

ESHRE 2022



Review of the European Society of Human Reproduction and Embryology (ESHRE) 38th Annual Meeting 2022

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THE 38th Annual Meeting of the European Society of Human Reproduction and Embryology (ESHRE) took place in Milan, Italy, and online between 3rd and 6th July 2022. During the opening ceremony, Giovanni Coticchio, Immediate Past Chairman of the Special Interest Group (SIG) Committee, highlighted the important role Italy has played in ESHRE history, having contributed three society chairs as well as hosting three previous annual meetings.

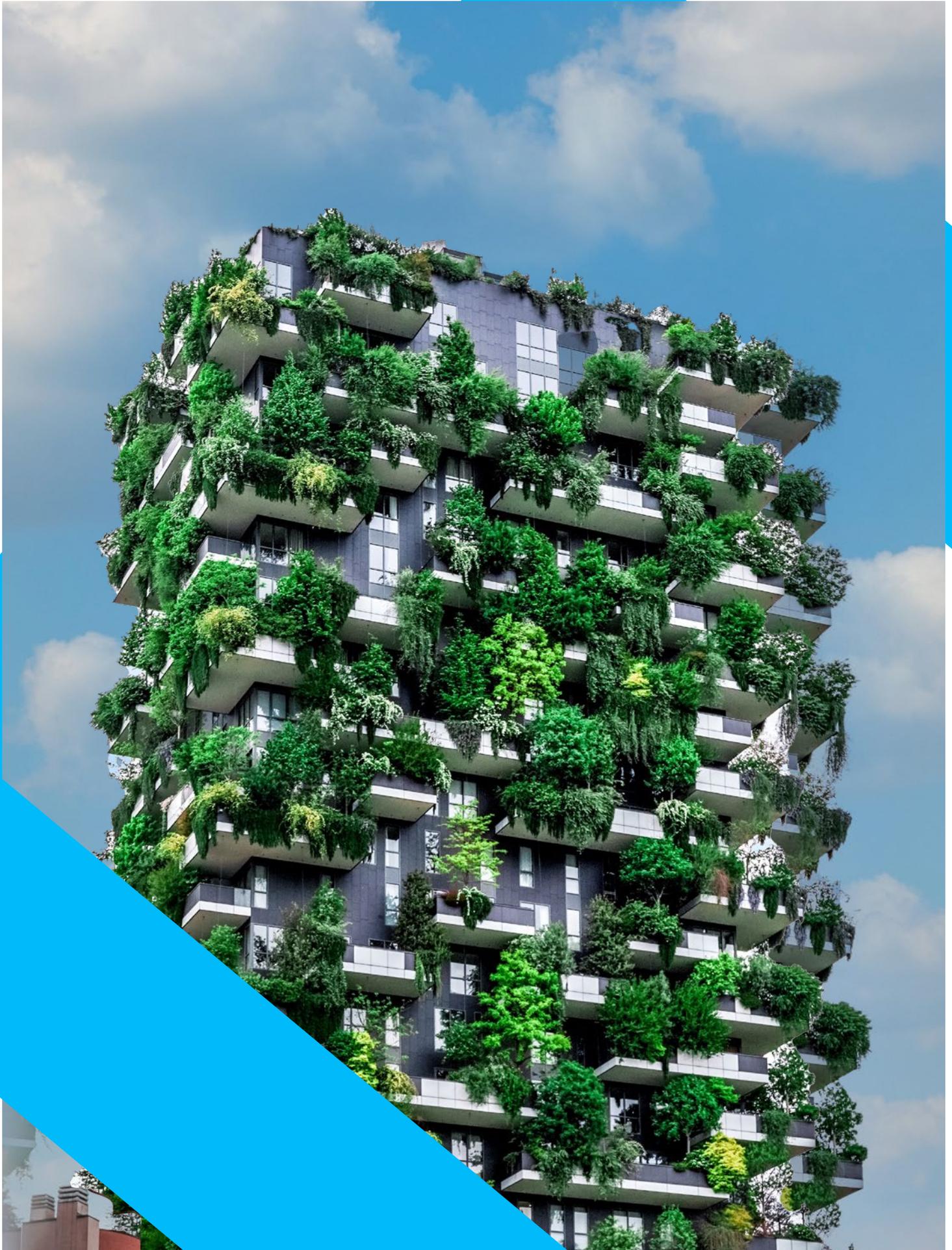
As of 3rd July, there were 10,006 registered participants (82% in-person and 18% virtual) from 130 countries across the globe. Furthermore, 1,623 abstracts were submitted. Similar to previous years, embryology, andrology, reproductive endocrinology, and implantation and early pregnancy were the most popular abstract topics.

