

# UNDERSTANDING FERTILITY

**03** DARING TO UTTER THE 'F' WORD

**06** SHOULD THE BOSS GET INVOLVED?

**14** CAN TECHNOLOGY GET YOU PREGNANT?



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Our clinics have been helping people start families for over 35 years. When all you want is to have a baby, you need to know that you're in safe hands: it's no wonder we're the largest provider of fertility treatment in the UK.

*"The care we received during the treatment was exceptional"*

Lucy, GCRM

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Visit [thefertilitypartnership.com](http://thefertilitypartnership.com) to find your nearest clinic and open event



The Fertility Partnership

Giving Life a Helping Hand

CARE

EXPERTISE

PASSION

TRUST

INNOVATION



\*(HFEA data published March 2016) \*\*(HFEA data published March 2018). Names have been changed to protect patient anonymity.

# UNDERSTANDING FERTILITY

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## PROGRESS

# Daring to utter the 'f' word

Advances in fertility treatments must be matched with greater understanding of the personal impact of dealing with infertility

### MAGDA IBRAHIM

**F**ertility: the "f" word so taboo that six out of ten women are more reluctant to talk about it than sexually transmitted diseases or mental health.

Yet 3.5 million people in the UK are affected by infertility at the same time as groundbreaking research is delivering leaps in scientific innovation.

In the 40 years since IVF was introduced, advances including gene editing, growth in reproductive medicine, egg freezing, donation and surrogacy have created a brave new fertility landscape.

But it's not hard to see why many facing fertility challenges stay silent. Societal pressure, lack of employment support, and feelings of confusion and despair can be overwhelming.

Stigma around fertility can stem from its personal nature, says Professor Tim Child at the University of Oxford's Nuffield Department of Obstetrics and Gynaecology.

"It involves sex and reproduction, and most people assume at some point they will have children," says Professor Child, who is the medical director at Oxford Fertility. "When that doesn't happen, some are embarrassed, or feel a sense of failure or shame."

Fertility Network UK chief executive Aileen Feeney adds: "There's a huge stigma. It is so unfair that people think they can't speak about it."

Look at the statistics though and it's clear the secret's out, at least within the fertility community. More than 1.1 million IVF treatment cycles have taken place in UK licensed clinics since 1991, while at least 20,000 babies are born here each year as a result of fertility treatment, around 3 per cent of all births.

Worldwide it is estimated 6.5 million people are alive today because of IVF technology.

The Human Fertilisation and Embryology Authority (HFEA), the independent regulator for the sector, believes sharing its data – like the fact that male infertility accounts for 37 per cent of IVF cycles carried out – can challenge stereotypes and shine a much-needed light on relatively new processes such as egg freezing.

Joanne Triggs, HFEA's head of engagement, says knowledge is a powerful tool. "Our aim



is to empower patients to make informed decisions and improve their chances of having a longed-for family," she says.

While high-level data engenders transparency, it's the grass roots that are critical in changing attitudes.

Despite running a successful podcast that has been downloaded 150,000 times in 50 countries since launching in 2014, *The Fertility Podcast* producer Natalie Silverman spent the first year hosting the show anonymously.

"Eventually I felt like a hypocrite discussing taboos around fertility, while not willing to share my own name," she reveals. "Now creating a constant digital dialogue is empowering people and challenging misunderstanding."

Education in schools has a role, with the British Fertility Society leading a task force to bring issues including future fertility on to the national curriculum.

Meanwhile, political cogs are turning and an inaugural All Party Parliamentary Group on Women's Health, including fertility, launched last month supported by health minister Jackie Doyle-Price.

"Fertility is a fundamental aspect of our society," says Professor Child. "More people talking about it has to be positive."

But an honest fertility narrative is a tough ask when faced with miraculous celebrity pregnancy tales. Researchers from New York University who analysed magazines covering 240 celebrities with an average age of 35 found they contributed to misunderstanding of reproductive ageing.

Only two mentions were made of celebrities over 40 using assisted reproductive technology with their own eggs, with no mentions of donated eggs.

TV presenter Julia Bradbury has been candid about her five IVF

rounds to have twin girls at 44 and explains. "The more we talk about fertility, IVF and what it means to have children for both sexes, the better," she says. "It's important to discuss fertility and decision-making that concerns creating a family freely and frankly in as many forums as possible, including the media, but also at home and in schools."

With official figures showing an increasing average age of mothers – it's 30.4 years in the UK – openness around fertility decline is evermore significant.

And while birth rates from IVF treatment have increased by around 85 per cent in the last 25 years, there are no guarantees, as a third of fertility treatment cycles result in a birth for women under 35, dipping to less than 15 per cent for those over 44.

"We are living longer, healthier lives, so people can be astounded by natural and IVF fertility rates," says Professor Child. "Many people think being healthy and going to the gym must help, but it doesn't help the genetic quality of eggs and sperm."

The complexities of the fertility question can make it tricky to grasp, especially for those who have never experienced the struggle. But a new exhibition launching at the Science Museum in London on July 5 will put fertility under the spotlight for around 370,000 visitors.

The five-month showcase will not only celebrate 40 years since the birth of the first IVF baby, Louise Brown, at Oldham General Hospital, following pioneering treatment from Patrick Steptoe, Sir Robert Edwards and Jean Purdy, but also explore the ongoing negotiation between science and society around the once-fringe technology.

Connie Orbach, content developer for the Science Museum exhibition, explains: "It is important this exhibition is a catalyst for conversations around fertility."

As the scientific world celebrates four decades of IVF contribution to reproductive health, Louise Brown emphasises the real-life impact of the sector. "I think my mum, Lesley, would be amazed at how many different techniques there are now to help both men and women with their fertility," she says. "Almost 40 years after my birth, doctors and scientists are still doing fantastic work. They should never forget at the heart of this are ordinary people who just want to have a family." ♦

**1/6**

couples have difficulty conceiving

**43%**

of women with fertility problems did not seek help when trying to become pregnant

**47%**

of men with fertility problems did not seek help

London School of Hygiene & Tropical Medicine 2016



**We want to empower women to take control of their fertility, whether that's to prevent or plan for a pregnancy**

trials the concept with fellow CERN colleagues, in Geneva, and discovered that many of her female colleagues were looking for an effective alternative to hormonal contraception.

"As the only certified contraceptive app, we are providing women with an additional option to choose from that is effective, non-hormonal and non-invasive," she says. "Our typical users, and those who we believe are most suitable for Natural Cycles, are 30 years old on average, in a stable relationship and for whatever reason find that hormonal options are not suitable for them. Most of our users were previously using less effective methods of contraception such as withdrawal or condoms."

The app is used in two thirds of cases to prevent pregnancy and in one third to plan a family.

"At Natural Cycles, we are pioneering a new era in which women are more aware and in control of their bodies than ever before. We want to empower women to take control of their fertility, whether that's to prevent or plan for a pregnancy," says Dr Berglund.

After helping discover the Higgs-Boson particle, Dr Berglund has continued on a route that is using science to make important advances in society. "We believe Natural Cycles offers exciting possibilities for the future in terms of providing healthcare professionals with valuable information that could help inform diagnoses, and on a macro-level, to better understand fertility as a whole," she says.

**For more information please visit [naturalcycles.com](http://naturalcycles.com)**

 **Natural Cycles**

# A contraceptive app that can map fertility

Technology is transforming every aspect of modern life for women – and health is no exception

**M**ore and more tech-savvy women are now turning to apps to monitor and track various aspects of their health and wellbeing, including fertility.

Natural Cycles is the only app to be certified for use as a contraceptive in Europe and now has more than 700,000 users worldwide. The app is powered by a sophisticated algorithm, which enables women to tune into their unique monthly cycles to map and predict ovulation, and is backed by a wealth of scientific data.

Users take their temperature with a basal thermometer each morning and

the data builds into an individualised fertility indicator that identifies green days, when it is safe to have unprotected sex, or red days, when condoms should be used. After approximately three months, users can expect to see roughly 60 per cent green days in one cycle.

"The algorithm behind Natural Cycles was created to help women understand their own unique cycles. It takes into account sperm survival, variation in cycle length, ovulation day, temperature fluctuations, and the length of the follicular and luteal phase," says particle physicist

Dr Elina Berglund, a former member of the CERN team that discovered the Higgs-Boson particle, who invented the app.

"Unlike other fertility awareness methods, Natural Cycles eliminates human error because the app does all of the calculations and interpretations for you."

Natural Cycles has received European Union certification as a Class IIb medical device, in the same classification as dialysis equipment, intensive-care monitoring and alarm devices, anaesthesia

machines and blood pumps for heart-lung machines.

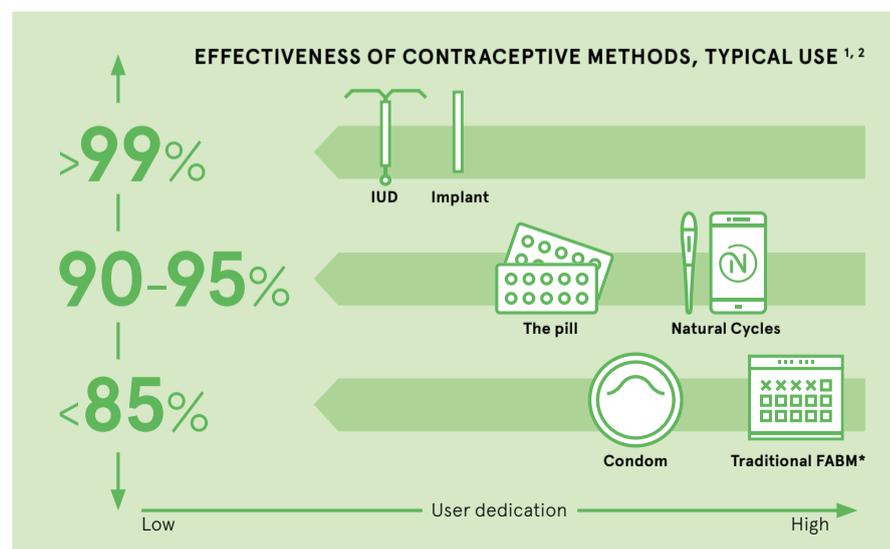
"Receiving EU certification indicates how Natural Cycles is leading the charge in digital health," adds Dr Berglund, who co-developed the app with husband Dr Raoul Scherwitzl, a fellow physicist. The couple researched how levels of progesterone, a hormone that plays an important role in the menstrual cycle, are increased after ovulation causing women's body temperature to rise by up 0.45C compared with the rest of their cycle. This provides the foundation of the Natural Cycles accurate fertility calibration.

In a study of 22,785 women aged 18-45, through 224,563 menstrual cycles across two years – the largest trial of a natural contraceptive to date and published in the peer-reviewed journal, *Contraception* – the "typical use" effectiveness rate of Natural Cycles was 93 percent, which is comparable with the pill.

Dr Berglund, 33, who is based in Stockholm, got the idea when she wanted to give her body a break from hormones before starting a family. She



**Dr Elina Berglund**  
Chief technology officer  
and co-founder, Natural Cycles



## Case study

Sofie, a search engine optimisation consultant, started using the Natural Cycles app a year ago and says: "It has helped me learn so much about my body."

The 27 year old says: "When a friend told me about Natural Cycles, I was excited as the idea of natural contraception really appealed to me.

"Because I'm in a relationship, it was important for me that my partner felt

that this was a good idea too. After discussing it together, we decided to give it a go.

"It only took one menstrual cycle for the app to detect my ovulation, I got to know my body and just how regular my cycle is, and with it came the understanding of my moods and emotions throughout my cycle. It has now been a year-and-a-half since I started using Natural Cycles and it feels amazing."

