A randomized controlled trial of fallopian tube sperm perfusion compared with standard intrauterine insemination for women with non-tubal infertility

C.M. Farquhar1,2,*, J. Brown1, N. Arroll1, D. Gupta2, C.V. Boothroyd3, Maha Al Bassam4, J. Moir5, and N.P. Johnson6

1Faculty of Medicine and Health Sciences, The University of Auckland, Private Bag 92019, Auckland 1142, New Zealand 2Fertility Plus, Auckland District Health Board, Auckland, New Zealand 3Assisted Conception Australia, Greenslopes Private Hospital, Newdegate St, Greenslopes, QLD 4120, Australia 4Tawam Hospital, OB/GYN Department, Al-Ain, United Arab Emirates 523 Elsa Wilson Dr, Buderim 4556, Australia 6Repromed, 105 Remuera Rd, Remuera, Auckland

*Correspondence address. Department of Obstetrics and Gynaecology and National Women’s Health, University of Auckland, Level 12, ACH Support Building, Auckland City Hospital, Park Road, Grafton Private Bag 92019, Auckland 1020, New Zealand. Tel: +64 9 3737599; Fax: +64 9 3035969; E-mail: c.farquhar@auckland.ac.nz

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STUDY QUESTION: Does fallopian tube sperm perfusion (FSP) result in better pregnancy and live birth rates than standard intrauterine insemination (SIUI) for couples with non-tubal infertility with or without gonadotrophin or clomiphene stimulation?

SUMMARY ANSWER: There was no evidence of an improvement in live birth rates with FSP compared with SIUI.

WHAT IS KNOWN ALREADY: Previous randomized controlled trials have suggested improved live birth rates with FSP but these trials were small. A systematic review published in 2004 suggested heterogeneity in results.

STUDY DESIGN, SIZE, AND DURATION: This pragmatic, multicentre, randomized controlled trial compared SIUI and FSP in 417 women with non-tubal infertility.

PARTICIPANTS/MATERIALS, SETTING, METHODS: The patients were treated at fertility clinics in New Zealand, Australia and the United Arab Emirates.

MAIN RESULTS AND THE ROLE OF CHANCE: Four hundred and seventeen women were randomized to SIUI (n = 210) or FSP (n = 207). Data were available for analysis from 198 women in the SIUI group and 198 women in the FSP group. There were 19 women with incomplete data because of cycle cancellation or withdrawals and 2 women who conceived prior to commencing treatment. There were no significant differences in live birth rates between the two groups with 27 (12.9%) in the SIUI group and 21 in the FSP group (10.1%) [Odds Ratio (OR) 1.31 (0.71, 2.39), P = 0.48]. Two ectopic pregnancies were reported in the SIUI group and one was reported in the FSP group.

LIMITATIONS, REASONS FOR CAUTION: Different ovulation protocols were used in the different clinics. Approximately 10% of the cycles involved donor sperm and ~5% of the cycles did not complete the assigned intervention.

WIDER IMPLICATIONS OF THE FINDINGS: There was no evidence of an improvement in live birth rates with FSP compared with SIUI.

STUDY FUNDING/COMPETING INTEREST(S): The study was funded in part by the A+ trust of the Auckland District Health Board. No commercial funding was received.

TRIAL REGISTRATION NUMBER: ANZCTR Number ACTRN12612001303831.

Key words: randomized controlled trial / intrauterine insemination / fallopian tube sperm perfusion
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Materials and Methods

A pragmatic, randomized (1:1), multicentre, parallel group, controlled trial of FSP and SIUI was undertaken. The trial was coordinated by the lead in-

...spermatozoa were re-suspended in 0.5 ml of medium as used in the recruiting laboratory is inserted into the uterine cavity using a small catheter at the time of ovulation with the aim of improving the chance of fertilizing the oocytes in the fallopian tube. The clinical pregnancy rate per cycle in women with unexplained infertility treated with SIUI in previous studies ranges from 6 to 18% (Veltman-Verhulst et al., 2012).