During his welcome address, ESHRE Chair Carlos Calhaz-Jorge highlighted the “rich and diversified” scientific programme. Indeed, symposia spanned across the discipline, with updates on the management of endometriosis, co- and pre-treatment for ovarian stimulation, novel aspects of recurrent pregnancy loss, fertility preservation in females with cancer, COVID-19 and implantation, new markers of male health and function, and the current

state of time-lapse technology. Of note was the session debating reproductive rights in this millennium, which saw two leading experts discuss the positive outcomes of the Sustainable Development Goals of the United Nations (UN) as well as challenges that are still experienced in reproductive health today. This forms the basis of our compelling in-house feature and is not to be missed.

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Alongside the impressive programme were the annual prizes for standout presentations. The Clinical Science Award for oral presentation was awarded to Christian Becker, Nuffield Department of Women's and Reproductive Health, University of Oxford, UK, for his report on relugolix combination therapy in females with endometriosis-associated pain. The Clinical Science Award for poster presentation was presented to Juan



"Read on for our key scientific insights from ESHRE's 38th Annual Meeting."

Giles, Reproductive Medicine, IVIRMA Valencia, Spain, for his presentation on medroxyprogesterone acetate as an alternative to gonadotropin-releasing hormone antagonists in oocyte vitrification for non-oncological fertility preservation and pre-implantation genetic test cycles. The work of Sara Somers, Department of Reproductive Medicine, Ghent University Hospital, Belgium, was celebrated when her presentation, discussing uniform communication by nurses and midwives in anticipation of *in vitro* fertilisation treatment, received the Nurses Award for best oral presentation by a nurse.

An overview of groundbreaking ESHRE press releases can also be found within this issue of *EMJ Reproductive Health*, including whether probiotics improve poor vaginal health, the association between anorexia and adverse pregnancy outcomes, and the effectiveness of frozen sperm for insemination treatments.

Calhaz-Jorge also spoke about some of the crucial activities carried out by ESHRE, such as the provision of education through the annual meeting, e-Learning platform, campus workshops, and webinars. ESHRE is

also responsible for setting standards, including the recent evidence-based guidelines for endometriosis, medically-assisted reproduction in patients with a viral infection or disease, and female fertility preservation. There are also a range of good practice guidelines, which cover pre-implantation genetic testing, information provision for those involved in reproductive donation, and more. ESHRE is also collaborating with the patient organisation Fertility Europe to create a roadmap for fertility awareness and advocacy across Europe.

"The strength of our society is the membership," concluded Calhaz-Jorge. ESHRE now has 9,379 members from 135 different countries. In contrast, there were less than 8,000 members in 2019. "We crossed the pandemic gaining more than 1,000 new members," said Calhaz-Jorge. Clearly, conferences such as ESHRE are crucial for the generation and exchange of scientific knowledge. With this in mind, we look forward to being part of the international human reproductive health and embryology community again at next year's congress in Copenhagen, Denmark. Until then, read on for our key scientific insights from ESHRE's 38th Annual Meeting. ●



Can Probiotics Improve Unhealthy Vaginal Flora?