# Stigma about male infertility remains

Fertility is a medical frontier where the gender gap is disturbingly wide and male infertility an under-researched part of the conception equation

DANNY BUCKLAND

**T**he biology of how a sperm swims to and fertilises an egg remains, largely, uncharted scientific waters, and lags behind understanding of female fertility.

The alarming statistic is that although a healthy, successful sperm is 50 per cent of a successful fertilisation, there is only one licensed fertility clinic dedicated to men, while the legions of others focus almost solely on women.

Research into male factors is minimal, allowing myths to proliferate and an undercurrent of placing responsibility on the female side.

"The lack of research is crucial. Men have not featured as heavily in research in reproduction and socially we construct reproduction much more as a female issue," says Dr Esmée Hanna, a researcher at the Centre for Health Promotion in the School of Health

and Community Studies at Leeds Beckett University.

"I am really surprised by how little research we have about men's infertility and their voices are lacking from the discussions. We don't ask about how they feel if they can't have children or about their desire to have children.

"There is a stigma about male infertility. Our social constructs of masculinity and being a man are about someone who is sexually active and virile, and we can conflate fertility with virility."

This barren zone of knowledge is pushing couples towards expensive and emotionally draining IVF cycles or intracytoplasmic sperm injections, which involves the direct injection of sperm into eggs obtained by IVF.

Allan Pacey, professor of andrology at Sheffield University, is among many academics and experts who confirm that levels of scientific evidence on sperm cell function fall way behind other branches of medicine.

Dr Sheryl Homa, who runs Andrology Solutions, a male fertility clinic licensed by the Human Fertilisation and Embryology Authority, believes couples are directed too readily towards IVF based on a rudimentary sperm analysis without full consideration of health issues that might be impinging on male fertility.

"It is a gold-standard test, but it is not the only test," says Dr Homa, a clinical embryologist and honorary senior lecturer in biosciences at the University of Kent. "It is a poor indicator of fertility and World Health Organization guidelines recommend that you cannot investigate male reproductive health based on just that test.

"You need a full reproductive health test looking at fertility history, general health – because systemic illness could be a cause of poor semen quality – medical and urological history, underlying infections, and issues such as varicoceles – enlarged veins in the



Hanny Naibaho/Unsplash

**“Our social constructs of masculinity and being a man are about someone who is sexually active and virile, and we can conflate fertility with virility**

IVF; you would investigate to make sure she doesn't have other confounding issues such as fibroids in the uterus that impair embryo implantation which if removed may result in natural pregnancy.

"So why would you send a man off without a testicular scan that might reveal the underlying cause of his sperm quality and infertility? Detection of a varicocele, for example, may explain poor semen parameters and indicate damaged sperm DNA, and there is evidence to show that varicocele repair can improve sperm DNA quality and increase both natural and assisted conception pregnancy rates."

Dr Homa also believes that more research is needed to gauge the impact of exposure to chemicals and medications, such as antidepressants, on male fertility, while educating young men on their role in conception needs to be improved.

"It is absolutely key that men look after their reproductive health if they are considering trying for a family," she concludes. "Men need to understand that the whole point of the sperm is to deliver healthy genetic material into the egg and any anomalies passed on will have consequences in every single cell of that embryo – they are 50 per cent responsible for the health of that embryo." ♦

scrotum – which can all contribute to poor fertility for men. A physical exam is also advised."

Results from detailed health checks give clinicians better options to address and manage male infertility, she adds.

"Treatment management should be assessed on these results rather than saying 'off to IVF' on the basis of the semen test," says Dr Homa. "I believe there are a lot of people having IVF who don't need it or who are handicapped because the man has an underlying infection, a varicocele that is damaging the sperm DNA or oxidative stress interfering with the functionality of the sperm including fertilisation.

"If you had a female patient who has problems with her hormones, you wouldn't simply send her straight to

## Three myths about male infertility

Allan Pacey, professor of andrology at Sheffield University and editor of the British Fertility Society's journal *Human Fertility*, puts the record straight

### Planning it like a military operation

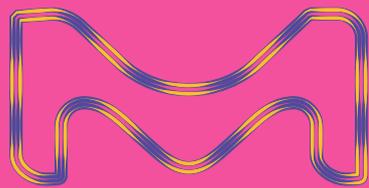
This can lead to stress for some men which in turn leads to poor sexual performance and can change the ejaculatory response. There might be something in theories that sperm quality is better at certain times, but this is insufficient to provide a marginal gain.

### Cycling is damaging

Cycling to work is not something you should worry about and moderate exercise is good for you. I would not suggest giving it up unless you were a triathlete because there is evidence that men at the edge physiologically have poorer sperm because they have pushed themselves to the max.

### Save it up

This is a bad thing to do as the stored sperm gets older, dies and releases free radicals which damage younger sperm. The point is to have a healthy sex life and, if a man is ejaculating two to four times a week in sex, this means the sperm production process is in tip-top condition.



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## CORPORATE FERTILITY

# Should the boss get involved?

Two thought leaders debate the pros and cons of corporate intervention in women's fertility through a "freeze your eggs" benefit scheme



**For**

**Aliya Vigor-Robertson**  
Co-founder of JourneyHR

### HAZEL DAVIS

If good mental or physical well-being are at risk, then a forward-looking business will take responsibility for assisting in any way it can to make sure staff are well cared for.

So if it has an impact on the employee, then it makes sense that fertility may well be the business of human resources.

Women are feeling more empowered than ever to achieve both motherhood and career fulfilment. Both are possible and, for some women, corporate fertility can help on this personal mission.

It's about responding to staff needs. The emphasis here is on benefits; they're an option that staff can utilise if they want and not something the employer forces on them. They are employee benefits not employer benefits and should be treated as such.

This may be helping to conceive a child where there are problems in doing so. Or, perhaps, it is about helping a woman to plan when she wants to have children, whether that's now or later in life.

Just as with shared parental leave or childcare support, not every member of staff will want to use fertility services, but if it could significantly improve the quality

of life for staff, then leaders and HR have a place to provide it.

If handled effectively, benefits that respond to the challenges around fertility can help improve staff wellbeing and create a supporting culture. But again, as with parental benefits such as shared leave, it takes time for these things to be adopted or seen as the industry norm and it all goes back to remembering who these benefits are for.

If the focus remains on the individual members of staff, then corporate fertility has the potential to support individuals wanting to start a family. The second this becomes a method to delay pregnancies or avoid parental leave, the business has taken a wrong turn.

To avoid slipping into this "employer benefit" trap, HR needs to stay aware of how this is being communicated and ensure no one is pressuring employees to take up the option for the wrong reason. But equally, information about the benefit should be easily accessible and openly discussed to keep any taboo at bay.

Ultimately, if you keep it employee led at all times, lives could be transformed. As with any benefit, the right package has to reflect the drives and motivations of employees, and establish the right balance between work and personal life.

My heart sank when I first heard about fertility benefits because it just seemed to me like another fix created to keep business as usual.

From the moment women entered the workforce, they've been forced to fit into a box – let's call it the business-world box – and as we all know, that box was created by men for men.

Women have been continuously trying to fit into that limiting box, bowing down to all sorts of demands to be accepted. Women are told they need to be competitive, to "lean in" and demand their space. At the same time, women should be cautious, making sure not to expose too much cleavage and heaven forbid women dress in a way that's too sexy.

In 2018, isn't it time to say goodbye to old boxes limiting 50 per cent of human beings?

This new "freeze your eggs" as a benefit scheme is, for me, a feeble and misguided attempt to fix a problem and a way to avoid looking at the whole picture. It might be done with good intentions, especially from a business perspective, but in my opinion, by encouraging women to plan for families by freezing fertilised eggs, businesses are not being authentic. They are not giving both parents the space to have a role in raising their family and also have a



career, and that is a step backwards.

If we want to live in a society where families prosper, we've got to move away from the unconscious behaviour of placing women into the outdated "mothers" box and fathers into another historically limiting box. It's time we started talking about the roles and responsibilities of both parents, and acknowledging that every child has the right to be raised by both parents.

It is vitally important for us all to raise our awareness about the historic gender-bias boxes and be brave enough to look at our responsibility for becoming the change we want to see in our world. There is a massive opportunity for

businesses to stand out in the marketplace by acknowledging this.

Organisations that are brave enough to do things differently can walk away from the gender-box bias and behaviour, and be seen as a sustainable and inclusive brand, creating a culture where both parents and their children thrive. This makes for a really magnetic brand, irresistibly attractive for both the right talent and clients. ♦

### Runa Magnus

Founder of The Change Makers and leader of the #NoMoreBoxes movement

# Against



Science Photo Library/Getty Images

Commercial feature



## Celebrating 350 years of dedicated service

With a long history of achievement, **Merck** is striving to help provide the best outcomes for couples hoping to have a family

**M**erck is celebrating its 350th anniversary this year. Founded in 1668, the world's oldest pharmaceutical and chemicals business has evolved into a science and technology company in healthcare, life sciences and performance materials. Around 50,000 employees work to further develop technologies that help create, improve and enhance life, from biopharmaceutical therapies to cutting-edge systems for scientific research and production.

Since the 1950s, Merck has provided healthcare professionals and patients with innovative fertility treatment options, devices and advanced fertility laboratory technologies.

Assisted reproduction technologies (ART) have made tremendous progress since the birth of the first IVF baby Louise Brown 40 years ago, and now provide options that were previously unavailable to women and couples experiencing fertility problems. Nevertheless, infertility remains not only an area of high clinical need, but is also a psychosocial issue, which needs to be addressed through a patient-centric approach. Merck is committed to addressing

these needs through investment in innovation, research and patient support.

Business unit director Phil Krzyzek says: "At Merck we are very proud of our long heritage in fertility treatment, primarily focusing on drug development to support the patient across key stages of fertility treatment. While the success rate of IVF has improved significantly over time, there are still phases of both the clinical and emotional journey that could be further improved.

"As a science and technology company, we are now applying our broader capabilities to provide fertility solutions beyond drug treatment to help drive success rates even further. We are investing in technologies, which are utilised within the IVF laboratory, as well as developing services to support clinics and patients throughout the whole IVF journey."

Merck's innovations are driven by a focus on areas that make the most relevant difference to patients, aiming to improve the treatment experience and success rates. In addition, Merck is actively exploring the use of novel services that may help make the treatment journey psychologically easier for the patient, and help improve communication channels between the patient and the fertility clinic.

This foundation and commitment to pioneering ideas makes Merck an expert in the field of fertility, offering a broad portfolio of fertility options at every stage of the reproductive cycle. By establishing Fertility Technologies and partnering with other experts, Merck has grown from

a drugs company into a holistic fertility provider, to help women and couples fulfil their dreams of parenthood.

Working with both the NHS and private sector, Merck Fertility strives to leverage the science behind the company's heritage, supporting clinics in their patient management decisions. The company recognises the importance of continuing to support the improvement of success rates in ART by investing in research and education in innovative technologies as research and development plays a critical role in increasing treatment success rates.

Merck has a strong commitment to training and medical education, which is designed to support fertility specialists, specialist nurses and laboratory technicians with their continuing medical education. Educational events are held at various locations throughout the UK and Republic of Ireland, and are well supported by healthcare professionals.

Mr Krzyzek concludes: "The innovation process requires that we leverage capabilities right across our own organisation, but also work in partnership with others. We believe that by working in partnership with other organisations, which share our strong commitment to innovation, quality and excellence, we can achieve the best outcomes for those hoping to have a family."