Fertilization typically occurs in the fallopian tube. There have been concerns that in IUI cycles there is a progressive decline in the sperm concentration along the fallopian tube and there could be as few as 200 spermatozoa present in the ampulla (Mamas, 1996). The number of spermatozoa in the cul de sac suggest very low numbers (Ripps et al., 1994). In response to these concerns an alternative method of injecting the spermatozoa to the upper re-
pродuctive tract was proposed (Fanchin et al., 1995; Nuojou-Huttunen et al., 1997). Fallopian tube sperm perfusion (FSP) was developed to increase sperm densities in the fallopian tubes at the time of ovulation compared with that achieved with SIUI. FSP involves injecting a higher volume (4 ml) of sperm suspension by using a catheter with an intra-

uterine balloon in an attempt to seal off the cervix to reduce efflux of sperm preparation to the vagina.

A number of randomized controlled trials have been published comparing the efficacy of FSP with SIUI. A Cochrane review of the trials of FSP compared with SIUI suggested a benefit in a subgroup of women with greater than 1 year of infertility but there was substantial heterogeneity in the results and no firm conclusions were able to be reached (Cantineau et al., 2004). Variation in the type of catheter used, in the semen preparation and in the volume of insemination was considered to have possibly explained the heterogeneity (Cantineau et al., 2004). It was recommended that the results need to be con-

firmed in larger studies with adequate power before replacing SIUI with FSP as standard practice. However, the 2004 NICE Fertility guidelines stated that the evidence supported the use of FSP routinely, and gave this a category A recommendation and this recommendation was not changed in the draft version of the updated Fertility guidelines in 2012 (NICE, 2004, 2012).

The aim of this randomized controlled trial was to evaluate whether FSP results in improved pregnancy and live birth rates when compared with SIUI, with or without ovulation stimulation.

Introduction

Assisted reproductive techniques (ARTs) offered by most fertility clinics typically includes intrauterine insemination (IUI) with controlled ovarian hyperstimulation (COH). IUI with ovarian stimulation is commonly offered to couples with no tubal pathology. Donor sperm in-

semination is offered where the male partner has azoospermia or where the women are single or in same-sex relationship. In standard IUI (SIUI) ~0.5 ml of sperm suspension that has been ‘washed’ in the laboratory is inserted into the uterine cavity using a small catheter at the time of ovulation with the aim of improving the chance of fertilizing the oocytes in the fallopian tube. The clinical pregnancy rate per cycle in women with unexplained infertility treated with SIUI in previous studies ranges from 6 to 18% (Veltman-Verhulst et al., 2012).

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The aim of this randomized controlled trial was to evaluate whether FSP results in improved pregnancy and live birth rates when compared with SIUI, with or without ovulation stimulation.

Materials and Methods

A pragmatic, randomized (1:1), multicentre, parallel group, controlled trial of FSP and SIUI was undertaken. The trial was coordinated by the lead in-

vestigator at Fertility Plus, the public fertility clinic at National Women’s Hospital at the Greenlane Clinical Centre, Auckland, New Zealand. Suit-

able patients were recruited from clinics facilitated by a special interest group of the Fertility Society of Australia, the REACT (Reproduction And Collaborative Trials) group that supports and facilitates clinical re-

search networks in fertility (listed below). Institutional Ethics approval was sought and approved in all sites. The coordinating centre ethics ap-

proval was provided by the New Zealand Ministry of Health Northern X Regional Ethics Committee (approval number NTX/05/10/126) and the trial was registered on the Australian and New Zealand Clinical Trials Register (ANZCTR Number ACTRN12612001303831).

The study was centrally coordinated by a research nurse at Fertility Plus, National Women’s Hospital, Auckland, New Zealand. A computer-
generated randomization sequence of random blocks of three different sizes, chosen randomly (with equal probability of getting 6, 8 or 10 in each block) was prepared by a third party (statistician). Allocation numbers were placed in individual, sealed, opaque envelopes that were numbered sequentially. Stratification by ovulation induction protocols or age was not used. Women who were attending public or private fertility clinics and who were recommended to have IUI were invited to participate in the trial either by verbal or postal information. A written patient infor-
mation sheet described the study and was given to the patients. A consent form to take part in the research was signed at the commencement of the cycle and up until the day of insemination. Randomization envelopes were distributed to each of staff responsible for the study in the participating clinics. The randomization envelope was opened by the clinical staff, usually on the day of receiving the consent form at the beginning of the cycle, although it could be as late as the day before insemination. Patients, embryologists, nurses and doctors were aware of the assignment of treat-

ment from the time of assigning. Women were randomized to either one cycle of SIUI or one cycle of FSP. If the patient deferred the cycle, they could participate in the study in the next cycle. If the cycle was cancelled, the patients could not be randomized again or complete another cycle.