THE TYPE of bacteria that naturally colonise the reproductive tract are known to influence pregnancy chances in *in vitro* fertilisation. Specifically, in females with a vaginal microbiota dominated by *lactobacillus*, pregnancy and live birth rates are known to be higher. Conversely, among those with a lower *lactobacillus* concentration, the chance of an embryo implanting in the uterus is reduced. For this reason, there is increasing interest in the role of probiotics as a treatment for females with an imbalance in the vaginal microbiota.

A study presented at ESHRE's 38th Annual Meeting explored whether a probiotic containing strains of *lactobacilli* could improve unhealthy vaginal flora when administered vaginally in a daily capsule to patients for 10 days before fertility treatment.

The trial was conducted between April 2019 and February 2021 at a university fertility clinic. In total, 74 females referred for *in vitro* fertilisation were enrolled. All participants had a *lactobacillus* profile that ranged from low to medium quality. The females were randomly assigned to receive the capsules (n=38) or a placebo (n=36). Samples were taken to determine the effect on the vaginal microbiome at two time points: following the 10-day course of probiotics and in the subsequent menstrual cycle (between cycle days 21 and 25).

Overall, the vaginal microbiome was found to improve by 40% in the placebo group and 29% in females taking the *lactobacillus* probiotic. However, this did not represent a significant difference.

Primary investigator Ida Engberg Jepsen from The Fertility Clinic at Zealand University Hospital, Denmark, summarised the research findings: "The study indicates that

administering vaginal *lactobacilli* products may not improve a suboptimal vaginal microbiome."

It is important to note that only two strains of *lactobacilli* were contained in the probiotic. Further, the authors indicated that the broad categorisation of the vaginal microbiome profile may not have captured the subtler changes that can affect fertility. Consequently, probiotics in general should not be discounted.

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Also of relevance, 34% of all females who participated in the trial, regardless of whether they received the probiotic or placebo, exhibited an improvement in the vaginal microbiome between 1 month and 3 months later. Based on this, Jepsen highlighted an alternative therapeutic approach: "The strategy would involve postponing fertility treatment until spontaneous improvement occurs, but further research is needed." ●



Anonymity at Risk in Egg and Sperm Donations

COMMERCIAL DNA testing is being used by individuals involved in donor conception to find information about genetic relatives. According to interim results from ConnecteDNA, a qualitative study presented at ESHRE's 38th annual meeting, individuals who are donor-conceived are using DNA testing to discover genetic family and their origins, including potential health risks.

A 2015 survey conducted by ESHRE found that 12 European countries had laws requiring anonymous egg and sperm donations; however, some countries had introduced non-anonymous schemes. For example, information on donors and individuals who were donor-conceived has been held in a register by the Human Fertilisation and Embryology Authority (HFEA) in the UK since 2005. Therefore, individuals conceived from donors can request identifying information about their donors when they turn 18 in 2023.

ConnecteDNA will continue into 2024, but the researchers have already performed interviews with 20 adults conceived through donors, 15 parents of children who are donor-conceived, and 14 donors. So far, the results indicate that commercial DNA testing is not just used for identifying a donor but also 'ethnicity estimates'. Meanwhile, some donors use these services to make themselves contactable to those

conceived by their donation(s) and parents of children who are donor-conceived use it to trace genetic relatives.

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However, commercial genetic testing and tracking family history from saliva samples matched against a DNA database means that there is no real anonymity for donors whose gametes have been used in donor conception, as they could have a close genetic relative who has used the service, making the donor traceable. Furthermore, there is a chance that a child who does not know that they were conceived through a donor could accidentally learn of their origins, which could be distressing. Therefore, adequate support and counselling if unexpectedly exposed.