## 40 years

of progress in assisted reproduction technologies (ART) since the birth of the first IVF baby Louise Brown

For more information please visit [merckgroup.com](http://merckgroup.com)

**MERCK**

# Growing pains of Japan's fertility drive

Low fertility rates and an ageing population are an unwelcome combination threatening Japan's economic future

OLIVER GRIFFIN

All is not well in the Land of the Rising Sun. Japan, a country whose gross government debt as a proportion of GDP rose to 253 per cent in 2017, faces the dual challenge of an ageing populace and dwindling births.

If left unsolved, these twin issues will squeeze Japan's shrinking workforce with the burden of paying for the old and young. Combined with a low fertility rate of around 1.4, which represents the number of children that an average Japanese woman will have in her lifetime – a sustainable rate is 2.1 – Japan's rising costs will have to be paid by an ever-smaller proportion of workers.

"There is a terrible labour shortage in Japan," says Dr Randall S. Jones, head of the Japan and Korea desk at the Organisation for Economic



Jason Ortego/Unsplash

Co-operation and Development (OECD). "Companies are starting to cut back their services, restaurants close early, delivery services won't cover parts of the country."

According to Dr Jones, if fertility rates do not improve, Japan can expect its population to fall from around 128 million at present to 98 million by 2050. As that happens, the proportion of elderly people aged over 65 will increase from about 26 per cent now to 45 per cent at the mid-point of the century.

As a result of the country's rapidly ageing population, April saw credit rating agency Moody's warn of near-term and long-term credit challenges, as well as slower GDP growth, caused by lower household savings, a narrower tax base and rising welfare costs.

"We're talking about losing 30 million people – the situation now is

very dramatic," Dr Jones says. "We're not going to be able to stabilise the population for quite some time. It's a very stark picture."

Aware that time is of the essence, prime minister Shinzo Abe has focused considerable effort on persuading Japanese families to up their game when it comes to baby-making. While Japan has seen its fertility rate grow since a low of 1.3 in 2005, Mr Abe is going to have to hope he can persuade his citizens to get on board if the country is going to meet his fertility rate target of 1.8.

To facilitate this, Japan's government has tried a number of different initiatives. Examples include the Plus One Proposal, which has tried to encourage Japanese families to grow by "plus one", as well as the Angel Plan and the New Angel Plan, which were used to make having children easier and more attractive. Incentives

## Low fertility rates, coupled with ageing populations, are testing nations across the Far East

included boosting the number of childcare places available throughout the country, with free childcare for infants aged three to five years old.

Japan has also doled out cash payments for new mothers. However, this can't be extended to paying women to take care of their own children, as Japan still needs to address its impending labour shortage.

"Giving people money to have babies, like an allowance, makes women less

likely to work," says Dr Jones. "If they get money for having babies they don't have to work, and the government wants them to work and have babies."

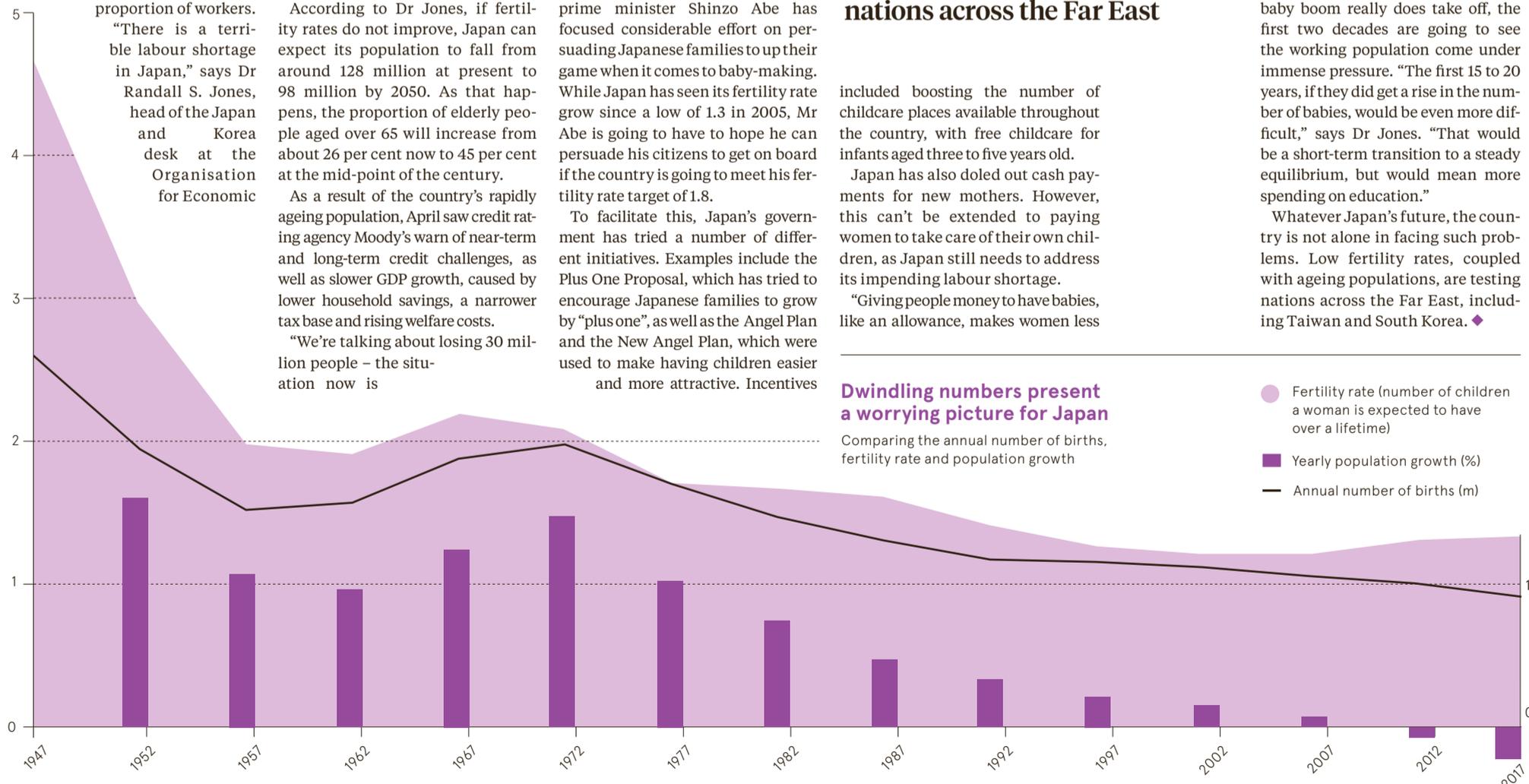
Another thing that needs to be tackled to kickstart a baby boom is Japan's culture of workaholicism, which is so severe that *karoshi* – literally death by overwork – is now an infamous phenomenon. Dr Jones says the government is currently considering legislation that would cap the total amount of overtime a worker could do at 100 hours a month, limited to 720 hours a year. By reducing the number of hours that people can work, Japan is trying to improve work-life balance and free people up to spend more time with their families.

So far, initiatives to boost Japan's fertility rate have had limited success, at least according to a case study published by the Centre for Public Impact. The organisation says that while Japan's fertility rate has increased, it continues to lag behind the OECD average of 1.7.

What's more, despite even limited success in growing fertility rates, the Centre for Public Impact also found that the number of women of child-bearing age leaving the labour force has increased; the exact opposite of what the Japanese government is hoping to achieve. With day-care waiting lists in the 20,000s, it is unlikely that returning to work for many young mothers will be an option any time soon.

One more side effect is that if the baby boom really does take off, the first two decades are going to see the working population come under immense pressure. "The first 15 to 20 years, if they did get a rise in the number of babies, would be even more difficult," says Dr Jones. "That would be a short-term transition to a steady equilibrium, but would mean more spending on education."

Whatever Japan's future, the country is not alone in facing such problems. Low fertility rates, coupled with ageing populations, are testing nations across the Far East, including Taiwan and South Korea. ♦



### Dwindling numbers present a worrying picture for Japan

Comparing the annual number of births, fertility rate and population growth

- Fertility rate (number of children a woman is expected to have over a lifetime)
- Yearly population growth (%)
- Annual number of births (m)

# Rebirth of a company for women's wellbeing

In an information-rich society, with women keen to make informed decisions about their general and reproductive health, an innovative healthcare company is garnering attention with its commitment to exclusively support women's health and wellbeing

UK-based Theramex is poised to work alongside women of all ages and their healthcare providers (HCPs) to offer products and solutions to meet contraceptive, fertility, menopausal and bone health needs.

Headquartered in London and operating across 50 countries, the revamped specialty pharmaceutical company dates back to the 1970s and has a reputable history among women and healthcare professionals with a portfolio of well-established brands. Its employees have decades of experience in the healthcare arena, with an in-depth knowledge of the clinical issues women face. Further, the company fuels its commitment to providing solutions for these challenges by working with specialists who are prevailing thought leaders in the field.

Anish Mehta, chief executive of Theramex, wants people to know that supporting women's health is the backbone of the "new" company.

"I have an ageing mother, a wife and a young daughter, all with individual

health concerns. Making sure those needs are addressed effectively, for them and for all women, is important to me, personally and professionally," he says. "At Theramex, we recognise there are unmet needs in women's healthcare and a discernable gap in innovation. Our team is committed to partnering with women, with healthcare providers and with development companies to present affordable and accessible treatment options."

As part of the commitment that Mr Mehta talks about, Theramex launched the CHLOE and LIFE initiatives to broaden the channels of communication between women and their healthcare providers. CHLOE (Contraception: Helping for Women's Choice) is a questionnaire designed to capture a woman's healthcare conditions, individual needs and preferences to facilitate choosing the best contraceptive option for them. The summary of responses is passed on to the healthcare provider, enabling the choice of contraception that best suits the patient's needs while optimising the HCP's time.

Mr Mehta is eager to point out that the company is as dedicated to providing accessible contraception to women wishing to prevent or delay pregnancy as it is to supporting women struggling to conceive.

He stresses: "We're here to support women at every age, every stage. Whether they are seeking contraception, fertility treatments, managing osteoporosis or the symptoms of menopause, we are working on solutions that empower women to live happier and healthier lives."

To this end, a recombinant follicle-stimulating hormone, the most commonly used biologic drug during in vitro fertilization (IVF), was launched across Europe in 2016.



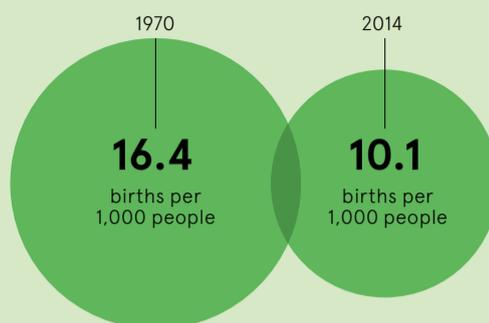
**Anish Mehta**  
Chief Executive Officer, Theramex

As world fertility rates drop, Theramex is committed to improving awareness of the impact infertility has on women and to providing access to solutions to manage the condition.

