

Fertility RESEARCH REVIEW™

Making Education Easy

Issue 24 – 2020

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Abbreviations used in this issue

AMH = anti-Müllerian hormone
ART = assisted reproductive technology
BMI = body mass index
HPV = human papillomavirus
ICSI = intracytoplasmic sperm injection
IUI = intrauterine insemination
IVF = in vitro fertilisation
OR = odds ratio



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Welcome to the 24th issue of Fertility Research Review.

Restrictions during COVID-19 alert level 4 have meant a delay in fertility treatments for some couples but may have provided opportunity to dedicate time and energy to healthy behaviours to help improve chances of conception. Factors related to the male partner are the focus of several studies included in this issue. Alcohol consumption in male partners, which may have been higher than usual during lockdown, was not found to be associated with a couple's chance of conceiving; an antioxidant formulation for males had no beneficial effect on semen parameters in men with male factor infertility; and ICSI did not improve reproductive outcomes in couples without male factor infertility. We hope you find these and our other selections for this issue interesting and welcome your comments and feedback.

Kind regards,

Dr Mary Birdsall

marybirdsall@researchreview.co.nz

Reduced pregnancy and live birth rates after *in vitro* fertilization in women with previous Caesarean section

Authors: Vissers J, et al.

Summary: A previous caesarean section was found to impair live birth rates after IVF or ICSI compared with previous vaginal delivery in a retrospective cohort study of 1317 women with secondary infertility and one previous delivery. Live birth rates after embryo transfer were 15.9% in 320 women with a previous caesarean section and 23.3% in 941 women with a previous vaginal delivery (OR 0.63; 95% CI 0.45–0.87). Similar differences were observed for rates of ongoing pregnancy, clinical pregnancy and biochemical pregnancy.

Comment: This study shows a reduction in live birth rates in women with a previous caesarean compared to women with a previous vaginal birth. Earlier data suggested a lower chance of a baby following a caesarean, and this study design suggests that at least part of that reduction is probably due to a uterine factor. It would be useful to determine the aetiology of this reduction and whether it is confined to women with a caesarean scar defect or is due to an altered microbiome or some other factor. This study information should be provided to women who are contemplating an elective caesarean for their first child and are wishing to have more children.

Reference: *Hum Reprod.* 2020;35(3):595-604.

[Abstract](#)

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Male alcohol consumption and fecundability

Authors: Høyer S, et al.

Summary: Little evidence of an association between male alcohol consumption and reduced fecundability was found in an analysis of pooled data collected from two ongoing preconception studies of 662 Danish couples and 2017 North American couples who had been trying to conceive for ≤ 6 cycles. 64.5% of couples conceived during 12 cycles of follow-up. After adjusting for the couple's age, female partner's alcohol consumption, intercourse frequency, previous history of fathering a child, race/ethnicity, education, BMI, smoking and consumption of sugar-sweetened beverages and caffeine, the fecundability ratio was 1.02 (95% CI 0.90–1.17) for male alcohol consumption of 1–5 standard servings per week; 1.10 (95% CI 0.96–1.27) for male alcohol consumption of 6–13 standard servings per week and 0.98 (95% CI 0.81–1.18) for male alcohol consumption of ≥ 14 standard servings per week.

Comment: I have included this study for all the men who are feeling a wee bit guilty about their alcohol consumption during lockdown. This study looked at couples trying to conceive for less than 6 months and the men self-reported their alcohol intake at the start of the study. There was little association between alcohol intake and the chances of a baby. I don't think this means that it is OK to binge drink or drink excessively but I suspect this shows that it is probably OK to drink modestly and there is no evidence that abstinence is required for men who are trying to conceive.

Reference: *Hum Reprod.* 2020;35(4):816-825.

[Abstract](#)

ICSI does not improve reproductive outcomes in autologous ovarian response cycles with non-male factor subfertility

Authors: Supramaniam PR, et al.

