964) | 0.928** (0.887 −0.970) | 0.925*** (0.887 −0.964) | 0.924*** (0.884 −0.965) | 0.929** (0.888 −0.971) |
| Infertility duration | 0.968 (0.916 −1.022) | 0.957 (0.900 −1.017) | 0.939 (0.881 −1.001) | 0.967 (0.915 −1.021) | 0.957 (0.902 −1.016) | 0.939* (0.883 −0.999) | 0.965 (0.914 −1.019) | 0.956 (0.901 −1.014) | 0.938* (0.882 −0.997) |
| Number of embryos transferred | 1.121 (0.930 −1.352) | 1.186 (0.977 −1.439) | 1.221 (0.999 −1.493) | 1.125 (0.934 −1.355) | 1.194 (0.983 −1.450) | 1.226* (1.002 −1.499) | 1.122 (0.931 −1.352) | 1.192 (0.981 −1.448) | 1.223 (1.000 −1.496) |

(*continued on next page*)

**Table 4** (*continued*)

| Pregnancy outcomes | Biochemical pregnancy | Ongoing pregnancy | Live birth | Biochemical pregnancy | Ongoing pregnancy | Live birth | Biochemical pregnancy | Ongoing pregnancy | Live birth |
|---|---|---|---|---|---|---|---|---|---|
| Variables | N = 601, n = 433 | N = 593, n = 427 | N = 578, n = 418 | N = 601, n = 433 | N = 593, n = 427 | N = 578, n = 418 | N = 601, n = 433 | N = 593, n = 427 | N = 578, n = 418 |
| | OR (CI) | OR (CI) | OR (CI) | OR (CI) | OR (CI) | OR (CI) | OR (CI) | OR (CI) | OR (CI) |
| Type of embryo transferred (i.e., frozen-thawed vs. fresh = ref.) | 1.389 (0.986 −1.956) | 1.259 (0.882 −1.799) | | 1.380 (0.983 −1.938) | 1.311 (0.923 −1.863) | | 1.370 (0.977 −1.921) | 1.305 (0.918 −1.854) | |

Abbreviations: IVF: *in vitro* fertilization, QoL: quality of life, OR: odds ratio, CI: confidence interval.
Notes: *significant at *p*-value <0.05; **significant at *p*-value <0.01; ***significant at *p*-value <0.001. "N" refers to the number of repeated embryo transfers (ETs); for every ET, the QoL and pregnancy outcomes were measured. "n" refers to the number of individual patients.

to preimplantation genetic screening (PGS). However, due to very limited study population that had used PGS (i.e., less than 4%), we did not further adjust for this in the analyses. Third, this study aimed to assess a prospective association of the QoL measured during IVF treatment (e.g., the date before ET) with subsequent pregnancy outcomes. However, the QoL of patients may vary by type of pregnancy outcome (e.g., chemical pregnancy, ongoing pregnancy, and live birth). Future research can measure the QoL of women receiving IVF treatment at different points of time during pregnancy to assess how the pregnancy outcomes of IVF treatment might influence QoL. Lastly, although this was a longitudinal design, the observed impact of emotional QoL on pregnancy outcomes is not completely certain because we did not manipulate the emotional QoL among our participants. That is, without a well-designed randomized control study, we were unable to observe whether a change in emotional QoL has a real impact on pregnancy. Future studies based on randomized control trials are thus recommended to corroborate our findings. In addition, further analysis in clinically meaningful subgroups (e.g., patients with repeated ET cycles, endometriosis) is needed to confirm the results of this study.

In conclusion, the results of this large cohort study support a prospective association between the QoL measured before ET and subsequent pregnancy outcomes of IVF treatment. The results highlight the importance and necessity of psychological counseling for patients undergoing IVF treatment to improve their QoL, especially the emotional aspect, which may consequently increase the pregnancy rates of this population.

## Authors' roles

M.H.W. and H.T.O. supervised the entire study, including the procedures, conception, design, and completion. N.G.H. and C.W.L. contributed to the data collection. P.F.S. and W.Y.C. contributed to statistical analyses. M.H.W., C.Y.L., and H.T.O. directed the critical discussion of the manuscript. H.T.O. wrote the initial manuscript and all authors approved the final manuscript.

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## Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jfma.2019.06.015.

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