The inclusion criteria were women aged 18–42 years old with non-
tubal infertility that was defined as ovulatory according to a raised luteal phase serum progesterone level, with proven potency of fallopian tubes and with a male partner having a normal semen analysis (WHO Laboratory Manual, 4th edition 1999: volume ≥2.0 ml, motility ≥50%, concentra-
tion ≥20 million/ml, morphology ≥14% normal forms until 2010 when the WHO criteria were changed to a concentration of ≥15 million/ml and morphology of ≥4% normal forms). Mild endometri-

osis was not an exclusion criteria. Women with ovulatory dysfunction who were also undergoing IUI were also included. In addition, women who required donor insemination (either because of azoospermia or same-sex couples) and who had an approved donor were also included. Public funding was only available if the women had failed to conceive after six cycles of insemination with donor sperm but women requiring donor sperm could also choose to pay without having any previous treatment cycles. Women were excluded if the female age was ≥42 years old, BMI was ≥40 kg/m² or if there was documented tubal occlusion (bilateral or unilateral). Cycles were cancelled if there were more than three follicles on ultrasound or if the sperm count or motility was low on the day of treatment. The only protocol change was the change in the semen analysis criteria from 2010 when the concentration was lowered to 15 million/ml. The sperm count requiring cancellation was at the discretion of the individual laboratories.

Women underwent ovarian stimulation and monitoring according to the policy of the individual clinics.

A Tomcat or Wallace catheter was used for the IUI procedure. The inseminate was prepared using a density gradient (Puresperm) and spermatozoa were re-suspended in 0.5 ml of medium as used in the recruiting centre. The catheter was passed gently through the cervical canal high up into the uterus and the specimen with a volume of 0.5 ml was slowly injected according to standard unit protocol.

An atrumatic insemination catheter (Cook catheter J-CHSG-503000) was used for the FSP procedure. The inseminate was prepared using a density gradient (Puresperm) and spermatozoa were re-suspended in 4 ml of human tubal fluid or equivalent medium as used in the recruiting
centre. The catheter was attached to a 5 ml syringe, and the dead space was filled with the suspension mixture. The catheter tip was passed gently through the cervical canal into the uterus and the balloon catheter was gently inflated. The specimen was slowly injected over 2 min, the balloon was deflated and the catheter was removed.

Demographic and clinical data were collected. The primary outcome measure was live birth per woman randomized. Secondary outcomes included clinical pregnancy rate (defined as a gestation sac), scores evaluating procedural pain immediately following the procedure, vaginal bleeding and spotting immediately following the procedure, ectopic pregnancy, miscarriage rate and multiple pregnancy rate.

For dichotomous variables, the test of statistical significance was the \( \chi^2 \) test. An intention-to-treat analysis was used for the primary outcome of live birth and the secondary outcome of clinical pregnancy rate and all data have been analysed in the groups that they were randomized to. For continuous variables, a two-tailed \( t \)-test was performed to test for differences and if the data were not normally distributed (as in the case of procedural pain and sperm count), a Mann–Whitney test for non-parametric data was used.

Power calculations were based on a doubling of the live birth rate per couple, from 10% for the SIUI cycle to 20% with FSP. These estimates were based on the results from studies reviewed in the Cochrane meta-analysis (Cantineau et al., 2004). In order to have 80% power to detect a difference between the two treatment groups at the 5% confidence level, using a two sided \( Z \)-test with pooled variance, 199 women were required in each group (http://www.stat.ubc.ca/~rollin/stats/ssize/). Therefore, it was planned to randomize 420 women allowing for losses from cycle cancellation and withdrawals.

**Results**

Between July 2006 and March 2012, 620 were invited to participate in the study and total of 417 women were randomized, 210 to SIUI and 207 to FSP. There were 21 women who did not complete the procedure following randomization. In the SIUI group, eight women had cycles cancelled (five were no given reason, two were overstimulated and one had a poor response), there were three withdrawals and there was one case where all the patient records were lost. In the FSP group, there were four women with cycle cancellation (one for no reason given, one was overstimulated, one had a poor response and one had a poor semen analysis), two women conceived before completing the treatment and there were three withdrawals. In three cases, women who were randomized to FSP received SIUI (because of difficulty completing the procedure) and their data have been analysed in the FSP group. Three hundred and ninety-six women had data suitable for analysis, 198 in the SIUI and 198 in the FSP group.