Summary: ICSI in the absence of male factor subfertility did not improve reproductive outcomes in women with poor ovarian response compared with IVF in a retrospective study of 569,609 fresh cycles recorded on the anonymised Human Fertilisation and Embryology Authority (HFEA) registry after 1998. ICSI was used in 52.2% of cycles and IVF was used in 47.8% of cycles. Poor ovarian response was reported for 62,641 cycles (11%); ICSI methods were used in 46.6% and IVF methods were used in 53.4%. The likelihood of live birth per treatment cycle was no better with ICSI compared with IVF based on poor ovarian response (adjusted OR 1.03; 99.5% CI 0.96–1.11; $p=0.261$) or for all autologous ovarian response categories (adjusted OR 1.00; 99.5% CI 0.98–1.02; $p=0.900$). Mean fertilisation rate in poor ovarian response cycles was 64.7% with IVF and 67.2% with ICSI ($p<0.001$). There was no significant difference between IVF and ICSI for failed fertilisation rate (17.3% vs 17.0%; $p=0.199$). A similar trend was observed for all autologous ovarian response categories.

Comment: Thank you for this study. I hope this finally puts to rest the fallacy that ICSI should be performed to obtain the best possible chances of a baby when the semen assessment is normal. The pressure to perform ICSI comes from a variety of sources, sometimes from patients or their friends and family, sometimes from the lab, sometimes from the clinician and yes also from the owners of the clinic. ICSI was invented as a technique to improve fertilisation where a significant male factor exists and this is where its application should rest.

Reference: *Hum Reprod.* 2020;35(3):583-594.

[Abstract](#)

Following the postponement of FSA 2020 due to the issues surrounding the COVID-19 situation, the FSA Board and Local Organising Committee are pleased to announce that dates in 2021 have now been secured with the International Convention Centre in Sydney.

The conference will now be held as follows.

11 – 15 September 2021

<https://www.fertilitysociety.com.au/home/events/fsa-2015/>



The effect of antioxidants on male factor infertility

Authors: Steiner AZ, et al.

Summary: Antioxidants were not found to improve semen parameters or DNA integrity in a multicentre, randomised, placebo-controlled trial in 174 men with male factor infertility (defined as sperm concentration ≤ 15 million/mL, motility $\leq 4\%$, normal morphology $\leq 4\%$, or DNA fragmentation $> 25\%$). The antioxidant formulation comprised daily doses of vitamin C 500 mg, vitamin E 400 mg, selenium 0.2 mg, L-carnitine 1000 mg, zinc 20 mg, folic acid 1000 μ g, and lycopene 10 mg. Men were randomised to receive this antioxidant formulation (n=85) or placebo (n=86) for 3–6 months, during which time couples attempted to conceive naturally for the first 3 months before female partners were given clomiphene citrate and IUI during months 4–6. All female partners were aged ≤ 40 years, ovulatory and had documented tubal patency. Cumulative live birth rates at 6 months were 15% for couples with the male partner receiving the antioxidant formulation and 24% for couples with the male partner receiving placebo. Antioxidant use in male partners decreased median sperm concentration by 4 million/mL at 3 months compared with an increase in median sperm concentration of 2.4 million/mL at 3 months in men who received placebo. No significant differences between antioxidant use or non-use were evident for sperm morphology, motility or DNA fragmentation. Use of antioxidants had no effect on sperm concentration in 66 men with oligospermia, no effect on sperm motility in 75 men with asthenospermia and no effect on DNA fragmentation rate in 44 men with high DNA fragmentation.

Comment: This well-conducted randomised controlled trial of a combination male antioxidant showed no improvement in any semen parameters nor the chances of a pregnancy or a baby in a group of men with mild-to-moderate male factor infertility. We have all been recommending male antioxidants based on level 1 evidence for men with poor sperm and on the basis that recommending a multivitamin is a low-cost and low-risk intervention. Whilst it might be argued that the combination supplement used in the trial was missing a particular ingredient, such as CoQ10, it might also be that antioxidants are not effective in the treatment of mild-to-moderate male infertility.

Reference: *Fertil Steril.* 2020;113(3):552-560.

[Abstract](#)

Independent commentary by Dr Mary Birdsall, BHB MB

ChB Auckland; FRANZCOG MSc (Oxon)



Dr Birdsall graduated from Auckland Medical School followed by post-graduate training at National Women's Hospital. She was awarded a Nuffield Scholarship and completed a Master's Degree in Human Reproduction at Oxford University. Mary is the Chair of Fertility Associates and works as a full time fertility specialist at Fertility Associates Auckland. She has a special interest in fertility preservation and lifestyle influences on fertility.