The LIFE (Listening in: IVF and Fertility in Europe) survey was launched by Theramex to assess the European perception of IVF and fertility preservation using oocyte freezing. The technique is currently aimed at women who delay family planning due to lifestyle choices as well as to women with cancer or other medical conditions, which may affect their fertility. A total of 6,110 people across six European Union countries took part in the survey, which indicated general acceptance of IVF and cryopreservation among Europeans. The findings

**Our team is committed to partnering with women, with healthcare providers and with development companies to present affordable and accessible treatment options**

## Changing demographic trends across the European Union<sup>1</sup>



**10%**<sup>3</sup>

of couples are experiencing infertility

**29**<sup>1</sup>

years is the average age of first time mothers

**80%**<sup>4</sup>

of respondents support egg-freezing when a woman becomes infertile due to medical reasons

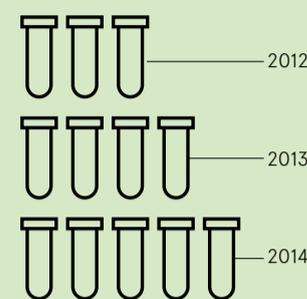
**60%**<sup>4</sup>

of respondents support eggfreezing for lifestyle reasons

**70%**<sup>4</sup>

of respondents under the age of 35 support egg-freezing

## Growth in egg-freezing rates<sup>2</sup>

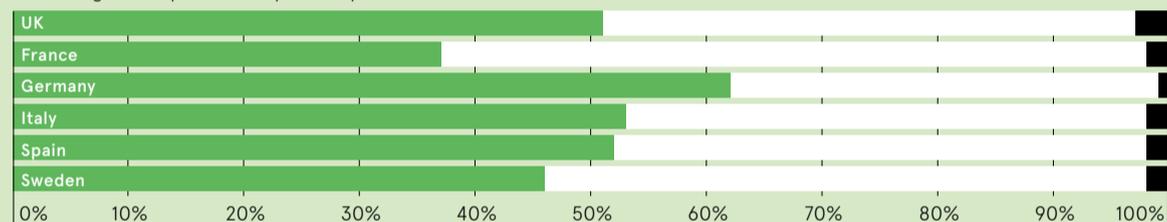


**25-30%**  
increase year on year in egg-freezing in the UK

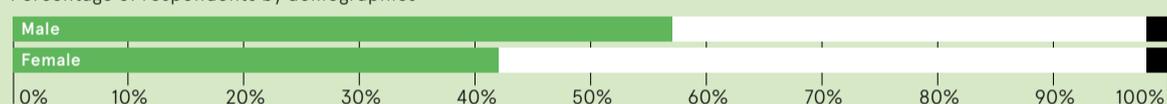
## Who should bear the cost of egg-freezing prior to undergoing cancer treatment?<sup>4</sup>

■ Individual/couple ■ Government ■ Other

### Percentage of respondents by country



### Percentage of respondents by demographics



<sup>1</sup> Eurostat. Fertility statistics. [http://ec.europa.eu/eurostat/statistics-explained/index.php/Fertility\\_statistics#Main\\_statistical\\_findings](http://ec.europa.eu/eurostat/statistics-explained/index.php/Fertility_statistics#Main_statistical_findings)

<sup>2</sup> Fertility treatment 2014. Trends and figures. Human Fertilisation and Embryology Authority. <http://ifqtesting.blob.core.windows.net/umbraco-website/1783/fertility-treatment-2014-trends-and-figures.pdf>

<sup>3</sup> Berg Brigham K, Cadier B, Chevreul K. The diversity of regulation and public financing of IVF in Europe and its impact on utilization. Hum Reprod. 2013 (2): 666-675

<sup>4</sup> LIFE Survey conducted in 6110 individuals from 6 European countries

could drive discussions among legislators and payers for the funding of these procedures.

Results from the LIFE survey are currently being analysed for further insights by a group of experts in the field of fertility treatment, in addition to sociology experts, and will be published in a peer-reviewed journal before the end of 2018.

Bart Fauser, emeritus professor of reproductive medicine at the University of Utrecht in the Netherlands, says: "These findings provide fascinating and compelling evidence of the shifting public attitudes around fertility procedures used for both medical and lifestyle reasons. I see many women, who face issues with fertility, not only because of existing medical conditions, but increasingly when personal circumstance precludes them from having a baby at the present time. Individuals and couples should feel confident about exploring egg-freezing and IVF treatment as possible solutions to their current fertility challenges."

Theramex hopes that the survey's findings will encourage more women and healthcare professionals to consider the importance of having a conversation about fertility preservation. This dialogue may be especially

beneficial to women whose fertility may be compromised as a result of cancer treatment or a family history of early menopause.

Dr Stuart Lavery, senior consultant at Hammersmith and Queen Charlotte's Hospitals, says: "No matter what their situation is, if cancer might affect their fertility, it is important to ensure they know there are steps they may be able to take to have children after treatment. Cancer could have a big impact on a patient's life, but if they are provided with the right information and given the right support, that impact can be managed."

As women live longer and take greater control of their health, the need for accessible and affordable products to manage their needs grows. Theramex is listening to what women want and will continue to deliver practical, dependable and affordable solutions for all women.

**For more information please visit [theramex.com](http://theramex.com)**



# FERTILITY FIRSTS

Assisted reproduction technologies have come a long way since the 1950s, with advances in research resulting in IVF births now accounting for more than 2 per cent of total births in the UK. This timeline charts some of the major milestones that have changed fertility treatment worldwide over the past 70 years

## 1953

**Birth using frozen sperm**

American professor Jerome Sherman pioneers the method of preserving sperm using glycerol as a protectant and dry ice as a refrigerant. The sperm, once thawed, is able to fertilise an egg as "normal" through artificial insemination

## 1970s

**Cryobanks founded**

The commercial cryopreservation (sperm banks) becomes possible through public acceptance

## 1983

**Birth from donated eggs**

Monash Group, an IVF centre in Richmond, Australia, achieves the first pregnancy by a woman without ovaries through the use of donor eggs



## 1978

**IVF baby born**

In vitro fertilisation (IVF), where an egg is fertilised outside the body, results in the birth of the first "test tube baby", Louise Jordan, at Oldham General, Manchester. The doctors involved were Patrick Steptoe and Jean Purdy. They were also trying at the time to help Louise's sister Natalie become pregnant. Dr Steptoe later won the Nobel prize in medicine



## 1984

**Birth from cryopreserved embryo**

Monash Group achieves the first birth from a frozen embryo, which had been preserved for two months before transfer into the uterus



## 1992

**Birth using intracytoplasmic sperm injection (ICSI)**

ICSI takes place in vitro, where a single sperm is injected into the cytoplasm of an egg with a fine needle. The process becomes the most common and successful treatment for male infertility, offering an opportunity where conventional methods are not an option



## 1990

**Genetic profile**

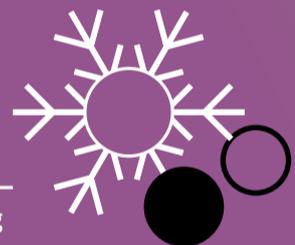
Preimplantation genetic diagnosis is introduced to determine the profiles of embryos before implantation, enabling doctors to screen for a specific genetic disease. Preimplantation genetic screening is later developed to screen for abnormal numbers of chromosomes in the embryo, the leading cause of miscarriage and implantation failure



## 1986

**Birth from cryopreserved egg**

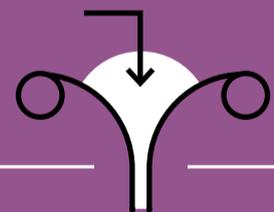
Human egg cryopreservation is developed to enable women to postpone their maternity beyond their most fertile years. Dr Christopher Chen, from Singapore, the scientist responsible for the breakthrough, said 80 per cent of eggs survived the freezing process and 85 per cent of those fertilised as normal; the survival rate is said to be almost double that of frozen embryos



## 2014

**Birth using uterine transplant**

A 35-year-old woman born without a uterus undergoes IVF with her partner before having a uterus implanted from a 61-year-old donor. The cryopreserved embryos are then transferred a year later, resulting in pregnancy. The results of the treatment prove the feasibility of uterus donation, even from a post-menopausal donor



## 20

**Drug-fr**

A revolutionary development in fertility treatment, safer and more effective than conventional medication, is used before the birth of the ovary, in vitro, to ensure maturity of the egg from the time of fertilisation. Little to no time is spent on the

### IVF treatment cycles, by age of patient in 2016

Latest UK statistics

**3%**

Over 44

**4%**

43-44

**14%**

40-42

**14%**

38-39

**42%**

Under 35

**23%**

35-37

**6.5m**

last published estimate of global births as a result of assisted reproduction technologies

European Society of Human Reproduction and Embryology 2016

Human Fertilisation and Embryology Authority (HFEA) 2018

### Reasons for IVF treatment

Percentage of recorded reasons only

Male infertility

**37%**

Unexplained

**32%**

Ovulatory disorder

**13%**

Tubal disease

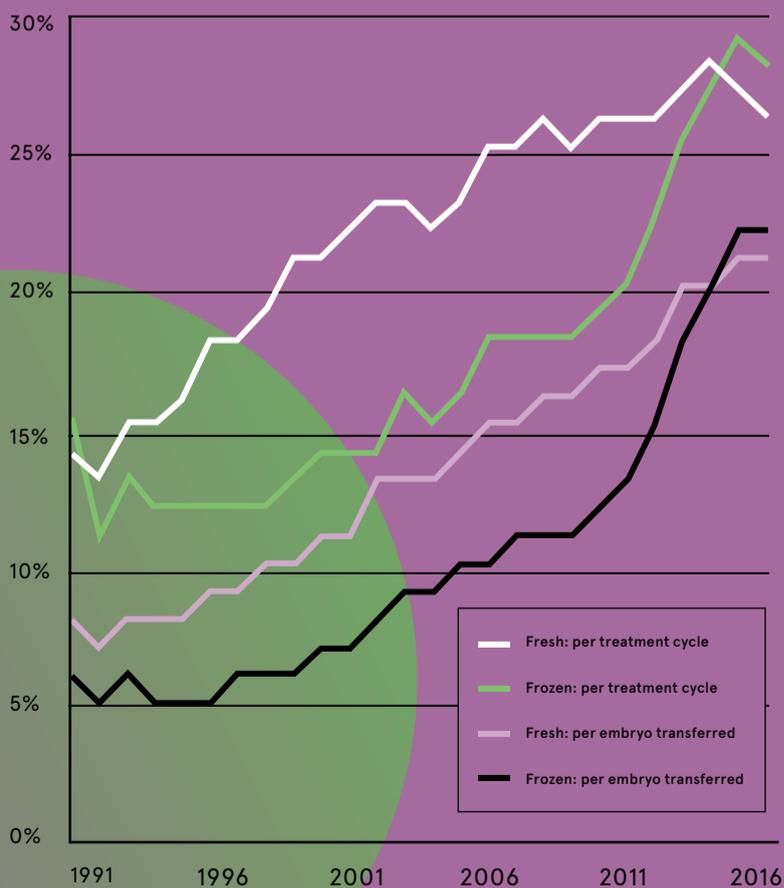
**12%**

Endometriosis

**6%**

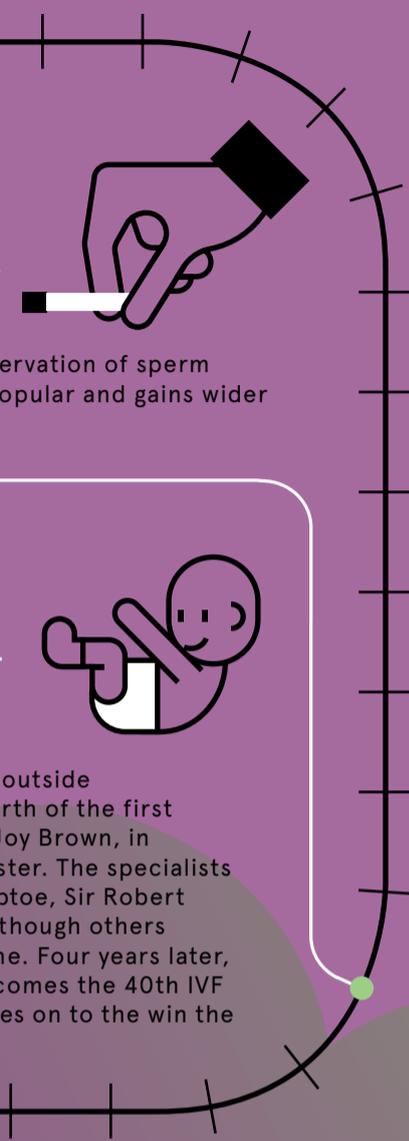
### Birth rates for IVF treatment 1991-2016

Latest UK statistics



HFEA 2018

HFEA 2018



**2018**

### Free IVM technique

onary treatment is d that could provide a cheaper alternative to onal IVF. While IVF uses on to bring eggs to maturity ey are removed from the vitro maturation (IVM) retrieves e eggs and brings them to in a ovarian cell culture taken patient, before ICSI is used for on. The new method involves o hormone stimulation of ovaries - contrary to IVF - and could be beneficial to women with polycystic ovarian syndrome or those recovering from cancer



# UK couples go abroad for IVF help

Access to NHS fertility services can be a postcode lottery, resulting in couples travelling abroad for treatment

KATE BRIAN

The UK may have been the birthplace of in vitro fertilisation (IVF), but cuts to NHS fertility services have led some people to consider travelling across the globe for fertility treatment.