The participating fertility clinics (numbers recruited are in parenthesis) were Fertility PLUS Auckland, New Zealand (239); Repromed Auckland, New Zealand (9); Repromed, Adelaide, Australia (38); Assisted Conception Australia, Brisbane, Australia (38); IVF Sunshine Coast, Birtinya, Australia (35), Tawam Hospital, Al-Ain, United Arab Emirates (58).

The flow of patients through the study is shown in Figure 1. The demographic and clinical data of participants is presented in Table I. The median duration of infertility was 24 months [interquartile range (IQR) 9–42] for the SIUI group and 24 months (IQR 11–36) for the FSP group (\( P = 0.56 \)). There were 101 women (48%) in the SIUI group and 113 women (54.5%) in the FSP group who had previously had IUI or an IVF cycle. There were 6 women in each group who had partners with semen analyses <15 million/ml but with one exception all had >1 million/ml available for insemination. There were 16 women in the FSP group and 11 women in the IUI group with mild endometriosis.

The treatment cycle characteristics are presented in Table II. Donor sperm were used in 20 women (9.5%) in the SIUI group and in 18 women (8.7%) in the FSP group. The median number of donor cycles was three with an IQR from one to six cycles. Ovarian stimulation was not used in 17 women (8.1%) women in the SIUI group and 22 women (10.6%) in the FSP group. Of the women having ovarian stimulation, 106 women (50.5%) in the SIUI group and 114 women (55.1%) in the FSP group had clomiphene citrate (50–100 mg for 5 days in the early follicular phase) and 71 women (33.8%) in the SIUI group and 56 women (27.1%) in the FSP group had gonadotrophin therapy (from 50 to 300 IU per day). Letrozole (2.5–5 mg for 5 days in the early follicular phase) was used in 11 women in each group. The median number of motile sperm inseminated was \( 15.0 \times 10^6 \) (IQR 5.7–35 \( \times 10^6 \)) in the SIUI group and \( 16.2 \times 10^6 \) (IQR 5.3–32 \( \times 10^6 \), \( P = 0.86 \)) in the FSP group.

The results for study are presented in Table III. The live birth rate was 12.9% (27/210) in the SIUI group and 10.1% (21/207) in the FSP group [OR 1.31, 95% confidence interval (CI) 0.71, 2.39, \( P = 0.48 \)]. The clinical pregnancy rate was 14.3% (30/210) in the SIUI group and 11.6% (24/207) in the FSP group (OR 1.26, 95% CI 0.71, 2.23, \( P = 0.45 \)). There were 2/18 live births (11%) from FSP and 5/20 live births (25%) from IUI amongst the women who had donor sperm. Of the 39 women who had unstimulated cycles, there were 2/18 live births from SIUI and 2/21 live births from FSP.

There were four multiple pregnancies in the SIUI group (three sets of twins and one set of triplets) and two sets of twins in the FSP group. There were two ectopic pregnancies in the SIUI group and one ectopic pregnancy in the FSP group. There were nine miscarriages in the SIUI group and nine miscarriages in the FSP group. There were two cases of ovarian hyperstimulation (OHSS), one in the SIUI group and one in the FSP group; both cases were associated with the use of FSH. There were no cases of post-procedural infection in any of the women in the study.

Only 141 (68%) of the 207 women who had SIUI and only 159 (74%) of the 205 women who had FSP had recorded the outcome of procedural pain. There were 54 women (37%) who had SIUI and 82 women who had FSP (55%) who recorded that the procedure was painful (OR 2.01, 95% CI 1.27–3.19, \( P = 0.003 \)). The median for the visual analogue scale for pain was 2 (IQR 1–4 and a mean of 2.5) for FSP and was 1 (IQR 0–2, \( P = 0.001 \)) for SIUI. Only eight women who had FSP and five women who had SIUI reported spotting out of the 344 (88%) who recorded data for this outcome.

**Discussion**

This randomized controlled trial of women with non-tubal infertility compared standard IUI with or without COH with FSP. There was no evidence of a benefit of FSP over IUI. IUI either by standard technique or by FSP in this population with prolonged infertility with non-tubal aetiology and normal semen analysis results in a live birth rate of between 10 and 12% per cycle per woman. Whilst the absence of benefit of FSP has been shown, we have also reported that there...
was a slight increase in pain associated with the procedure when compared with SIUI, although only \(~\sim\) 70% of women completed data collection for pain outcomes. There was also no evidence of increased ectopic pregnancy rates or episodes of pelvic infection in the women who received FSP.