For full bio [CLICK HERE](#)

Consistency and objectivity of automated embryo assessments using deep neural networks

Authors: Bormann CL, et al.

Summary: The consistency and objectivity of deep neural networks in assessing embryo morphology was evaluated in a prospective double-blind study using images of embryos recorded at 70 hours post-insemination (n=748) and 113 hours post-insemination (n=742). The coefficient of variation across 8 embryologists was 82.84% for grading embryo morphologies at 70 hours post-insemination and 44.98% across 7 embryologists grading embryo morphologies at 113 hours post-insemination. Consistency among 10 embryologists in the evaluation of 56 embryos for biopsy and cryopreservation was 52.14% and 57.68%, respectively, compared with 83.92% for the neural network. Cronbach's α analysis showed the deep neural network introduced improved reliability of embryo selection and disposition.

Comment: Artificial intelligence would seem to hold great promise in the subjective world of IVF and in particular embryo grading. We are waiting for a non-invasive technique which will enable the best embryo to be selected and hope that artificial intelligence may be the answer. This study shows that artificial intelligence is more consistent at selecting high-grade embryos but what I want to know is: do you get more babies? This study doesn't give us that information.

Reference: *Fertil Steril.* 2020;113(4):781-787.

[Abstract](#)

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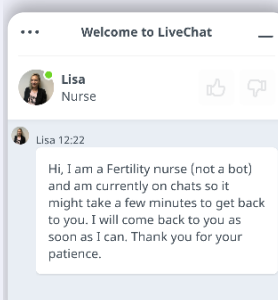


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Effect of endometrial thickness on ectopic pregnancy in frozen embryo transfer cycles

Authors: Liu H, et al.

Summary: The influence of endometrial thickness on the incidence of ectopic pregnancy in frozen embryo transfer cycles was investigated in a retrospective study of 16,556 patients and a total of 17,244 pregnancy cycles. Pregnancy locations comprised intrauterine (n=16,701), ectopic (n=498) and heterotopic (n=45). Thinner endometrial thickness was a significant risk factor for ectopic pregnancy. Endometrial thickness was inversely proportional to rates of ectopic pregnancy with odds ratios ranging from 2.70 (95% CI 1.65–4.40) for women with endometrial thickness <8 mm to 1.66 (95% CI 1.07–2.58) for women with endometrial thickness of 10–11.9 mm compared with women with endometrial thickness ≥14 mm. The risk of ectopic pregnancy was also increased in women who received hormone replacement treatment for endometrial preparation during frozen embryo transfer.

Comment: This study suggests that frozen embryo transfer cycles resulting in ectopic pregnancies are associated with thinner endometrial thicknesses and also occurred more commonly in hormone replacement cycles. This is interesting and further work is needed to see where this fits into clinical practice.

Reference: *Fertil Steril.* 2020;113(1):131-139.

[Abstract](#)

Comparison of pregnancy outcomes following intrauterine insemination in young women with decreased versus normal ovarian reserve

Authors: Tiegs AW, et al.

Summary: Conception rates and cumulative pregnancy outcomes per cycle following IUI were no different for 370 women aged <35 years with diminished ovarian reserve (AMH <1.0 ng/mL) compared with 2649 age-matched controls (AMH ≥1.0 ng/mL). The sample size in the retrospective study had >80% power to detect a 7% difference between groups in the primary outcome of a positive serum hCG pregnancy test (>2 mIU/mL) obtained 2 weeks after the IUI procedure. Women aged <35 years with diminished ovarian reserve conceived as often as age-matched controls after IUI, irrespective of the treatment strategy.