The National Institute for Health and Care Excellence recommends three cycles of IVF for those who are eligible, but whether you get anything approaching this depends entirely on where you live.

A survey carried out by Fertility Network UK and Fertility Clinics Abroad found that patchy NHS provision and the high cost of private IVF were the main drivers for people travelling overseas. Spain, Greece, Cyprus and Eastern Europe are all popular, along with destinations further afield such as the Caribbean.

IVF treatment overseas may look much cheaper, but headline prices on clinic websites are only part of the picture. The cost of drugs, scans, blood tests and specialist medical insurance are

rarely included and can quickly mount up. There is also travel and accommodation to factor into the budget, as well as living expenses abroad.

It is not just cost, but also success rates which can tempt people to travel overseas and half the respondents to the Fertility Network UK and Fertility Clinics Abroad survey believed overseas clinics were more successful.

It is worth noting that the high success rates quoted on clinic websites are often pregnancies rather than live births which are not comparable. Also clinics can be selective about their figures by excluding older patients or selecting a short period when success rates were unusually high.

In the UK, the Human Fertilisation and Embryology Authority, which regulates fertility clinics, gives verified success rates for every licensed clinic, but there is not the same verification process overseas. If you see a figure which appears to be completely out of line with anything you have come across elsewhere, caution is advisable.

One of the reasons people started travelling overseas for fertility treatment was to access donor eggs and sperm. In the past, there were long waiting times for donor eggs and overseas clinics could offer a quick route to treatment. Now many UK clinics have donor eggs available and most can access donor sperm, although this may be imported.

The way donors are recruited, screened and counselled is also something worth checking. In the UK, people conceived using donor eggs and sperm can find out about

their donor once they are 18, but some countries only allow anonymous donations, so nothing will be known about the donor.

Nina Barnsley, director of the Donor Conception Network, says it is important not to forget the impact this may have. "We need to keep in mind that if treatment is successful, this new child will have their own thoughts and feelings. Keeping doors open for them in terms of access to information about the donor and/or half-siblings might be really important in the future."

It has been recognised, in the UK, that multiple births are the biggest risk from IVF to both babies and their mothers, and it is best practice for women to have a single embryo transferred where appropriate. Some overseas clinics do not take the same approach and regularly put back multiple embryos in women most likely to get pregnant with more than one baby.

**There is a well-regulated system in the UK where clinics have to meet certain standards and are regularly inspected, but this is not replicated elsewhere**

Jane Denton, director of the Multiple Births Foundation, says this is a real concern. "Miscarriage, high blood pressure and pre-eclampsia, haemorrhage and caesarean sections are more common in multiple pregnancies putting mothers at greater risk," she says. "The babies are much more likely to be born prematurely so more die, and have disabilities and long-term health problems. Having one child at a time is much safer for mothers and babies."

There is a well-regulated system in the UK where clinics have to meet certain standards and are regularly inspected, but this is not replicated elsewhere. It is, therefore, important to check the rules and regulations, and also the legal situation if you are using an overseas donor or a surrogate.

In addition, there are practical issues to consider, such as potential language barriers, as it can be difficult to talk to a doctor through a translator and it is advisable to check how communications with the clinic are handled.

The key piece of advice to anyone thinking of travelling for treatment is to do your homework before making any decisions. Fertility treatment always involves a significant financial and emotional investment, and making sure you are happy with the clinic you choose will lead to a more positive experience, whatever the outcome. ♦

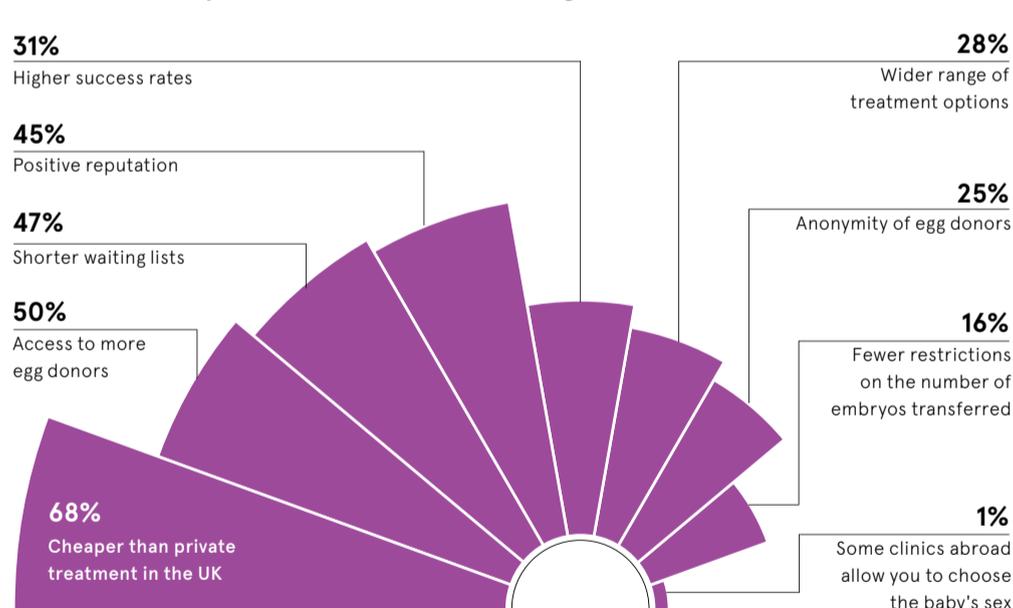
## Attitudes towards fertility tourism

Survey of UK women and couples undergoing or considering fertility treatment

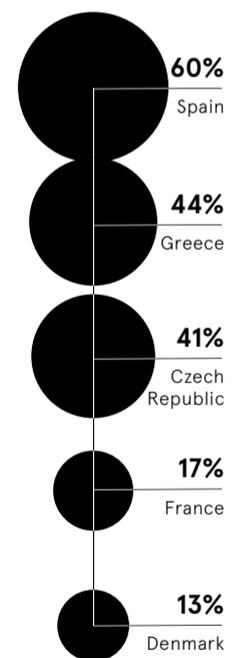
### Would you consider going abroad for treatment?



### What would be your main reasons for seeking treatment abroad?



### Which countries would you consider for treatment?



Fertility Network UK/Fertility Clinics Abroad 2017

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MY FUTURE,  
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# ‘Is it negligence or ignorance that fertility is seen as a female problem?’

**T**hirty thousand years ago unknown artists chose to carve exquisite ovals each with an inner cleft on the walls of a cave in La Ferrassie, France. These Stone Age sculptors were not alone: across the globe and throughout millennia, our ancestors depicted female genitalia in myriad ways. The story these vaginal symbols tell is a vital one that fertility is the most important aspect of human life; we must protect it. Without fertility, we are dust.

Fast forward 30,000 years to our apparently advanced age and it seems we have learnt nothing. We do not teach our children how important fertility is. They do not know its basics, its possibilities and limitations. They are not aware of how easily the flame of fertility is extinguished by age, weight, drugs, disease, occupation and environment. Collectively, we are only now beginning to recognise the potentially devastating impact that 21st-century lifestyles may be having on fertility, especially sperm health.

Which young adult leaves education knowing the female fertility vital statistics? 28: female fertility is already falling. 35: female fertility plummets. 42: the chance of becoming a biological mother is vanishingly small. Did you know the upper age limit for egg donation is 35? That’s because above 35 substantially reduced egg quality increases the risk of miscarriage. Yet in the UK, more than 68 per cent of women freezing their own eggs are over 35. The message isn’t being heard or are these women being exploited?

Everyone has heard of the female biological clock, but did you know the male reproductive system suffers the same fate? Men over 40 are half as likely to get their partners pregnant as men under 25. There is a significantly higher risk of miscarriage too. That’s why the recommended age limit for sperm donation is 40. We are failing our offspring and future generations if age and fertility are not part of sex education.

Myths about fertility are numerous. The recent *Fertility Trends* report from the Human Fertilisation and Embryology Authority (HFEA) shatters several fertility misconceptions. The average age of women having IVF in the UK is just 35.5, but couples will have been trying to conceive for several years before fertility treatment, so on average women having

IVF started trying for a baby in their early-30s. Fertility treatment is not the preserve of older women.

To date, fertility has been firmly cast as a female issue, irrespective of men being half of the fertility equation. But the HFEA’s data reveals infertility is now predominantly a male factor in origin. Male fertility problems are the most common reason for couples to seek fertility treatment (37 per cent), with female fertility problems and unexplained problems representing 31 per cent and 32 per cent, respectively.

Fertility problems are common, affecting one in six couples, so you will have a friend, family member or colleague affected. Despite this, infertility is too often ignored as the majority of couples (60 per cent) have to pay for their treatment, they are let down by their GP not providing appropriate information (74 per cent) and they are not supported at work by an effective fertility workplace policy (75 per cent). Why do so few firms enable employees to have time off for fertility treatment? Does your employer have a fertility policy?

Is it negligence or ignorance that fertility is seen as a female problem, not spoken openly about and insufficient support provided in the workplace? Will the way in which society views and responds to fertility issues change with the increasing recognition of fertility’s toll on men? For Palaeolithic people, female genitalia could symbolise fertility: the male role in reproduction was not fully recognised. Today, we know more about fertility, but we still have a long way to go in respecting it.



**Aileen Feeney**  
Chief executive  
Fertility Network UK

# How flash freezing is revolutionising fertility treatment

The flash-freezing technique of vitrification is rapidly proving a revolution in assisted reproduction



Ali froze her eggs at the age of 40 at the London Women’s Clinic. At 46 she thawed her eggs and successfully had twins Molly and Monty. To see Ali’s story search London Women’s Clinic Ali in YouTube

**N**ot only has vitrification made embryo freezing more efficient, with delivery rates apparently improved when thawed embryos are transferred but, for the first time in 40 years of IVF, human eggs can be frozen for viable use at a later date.

Never before was it possible to freeze eggs without damage to their microstructure. Thus, while the old slow freezing methods were adequate for sperm storage, eggs were not so robust when ice crystals formed within the cells. Vitrification, however, which reduces eggs to a glass-like state in just a few seconds, avoids the ice crystals and any micro-damage to the egg.

The result has seen the emergence of egg banks in the ever-growing treatment of egg donation and an upsurge in the numbers of women, usually in their mid-30s and single, having their eggs frozen for use some time in the future.

“We’ve seen a huge growth in egg freezing in the past two or three years,” says Professor Nick Macklon, medical director of the London Women’s Clinic. “Most patients are women without a partner hoping to preserve their fertility and put their family plans on hold.”

A recent audit of treatments at the London Women’s Clinic shows a dramatic increase in egg freezing, up from just six treatments in 2012 to 229 in 2017. Most of these treatments (74 per cent) were for freeze storage for single women, whose average age was 37.