ConnecteDNA researchers will also examine legal regulations governing access and storage of donor information across the UK; the Netherlands; Victoria, Australia; and Sweden, with the aim to make regulatory recommendations. ●





Anorexia Nervosa Linked to Unfavourable Outcomes in Pregnancy

FEMALES diagnosed with anorexia nervosa are 500% more likely, on average, to give birth to underweight babies. Researchers found that the incidence of newborns born to mothers with anorexia who were born small for their gestational age was far higher when compared to babies born to females of a healthy weight.

A study, presented at ESHRE's 38th Annual Meeting, has discovered that there is a substantially increased risk of premature birth (298%), and more than double the chance of the mother experiencing placental abruption compared with mothers without anorexia.

The study was based on data collated from over 9 million females, both with and without anorexia. Records were taken from a large public-accessible database of hospital inpatient care documents across the USA. The study included all deliveries in the decade between 2004 and 2014, with a cohort of 214 females who had anorexia during their pregnancies, and more than 9 million females who did not.

Whilst eating disorders often have an impact on menstruation, females who have anorexia are able to conceive naturally, or with the assistance of fertility drugs to restore ovulation. Although marked differences in birth weights were recorded in this study, researchers did not find variance in other conditions that affect females who are pregnant, including gestational

diabetes, post-partum haemorrhage, placenta previa, or hypertensive diseases. The necessity of performing a Caesarean section was also no greater in either cohort.

Researchers stressed that the risks associated with pregnancy in females diagnosed with anorexia need to be more widely understood by fertility specialists. Lead study author Ido Feferkorn, McGill University, Montreal, Canada, commented that the study's results carried a serious health message about the management of females with anorexia both during and following pregnancy. He remarked: "Clinics should be aware of the magnitude of adverse outcomes related to pregnancy among those patients with anorexia who do conceive."

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Feferkorn advocated that, based on the wider implication of the study's findings, females should be screened for anorexia before beginning fertility treatment. Current evidence suggests that the majority of healthcare professionals working in the field of reproductive health do not screen their patients for eating disorders. ●

Timed Intercourse Assisted by Urine-Monitoring May Increase Changes of Pregnancy

DATA presented at ESHRE's 38th Annual Meeting has suggested that females may be able to increase their chances of conceiving by timing intercourse to 'fertile windows' by using urine-testing monitors. In recent years, timed intercourse has become more widely practised due to the surge in the availability of health apps focusing on ovulation detection.

The researchers emphasised that definitive conclusions could not be made about the efficacy of fertility tracking through other home-based methods such as fertility awareness-based methods (FABM), which are used in most menstrual tracking apps. FABM use calendar predictions and identify physiological changes to cervical mucus or body temperature with wearable detection devices to detect when ovulation is most likely.

The study focused on timed intercourse decided by urine monitors and urine ovulation tests as well as FABM. Data from six studies which included 2,374 females. The aim was to measure the impact this has on live birth rates, pregnancy rates, time of pregnancy, and overall quality of life. However, researchers were also interested in the negative impacts of timed intercourse, stress, lack of spontaneity, and pressure on sexual performance.

The authors found that the chance of pregnancy using timed intercourse, judged by urine-testing was between 20–28%. Whereas individuals who were practising spontaneous intercourse had comparably lower chance of pregnancy at 18%.

'This update suggests a benefit of timed intercourse using urinary ovulation detection. However, more evidence is needed on the adverse effects of

timed intercourse and its effectiveness in different groups, such as those with unexplained infertility, before clinicians are able to promote this practice,' stated first investigator, Tatjana Gibbons, Nuffield Department of Women's and Reproductive Health, University of Oxford, UK.

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In contrast, the study found no conclusive benefit of timed intercourse using FABM in live birth rate and pregnancy rates. However, the authors conceded that data was only available from two studies involving 160 females and, therefore, evidence was low grade.●



Reducing the Risk of Ovarian Hyperstimulation Syndrome: Are Short Gonadotrophin Releasing Hormone Antagonists the Key?