Comment: We have good data in our IVF programme that women with a very lowered ovarian reserve (less than 5 pmol/L) have a reduced chance of a baby compared to age-matched controls with an AMH greater than 5. This is a useful study as it gives information about IUI and suggests that IUI is not any less effective in women with a reduced ovarian reserve. The next obvious question to ask is which is better: IUI or IVF in women with a reduced ovarian reserve but no other fertility pathologies? [Fuji et al. 2018](#) looked at all the trials of women with unexplained infertility doing IVF and found that women who had 4 or fewer follicles continuing on with IVF had a better chance of a baby compared to converting to IUI, except when there was only 1 follicle there was no difference. I cannot find a randomised controlled trial looking at women with very lowered ovarian reserve, patent tubes and normal sperm and then randomising to IUI or IVF. That would be interesting.

Reference: *Fertil Steril.* 2020;113(4):788-796.

[Abstract](#)

Reporting assisted reproductive technology success rates on Australian and New Zealand fertility clinic websites

Authors: Goodman LK, et al.

Summary: Compliance with guidelines for reporting clinic success rates was assessed for fertility clinics offering IVF treatment in Australia or New Zealand. The guidelines were adapted from code of practice recommendations by the Reproductive Technology Accreditation Committee (RTAC) for reporting success rates in the public domain. Success rates were reported on 20/30 fertility clinic websites and were broadly compliant with the guidelines (median compliance score 8/8). However, the authors commented that the guidelines do not provide a clear definition of success and they observed 32 different combinations of reporting variables on clinic websites. Live births were reported in 17 websites and clinical pregnancy rates were reported as the only outcome measure in 5 websites. There was variability in use of denominators for reporting success rates, e.g. 'per embryo transfer' (37/41 reported figures) and 'per egg collection' (2/41 reported figures). No websites reported success rates for 'per cycle started'.

Comment: Fertility clinics need to report meaningful data on their websites and they should be mandated to do so by their accrediting bodies. They must ask the question: what does the consumer wish to know? Every consumer wants to know the same thing: 'what are my chances of taking home a baby if I start an IVF cycle with a particular clinic?'. This data would seem on the surface to be easy to collect, however for the information to be accurate, this should include the outcome data from all the frozen embryos from that cycle. This is where data collection becomes more challenging as many people do not return to use their embryos in a timely way. This means the reported data may be 2 to 3 years old before it is published.

Reference: *Aust N Z J Obstet Gynaecol.* 2020;60(1):135-140.

[Abstract](#)

The association between reproductive health smartphone applications and fertility knowledge of Australian women

Authors: Ford EA, et al.

Summary: The usefulness of smartphone applications as a medium for sharing information on reproductive health was investigated in an online survey of adult women living in Australia. Mobile phone applications relating to female reproductive health were used by 43% of 673 women who completed the survey, with menstrual tracking functions being the most commonly used (82%). Knowledge about general fertility and factors such as age, menstrual cycle, smoking, obesity, miscarriage rates and success of ART was assessed in 6 questions. On average, 3 of these questions were answered correctly and users of reproductive health applications were more likely to correctly answer the question related to fertility during the menstrual cycle (p<0.001).

Comment: Most women coming for a fertility consult today are using a fertility app. When I ask when was your last period, the almost universal response is: 'Let me check my phone, it has an app.' Women are using these apps to track their cycles and to guide them on the best days to have sex in order to conceive. These apps are not being used for education of fertility-related issues such as smoking, obesity and age. It would seem a wasted opportunity for education around fertility.

Reference: *BMC Womens Health.* 2020;20(1):45.

[Abstract](#)

No association between HPV vaccination and infertility in U.S. females 18–33 years old

Authors: Schmuhl NB, et al.

Summary: No evidence of increased infertility was found among 1114 women aged 18–33 years who had received the HPV vaccine. The association between infertility and HPV vaccination was assessed by logistic regression analyses of data from the National Health and Nutrition Examination Survey for 2013–2016. Overall, 8.1% of women reported having ever experienced a 12-month period of infertility. No association between HPV vaccination and self-reported infertility was found; this applied to primary infertility in women who had never been pregnant and for latent and/or non-permanent post-vaccine infertility.

Comment: This is included for everyone's knowledge. There is no association between the HPV vaccine and infertility and that message needs to be heard loudly and clearly throughout our community. HPV cancers of the cervix, vagina, vulva, throat, anus and penis cause a hefty health burden and can be largely prevented with vaccination.

Reference: *Vaccine.* 2020;38(24):4038-4043.

[Abstract](#)



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