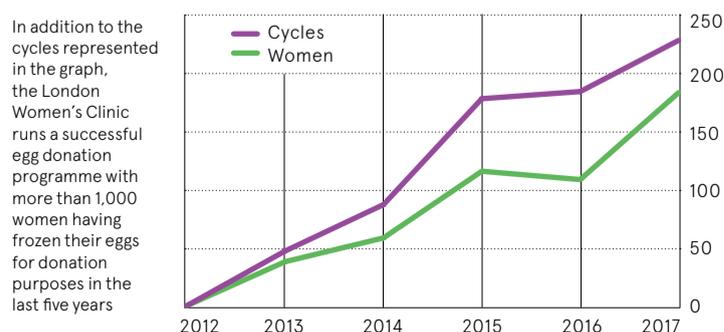
The few studies available suggest that these are women concerned with the biological decline in fertility, which inevitably comes with advancing age; egg freezing represents a way to stop the biological clock and increase a woman’s chance of motherhood in the future.

With more than 200 cycles completed in 2017, the cumulative total,

**“Egg freezing represents a way to stop the biological clock and increase a woman’s chance of motherhood in the future”**

## Five years of egg freezing at the London Women’s Clinic

Number of cycles and number of women 2012–2017



In addition to the cycles represented in the graph, the London Women’s Clinic runs a successful egg donation programme with more than 1,000 women having frozen their eggs for donation purposes in the last five years

says Professor Macklon, now makes the London Women’s Clinic one of the UK’s most experienced centres in egg freezing.

The trend has also been seen in egg donation, a treatment method for women unable to produce their own eggs, usually as a result of increasing age. Once gone, the store of eggs in the ovary can never be replaced, and egg donation offers the only chance of pregnancy.

Before efficient freezing, egg donation required a donor suitably matched to the recipient and embryo transfer in menstrual cycles hormonally synchronised in both donor and recipient.

“This inevitably meant long waiting lists or travelling abroad to countries where donor eggs were more plentiful. But banking eggs means that we have a greater choice in storage and the prospect of more immediate treatment without having to synchronise both parties,” says Professor Macklon.

The analysis of egg freezing at the London Women’s Clinic comes at a time when the Human Fertilisation and Embryology Authority (HFEA), the UK’s regulator of IVF clinics, described freezing in its latest report as “particularly striking”. It noted that birth rates from egg-freezing treatments have increased year on year, “with 26 per cent of patients finishing their treatment cycles with a live birth in 2016, compared to 20 per cent in 2013”. In 2016, all UK IVF clinics reported 1,173 cycles of egg freezing, up 10 per cent on the previous year.

The HFEA recognised that this cryo-revolution has not just brought egg freezing in from the cold. More and more routine IVF treatments in couples are now freezing all embryos generated, with the aim of transferring a single embryo in a later cycle unaffected by ovarian stimulation and storing the rest.

Not only are these “freeze-all” treatments associated with a higher success rate than fresh, they are also safer in encouraging the transfer of just one embryo and lowering the rate of multiple pregnancy. Summarising trends in the two years to 2016, the HFEA described IVF as “safer, more available and more successful than ever before”.

For more information please visit [www.londonwomensclinic.com](http://www.londonwomensclinic.com)



# Can technology really get you pregnant?

Smart technology, including apps and wearable devices, can now aid women to monitor their fertility

ANNA CODREA-RADO

Technology companies are getting serious about the baby-making business. In the last few years smart devices and apps, from bracelets that tell you if you are ovulating, to at-home hormone testing kits, have radically changed our understanding and approach to fertility. Investors are also paying attention, with the global fertility services market predicted to grow to \$21 billion by 2020.

Women now have access to a wealth of data to help them self-regulate, monitor and enhance the chance of pregnancy, as well as smart devices that offer a hormone-free contraception alternative. As these apps and products continue to play an increasingly major role in reproductive health, it raises the question: what happens when technology gives fertility a reboot?

“There has been little innovation within this space since the creation of the contraceptive pill,” says Ida Tin, chief executive of the period and ovulation tracker Clue. “Now, taboos around fertility and menstruation are disappearing, and as they do, women want to know more about their bodies and the unique patterns of their menstrual cycle.”

The Berlin-based company was one of the early period trackers that gave fertility an injection from the startup sector. By the end of 2015, Clue had 2.5 million users in 180 countries and had raised €10 million. Competitors in the market are Kindara, which launched in 2012 as a fertility tracking app, and Glow, launched by PayPal co-founder Max Levchin. The most basic functionality of these apps is to tell women when their periods are due, but some can also be used to prevent or plan pregnancy.

**More companies offering technology-driven contraception dovetails with women’s increasing dissatisfaction with existing hormonal options**

The fertility awareness method (FAM) is a misunderstood form of contraception. It relies on the physiological symptoms, such as changes in body temperature and cervical fluid, which reveal where a woman is in her cycle to determine her six-day fertility window. By monitoring and tracking these signs, a woman is able to pinpoint if she is fertile.

Often confused with the rhythm method, the crudest and most unreliable way to use FAM, many women do not believe FAM works. And while it’s rarely, if ever, offered as an option by a GP, according to the NHS website: “If natural family planning is followed correctly, it can be up to 99 per cent effective.” By comparison, the NHS says the pill and IUD (intrauterine device or coil) are both more than 99 per cent effective.

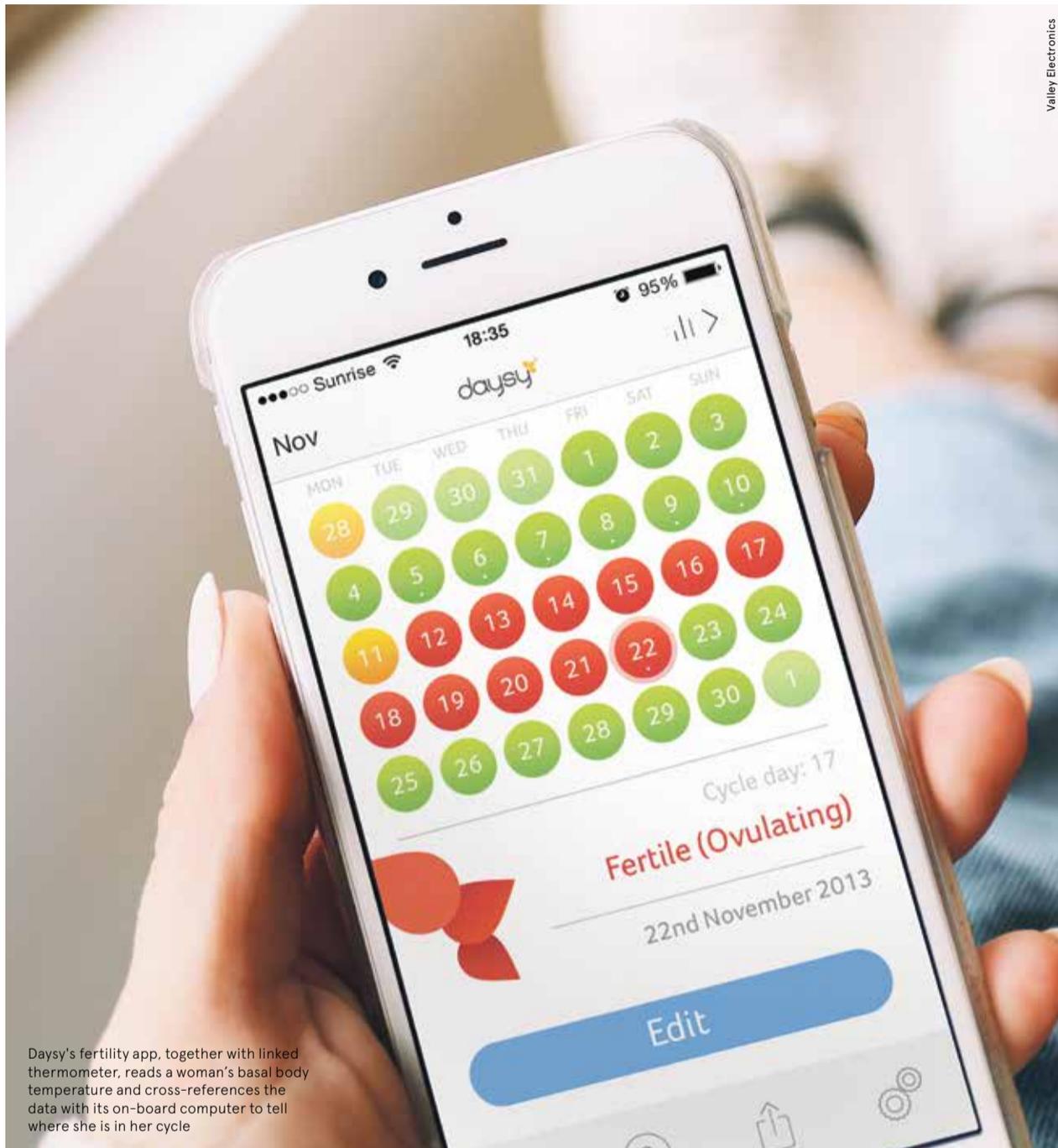
To be able to achieve that level of effectiveness with FAM, however, an app alone will not be enough. Many of the period tracker apps, including Clue, state they cannot be used as contraception alone. That’s where wearables and connected devices have come in.

“We’re all really comfortable with technology these days, especially to do with tracking health, calories, diet, exercise, sleep, heart rate,” says Holly Grigg-Spall, author of *Sweetening the Pill*. “And so we’re more able to understand the concept of monitoring, data and algorithms, and that it can help you understand what is going on with your body.”

Ms Grigg-Spall also works for Daysy, a fertility calculator. Daysy is a highly sensitive thermometer that reads a woman’s basal body temperature (the lowest body temperature attained during sleep) and cross-references the data with its on-board computer to tell where she is in her cycle. It can be used to both plan and prevent pregnancy. Its effectiveness rate for avoiding pregnancy is 99.4 per cent.

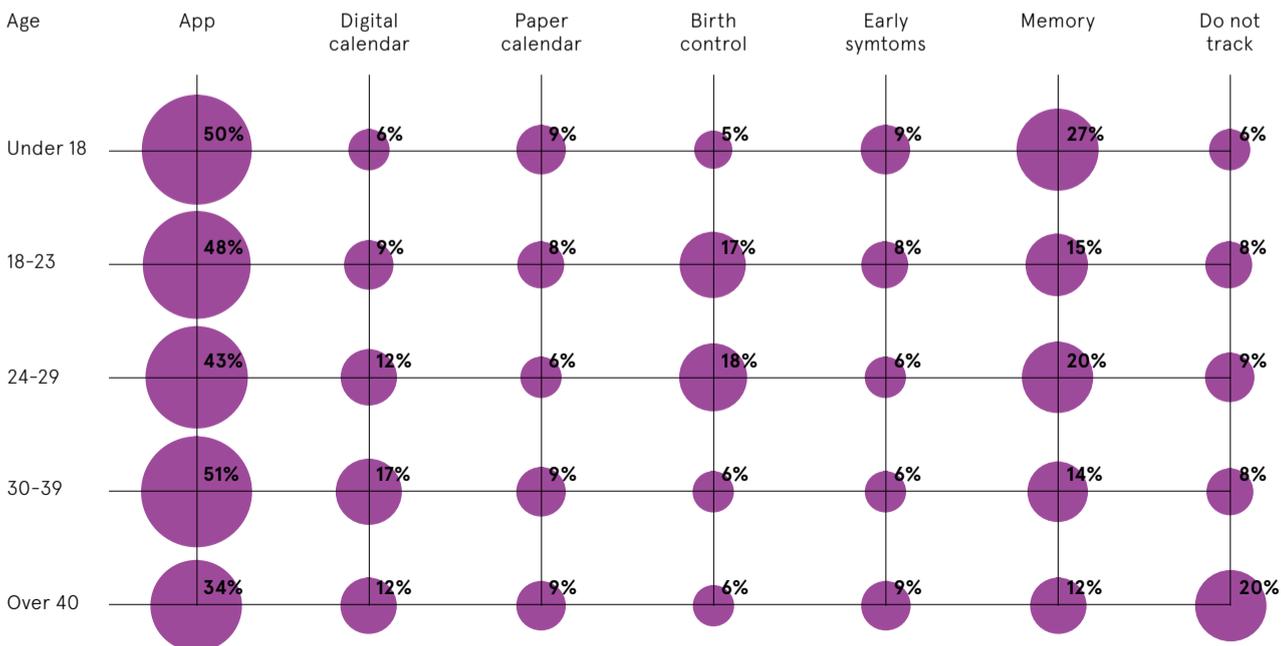
Daysy launched in 2014, but the company behind it has been offering a similar product, Lady-Comp, for more than 25 years. It’s only been in the last few years that similar products have started to come on the market, including Wink, the custom thermometer Kindara offers to work in conjunction with its app, and Natural Cycles.