The study design was pragmatic which allows for effectiveness to be tested in everyday practice and under flexible conditions. Such studies are considered the best way of informing decisions about practice as the patients in the study should represent the patients in most fertility clinics (Zwarenstein et al., 2008). Our study design included women with non-tubal infertility and included both women with unexplained infertility and women who required donor sperm. In addition, the trial recruited women from seven different clinics in three different countries and allowed each clinic to choose their local protocol for ovarian stimulation and sperm preparation. Within each centre however the single intervention of method of IUI was consistently compared with FSP of 4 ml of sperm suspension; these results therefore can be extrapolated to a variety of clinical settings.

The study has a number of limitations. Donor sperm were used in almost 10% of cycles. A small protocol violation occurred with regard to the inclusion criteria with 12 women with partners who had sperm concentrations \(\leq 15\) million/ml, although only one woman in the study had \(< 1\) million/ml inseminated. Clinics were able to choose their preferred ovulation stimulation protocols and of all cycles, the majority (\(~\sim 30\)% were with gonadotrophins and 9% were unstimulated cycles. However, this variation in the stimulation protocols is unlikely to have made a difference to the outcomes as it has been previously reported that there is no evidence of a difference between clomiphene and FSH protocols for IUI (Cantineau and Cohlen, 2007). The day of randomization was variable and included from Day 1 of the cycle to the day before the insemination. Finally, data on the

**Figure 1** Diagram illustrating the flow of patients through the study.
pain of the procedure were incomplete, with 30% not reporting this outcome. The reason for the incomplete data collection was not clear and it occurred in a similar proportion in both groups. However, the data that were collected does show a small increase in pain in FSP cycles compared with SIUI cycles.

The original Cochrane review was published in 2004 (Cantineau et al., 2004) and updated in 2009. The conclusions from 2004 were that ‘FSP may be more effective for non-tubal subfertility, but the significant heterogeneity should be taken into account. As a result no advice based on the meta-analysis could be given for the treatment of non-tubal subfertility (Cantineau et al., 2004). The conclusion of the updated review in 2009 (with two new trials) was that the results indicate no clear benefit for FSP over IUI (Cantineau et al., 2009). There are two RCTs not in the Cochrane review (Noci et al., 2007, El-Khayat et al., 2012). One trial of 102 women did not suggest a benefit (Noci et al., 2007), while the other did suggest a benefit with FSP, although the latter only just reached statistical significance (El-Khayat et al., 2012) and only includes men with < 15 million/ml (El-Khayat et al., 2012). Furthermore, both trials were underpowered (the largest trial included 120 women) and neither reported live birth rates.

In conclusion, this trial compared two different techniques for IUI with ovarian stimulation in women with unexplained infertility and in women who required donor sperm and did not report a difference in live birth outcomes. FSP should be discouraged as it does not increase live birth rates compared with IUI, while it significantly increases pain during the procedure. There is no indication for the use of FSP in fertility clinics and fertility guidelines and protocols should be updated to reflect this.

### Table I Baseline characteristics for women undergoing SIUI and FSP.

<table>
<thead>
<tr>
<th></th>
<th>SIUI (n = 210)</th>
<th>FSP (n = 207)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>33.67 ± 4.87</td>
<td>34.23 ± 4.62</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.43 ± 4.50</td>
<td>24.26 ± 4.09</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>140 (66.6)</td>
<td>140 (67.6)</td>
</tr>
<tr>
<td>Maori/Pacific</td>
<td>0 (0)</td>
<td>3 (1.4)</td>
</tr>
<tr>
<td>Asian/Chinese/Indian/Other Asian</td>
<td>64 (30.5)</td>
<td>57 (27.5)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (2.4)</td>
<td>6 (3.0)</td>
</tr>
<tr>
<td>Not reported</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Median duration of infertility (months)</td>
<td>24 (IQR 9–42)</td>
<td>24 (IQR 11–36)</td>
</tr>
<tr>
<td>Parity ≥1 (%)</td>
<td>38 (18.0)</td>
<td>44 (21.4)</td>
</tr>
<tr>
<td>Previous IUI/IVF cycles (%)</td>
<td>101 (48.0)</td>
<td>113 (54.5)</td>
</tr>
<tr>
<td>Median sperm concentration × 10⁶ (IQR)</td>
<td>68 (38–115)</td>
<td>72 (40–115)</td>
</tr>
<tr>
<td>Mean sperm motility ± SD (%)</td>
<td>62 ± 14.4</td>
<td>66 ± 15.9</td>
</tr>
</tbody>
</table>