META-ANALYSIS data from 171 randomised trials investigating the safety and efficacy of 56 different *in vitro* fertilisation (IVF) stimulation protocols, including almost 37,000 individuals, was presented by Pedro Melo, Tommy's National Centre for Miscarriage Research, University of Birmingham, UK, at the 38th Annual ESHRE Congress, 4th July 2022, Milan, Italy. The data reveals that use of short gonadotrophin releasing hormone (GnRH) antagonists reduces the risk of ovarian hyperstimulation syndrome (OHSS) and does not significantly affect live birth rate.

OHSS is a serious complication associated with use of exogenous gonadotrophins in IVF and occurs most frequently in patients who display a normal or high response to ovarian stimulation following gonadotrophin administration.

Previously, multiple gonadotrophin and GnRH agonist protocols have been trialled in order to improve outcomes and reduce risk. Traditionally pituitary downregulation has been achieved using GnRH agonists. This takes several weeks and is, therefore, referred to as 'long protocol'. However, it has recently been noted that using a GnRH antagonist leads to much faster pituitary downregulation. As such, these GnRH antagonists are referred to as 'short protocol'.

Data from this meta-analysis show that use of short GnRH antagonist protocols in patients with normal or high ovarian stimulation responses does not affect live birth rates and leads to a reduction in OHSS by up to 52%. The mechanism is not fully understood, but Melo stated that "it seems likely that this results

from a combination of factors, including the absence of an ovarian 'flare' effect with GnRH antagonists". However, the meta-analysis findings do not include cumulative live birth rates, which are considered "the most effective measure of IVF success."

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Whilst severe OHSS is rare, affecting 1% of patients, mild OHSS is more common, affecting up to 33%. Symptoms occur secondary to ovarian enlargement and include abdominal distension and pain, and in rarer circumstances leads to serious cardiovascular, respiratory, and renal complications. Therefore, identifying methods to reduce OHSS risk is important. These findings are promising, and use of short GnRH antagonist protocols could lead to reduced patient harm. Further evaluation of their effect on cumulative live birth rates will provide more insight into their efficacy and impact of IVF success rates. ●



Frozen and Fresh Sperm Equally Are as Effective at Insemination

IN THE largest study of its kind, researchers have found that cryopreserved sperm is not associated with any inferior outcomes compared with fresh sperm in patients undergoing intrauterine insemination. The results, presented at ESHRE's 38th Annual Meeting, identified no difference in pregnancy rates between cycles using cryopreserved and fresh sperm.

In most jurisdictions, cryopreservation is the favoured method of sperm sample preservation. However, although its use is now widespread and is a requirement for some donor samples, patients still harbour concerns that the process of cryopreservation may reduce the viability of sperm with the freezing and thawing process impacting mobility, structure, and DNA content.

The study analysed 5,335 intrauterine insemination cycles performed at Massachusetts General Hospital, Harvard Medical School, Boston, USA, between 2004 and 2021, analysing a range of outcomes with either fresh or preserved sperm, including positive pregnancy test, clinical pregnancy, and miscarriage. The study was further controlled for the type of ovarian stimulation administered and whether it was administered or not.

The results of the study demonstrated that similar clinical pregnancy rates were found with both fresh and frozen sperm samples. The investigators noted some small differences in the sub-group analysis of patient having pre-treatment ovarian stimulation with oral medications; however, the differences were limited to the first cycle treatment and beyond this were negligible. The only notable, lasting difference was that time-to-pregnancy was slightly longer in the frozen sperm group than the fresh group.

“The fact that our data did not reveal any significant difference in success between the utilisation of fresh ejaculated and frozen sperm, except in a sub-group of patients given oral ovulation-inducing agents, is very reassuring to all involved,” stated Panagiotis Cherouveim from Massachusetts General Hospital.

Cherouveim highlighted the importance of this research and the reassurance it should provide to single females and same-sex couples where cryopreserved sperm may represent the only opportunity for conception. ●