The trend of more companies offering technology-driven contraception dovetails with women’s increasing dissatisfaction with existing hormonal options. Two recent studies from Danish



Daysy's fertility app, together with linked thermometer, reads a woman's basal body temperature and cross-references the data with its on-board computer to tell where she is in her cycle

## How women track their menstrual cycles



\*Survey of US women only

DUB Group/University of Washington 2017

**It's about improving treatment and therefore chances of success, which is very important because ultimately it's about getting pregnant**

researchers linked the pill to an increased risk of breast cancer and also depression, prompting many women to rethink their options.

"There wasn't really a situation where women who didn't want to use synthetic hormones at all had something they could go to," says Ms Grigg-Spall. "People are now happy to and want to learn more about fertility awareness."

FAM monitors and apps can also be used in planning pregnancy, as they enable women to track when they are likely to be ovulating. There are now also plenty of products specifically geared towards women trying to conceive, such as Ava, a bracelet that tracks when a woman is ovulating.

There are also technology options available for women who are struggling to conceive. At-home hormone testing kits made by companies including Modern Fertility and LetsGetChecked offer a way for women to check their hormone levels. These kits are not without their drawbacks; perhaps one of the fundamental limitations is that if there is an underlying fertility issue, couples hoping to become parents still need to turn to medical help.

More recently, new startups are offering in-clinic services to address this need, working with established healthcare providers to turbo-charge their clinic's tech offerings.

An app attempting to help ease the emotional process of undergoing IVF treatment is Salve, an early-stage company whose mission

is to make a difficult process easier for both the patient and medical provider. The app works by syncing with the clinic to provide the patient with personalised treatment information. It has all the data regarding the patient's care, acting as a medication manager, appointment reminder and also resource centre.

"It's about removing someone's stress and anxiety around the practice," says Charlie Kennedy, Salve's chief executive and co-founder. "That could be all of the drugs they have to take, all their appointments they have upcoming, with supporting information, so this will be videos, texts, images, to ensure they understand everything."

The Manchester Fertility Clinic was one of the first to use Salve and says they have seen an improvement in their internal processes as a result. Jonathan Koslover, the clinic's managing director, says one of the biggest advantages for clinics to use an app such as Salve is an improvement in the level of patient service the clinic is able to offer.

"We're using it to educate patients about what their treatment will involve," says Mr Koslover. "This is particularly important in fertility because people are nervous. It's an intrusive and emotional treatment."

He emphasises that these apps will never replace the doctors' work. "It's a very personal treatment, so you still have to have that nurse or doctor contact," he says. "We still make sure that we're talking with patients. You can't do it all electronically."

For clinics like Mr Koslover's, technology will continue to improve fertility services by offering supplementary options that ultimately enhance a couple's chance of success. He sees a future where ultrasound scanners will use artificial intelligence to help determine patients' treatment. "It's about improving treatment and therefore chances of success, which is very important because ultimately it's about getting pregnant," Mr Koslover concludes. ♦

Ida Tin, founder of period and ovulation tracker Clue, says women want to know more about their bodies as taboos around fertility and menstruation are disappearing



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# Landmark research set to boost IVF

Latest research into growing human eggs outside the body has been hailed as a breakthrough, but it could be some time before childless couples benefit

JOHN ILLMAN

The growth of human eggs from the earliest stage to full maturity outside the body has been acclaimed as a landmark development that could widen the scope of fertility treatments.

But does it offer real hope to the reported one in six UK couples with fertility problems? Expert opinion is mixed. The consensus is that it represents an important step forward, but progress in research into the most basic secrets of all – the origin and creation of life – is measured by decades rather than years.

For example, two thirds of women under 35 undergoing in vitro fertilisation will not have a baby after their

treatment cycles, even though it is 40 years ago this year since the birth of Louise Brown, the world's first test tube baby. Specialists don't know why most IVF treatment cycles fail, but advances in knowledge arising from the development and study of lab-grown human eggs could help boost IVF success rates.

IVF success rates may be disappointing but, thanks to ongoing research, they are about 85 per cent better than in 1991 when the Human and Fertilisation Embryology Authority (HFEA) started keeping records.

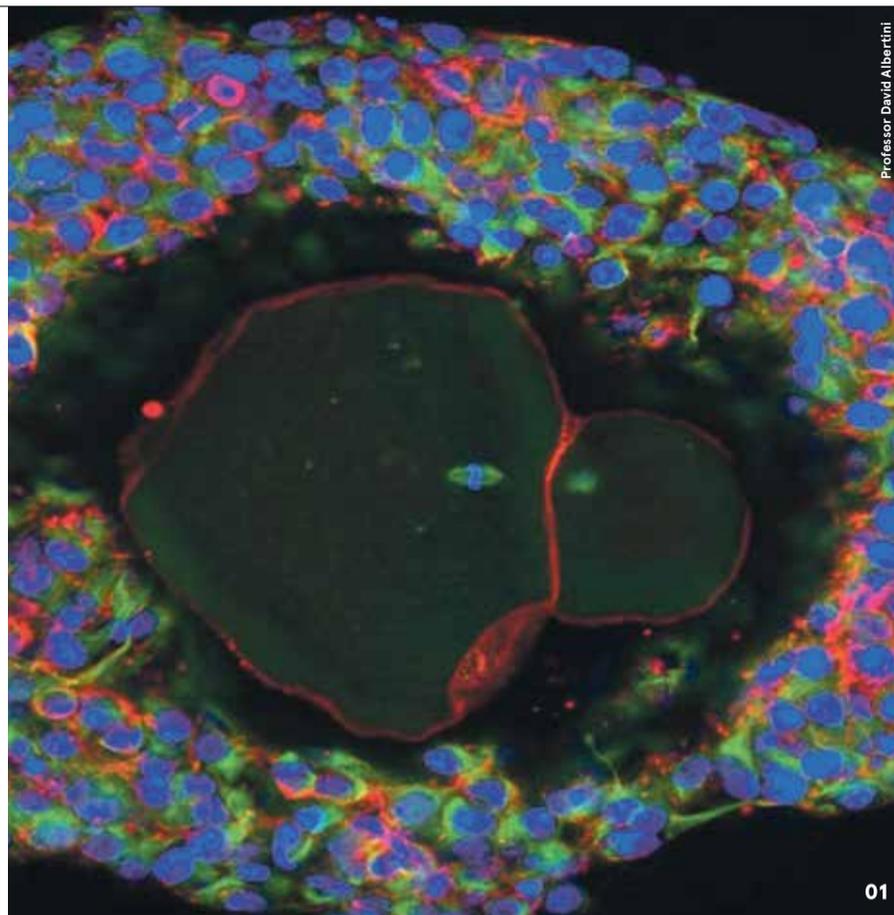
Transforming lab-grown human eggs into viable treatments could follow a similar pattern; the research programme started more than 30 years ago and has produced live offspring from lab-grown mice eggs.

The latest work was carried out by Professor Evelyn Telfer and colleagues at Edinburgh University, the Royal Hospital for Sick Children, Edinburgh, and the New York Center for Human Reproduction. The eggs were grown from ovarian tissue donated by ten women undergoing caesarian-section births.

Reported in the journal *Molecular Human Reproduction*, the research has provoked critical questions. For example, why did some of the developed eggs mature in just 22 days, compared with the five months it would have taken in the body? And why did only 10 per cent of the eggs reach full maturity?

Challenging the idea that maturation of lab-made eggs should mimic that of the natural cycle, Professor Telfer says: "The process takes much longer in the body because eggs have to work in tandem with a woman's hormonal cycle – there are lots of control mechanisms in the body.

"We prefer to describe the way eggs grow outside the body in our system not as accelerated development, but rather as development without brakes. That's a big difference. Logically there is no reason



Professor David Albertini

01

01 Magnification of a lab-grown, fully matured human egg ready for fertilisation

02 Analysis of embryo development following intracytoplasmic sperm injection at the IVF Centre, University Women's Hospital Bonn, Germany

why it should take human eggs months to mature.

"The real problem is the basic lack of knowledge about human eggs. We speak about lack of progress in IVF in the last 40 years. This is because we lack a fundamental understanding of human egg development. It's only this kind of work that will give us the kind of insight we need."

Professor Telfer also dismisses the criticism that only 10 per cent of eggs in the study reached full maturity. "In the human body, only 0.1 per cent reach full maturity – 99.9 per cent degenerate – so what we are doing in our in vitro system in the laboratory is circumventing what happens in nature."

With her colleagues, she is now planning to develop better quality eggs and to use IVF to fertilise them with sperm to test their viability; a procedure the HFEA will have to authorise. A big challenge is to create a receptive laboratory environment. Natural growth and development of eggs and the follicles or sacs containing them is controlled by the release of changing concentrations of hormones and a soup of growth-promoting nutrients.

Professor Telfer says: "We're working on some ideas to change the lab environment. We're on the path. We're not where we need to be yet, but I'm confident we'll get there."

Patience and determination is essential. It took Sir Robert Edwards and Patrick Steptoe more than ten years and 467 attempts at IVF before Louise Brown became the world's first test tube baby in 1978.

The Edinburgh research could help cancer patients. Stuart Lavery, consultant gynaecologist at Hammersmith Hospital's Department of Reproductive Medicine in London, says it offers hope to women having sterilising treatment such as chemotherapy.