### Table II Treatment cycle characteristics for women undergoing SIUI and FSP.

<table>
<thead>
<tr>
<th></th>
<th>SIUI (n = 210)</th>
<th>FSP (n = 207)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor sperm</td>
<td>20 (9.5%)</td>
<td>18 (8.7%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Ovulation induction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clomiphene cycles</td>
<td>106 (50.5%)</td>
<td>114 (55.1%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Letrozole</td>
<td>11 (5.2%)</td>
<td>11 (5.3%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Gonadotrophin cycles</td>
<td>71 (33.8%)</td>
<td>56 (27.1%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Unstimulated cycles</td>
<td>17 (8.1%)</td>
<td>22 (10.6%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Not reported</td>
<td>5 (2.4)</td>
<td>4 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Median number of motile sperm inseminated × 10⁶ (IQR)</td>
<td>15.0 (5.7–35) (n = 199)</td>
<td>16.2 (5.3–32) (n = 191)</td>
<td>0.86</td>
</tr>
<tr>
<td>Maximum median estradiol level</td>
<td>1116 (IQR 828–1700) (n = 165)</td>
<td>1165 (IQR 755–1685) (n = 162)</td>
<td>0.45</td>
</tr>
<tr>
<td>Mean number of follicles &gt;16 mm ± SD</td>
<td>1.14 ± 1.13 (n = 134)</td>
<td>1.15 ± 0.76 (n = 141)</td>
<td>0.95</td>
</tr>
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</table>

### Table III Reproductive outcomes for women undergoing SIUI and FSP.

<table>
<thead>
<tr>
<th></th>
<th>SIUI (n = 210)</th>
<th>FSP (n = 207)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live birth rate per woman</td>
<td>27 (12.9%)</td>
<td>21 (10.1%)</td>
<td>1.31 (0.71, 2.39)</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>30 (14.3%)</td>
<td>24 (11.6%)</td>
<td>1.26 (0.71, 2.23)</td>
</tr>
<tr>
<td>Multiple pregnancy rate</td>
<td>4⁵</td>
<td>2⁶</td>
<td>1.69 (0.28, 10.13)</td>
</tr>
<tr>
<td>Pregnancy loss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ectopic</td>
<td>2 (1.0%)</td>
<td>1 (0.5%)</td>
<td>—</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>9 (4.3%)</td>
<td>9 (4.3%)</td>
<td>0.71 (0.22, 2.30)</td>
</tr>
<tr>
<td>OHSS</td>
<td>1 (0.5%)</td>
<td>1 (0.5%)</td>
<td>—</td>
</tr>
</tbody>
</table>

⁵Three twins and one set of triplets.  
⁶Two twins.
Acknowledgements

Dr Sonya Jessup of Fertility Plus initially conceived the study and prepared the study protocol. Dr Jye Ru assisted with the original ethics application. Dr Virginia Griffiths was the research assistant who recruited women in 2008 and 2009. Dr Bruno Radesic, Dr Emily Liu and Dr Elizabeth Glanville also assisted with recruitment. The authors are grateful to the following fertility clinics and their staff for recruiting patients on behalf of Reproduction and Clinical Trials in Australia and New Zealand (REACT-ANZ): Fertility PLUS, Greenlane Clinical Centre, Auckland, New Zealand; Repromed, Auckland, New Zealand; Repromed, Adelaide, Australia; Assisted Conception Australia, Brisbane, Australia; Australia; IVF Sunshine Coast, Birtinya, Australia, Tawam Hospital, Al-Ain, United Arab Emirates.

Authors’ roles

C.M.F. was involved in the protocol design, ethics application, study recruitment, data analysis and drafting and revising the manuscript. J.B. was involved in the data cleaning and analysis and an earlier draft of the manuscript. N.A. was involved in data cleaning and analysis and editing the manuscript. D.G. was involved in recruitment and data entry. C.B., M.A.B., J.M. and N.P.J. were involved in recruitment and contributed to editing the draft version of the manuscript.

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Conflict of interest

None declared

References