At present, freezing eggs or embryos before treatment can help

**Advances in knowledge arising from the development and study of lab-grown human eggs could help boost IVF success rates**

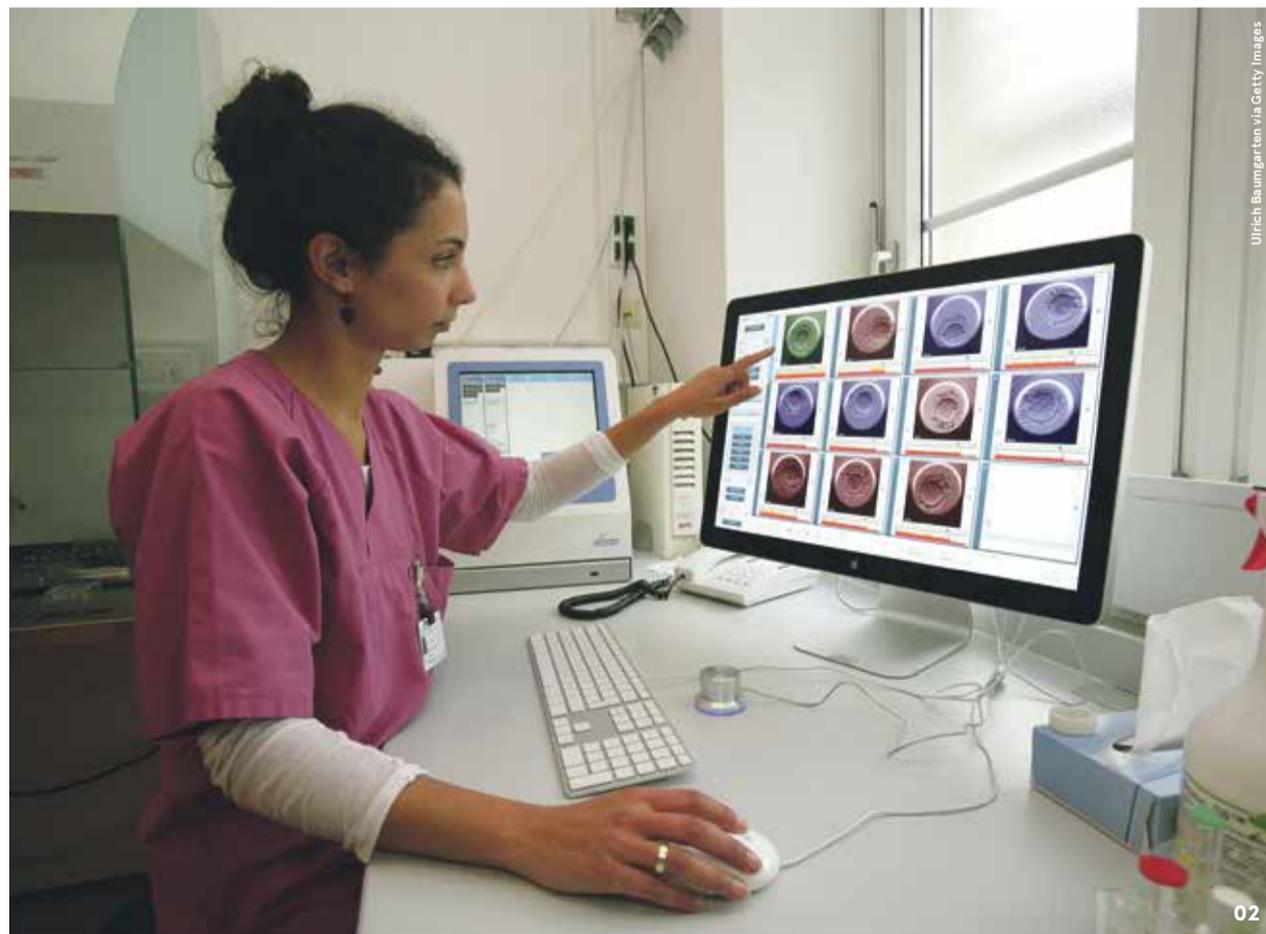
to preserve their fertility, but this is not an option for women who require immediate therapy or for young girls. A girl's eggs do not become viable until she starts her periods.

Ovarian tissue taken from such patients can be frozen for later pre-implantation, but there is a risk in some cases of reintroducing tissue contaminated with cancer cells back into the patient. Laboratory-grown eggs would bypass the need to reimplant the tissue.

Improved treatment could also prevent financial exploitation. Ying Cheong, professor of reproductive medicine at the University of Southampton, says: "It is hugely disappointing that more than two thirds of patients who undergo an IVF cycle will not have a baby at the end of their treatment cycle. Doctors do not yet have the magic wand.

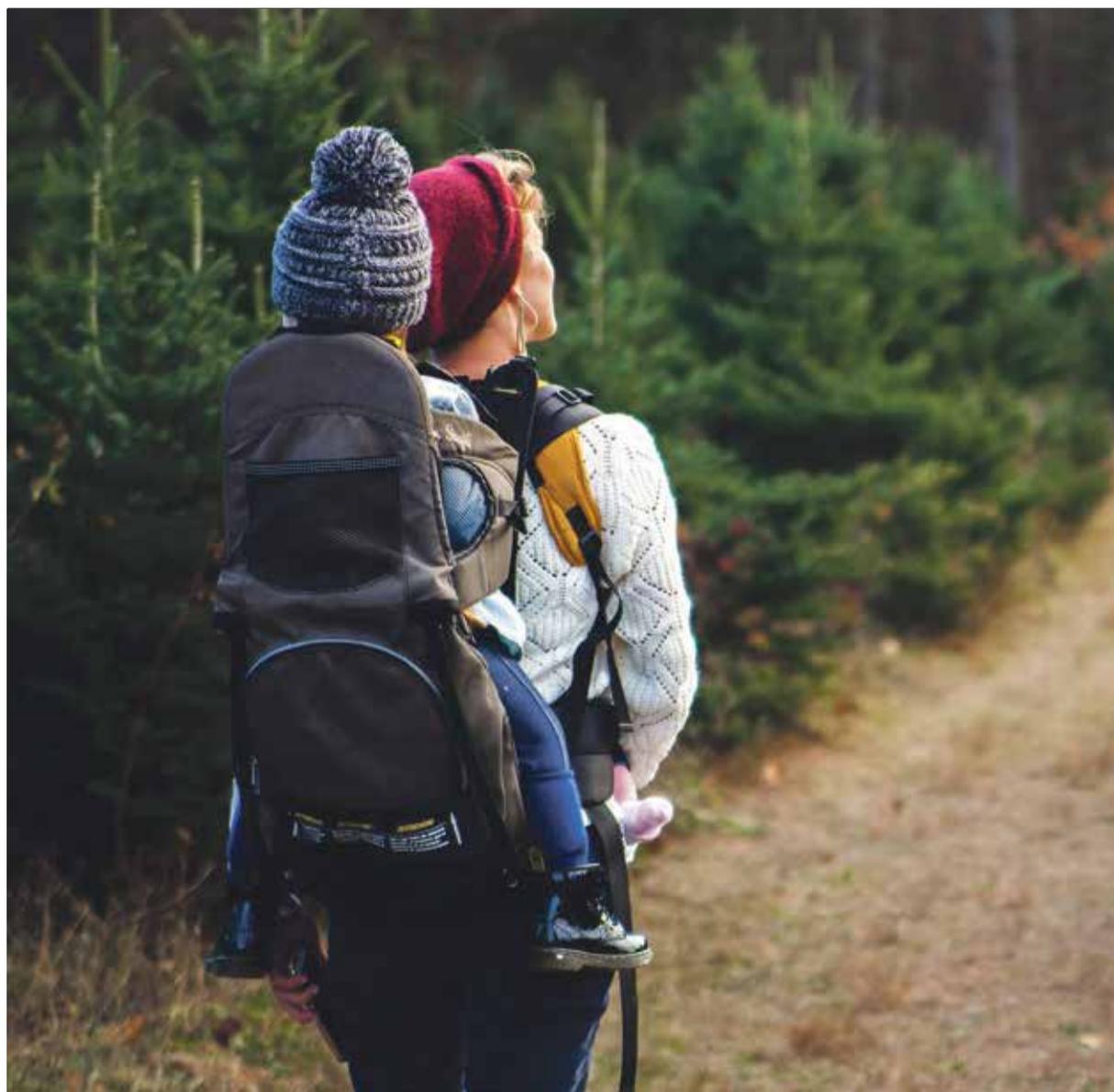
"With no scientific answers to explain the majority of the failures, many clinics resort to offering pointless, expensive add-ons to try to improve their success rate to no avail."

This does not deter childless couples who are encouraged by the many success stories. More than 300,000 babies have been born in the UK from licensed fertility treatments since 1991. The secret to future increased success may well lie in eggs assuming shape and definition in Edinburgh. ♦



Ulrich Baumgarten via Getty Images

02



# IVF 'breakthrough' treatment

Pioneering use of the first oral medication of its kind in IVF treatment is showing remarkable trial results

**O**bsEva, which develops reproductive health treatments, has reported trial results of a therapy with the potential to increase in vitro fertilisation (IVF) success rates by more than 10 per cent.

The reported findings are said to represent the biggest innovation in the field in 20 years and are one of many examples of small niche companies producing some of healthcare's biggest advances. Many of these focus on some of the areas with great unmet need that large companies often ignore.

In fertility treatment, timing can be everything and the same is true of new companies. ObsEva was founded in 2012 as demand for reproductive healthcare was rising rapidly. Vast numbers of Western women were delaying having children to pursue their careers and then in 2015 China suspended its one-child-per-couple policy.

Worldwide, the annual number of treatment cycles for assisted reproduction technology is estimated to have risen within the last decade from 1.6 million to 2.4 million. In China it is reported to be more than 800,000 a year.

Unfortunately for couples seeking fertility aid, quantity in demand does not equate to quality of outcome. The World Health Organization has estimated that only one in four infertility treatments end with a "take-home" baby.

ObsEva's founder and chief executive Dr Ernest Loumaye wants to fill what is for all too many women a therapeutic vacuum. He is a dedicated gynaecologist whose prime interest is looking after patients. But he felt that reproductive health had been left far behind in the biotech revolution.

As a clinician he was limited in what he could do. Wanting to develop innovative treatments, he moved into the pharmaceutical industry. Twelve years ago, he founded and was chief

executive of another successful company, PregLem, which was sold in 2010 before the launch in Europe of its lead medicine.

ObsEva's pipeline also includes a novel hormone-based therapy to treat both endometriosis, a common, painful condition that can cause infertility and pain during sex, and uterine fibroids, causing non-cancerous growths in and around the womb, heavy menstrual bleeding that may result in anaemia and other possible symptoms, including a frequent need to urinate.

**"In fertility treatment, timing can be everything and the same is true of new companies"**

## O&A

Founder and chief executive **Dr Ernest Loumaye** tells of the exciting trial results from ObsEva's pioneering use of the first oral medication of its kind – nolasiban – in IVF treatment

### What's so special about the results you've just reported?

Imagine 100 women undergoing in vitro fertilisation receiving nolasiban and another 100 patients receiving a placebo: our results show that 46 women in the first group may be able ultimately to go home with a baby compared with only 35 in the second. This 11 per cent difference represents a fantastic result in our view. In gynaecology, a 5 per cent increase in positive outcomes is considered a breakthrough – we more than doubled that threshold in this clinical trial.

### What is nolasiban?

An oral treatment to prevent expulsion of the embryo from the womb. It is taken four hours before "embryo transfer" – the implanting of the embryo in the uterus or womb.

### How many patients were in the trial?

There were 778 from 41 European fertility clinics.

### How does nolasiban work?

Nolasiban has a quietening or blocking effect on oxytocin, a naturally occurring hormone. It's known as the "love hormone" because it is released during orgasm and can generate feelings of peace. But calling it the love hormone is a bit like calling a computer a writing tool. It also stimulates the uterus or womb to contract to begin childbirth. Contractions also occur during IVF as the embryo is being implanted. Rapid rises in contractions can expel the embryo from the womb and prevent pregnancy. Nolasiban also – and we believe this may be critical – increases blood flow in the womb and womb lining.

### Is there any way to identify women who are prone to these problematic uterine contractions?

That's a very good question. Our nolasiban studies have focused on two groups: women with high contraction rates and those with low contractions. We found no



**Ernest Loumaye**  
Co-founder and chief executive  
ObsEva

clear relationship between any reduction in contractions and pregnancy outcomes. And so we didn't measure contractions in the latest trial. We just enrolled women undergoing either their first or second IVF treatment cycle. The results confirmed that it's not necessary to measure contractions to achieve a benefit. They also suggest that increased blood flow may be the real benefit. Blood flow is a critical factor in embryo implantation.

### The study has also shone a very bright light on the ongoing controversy over the best time for embryo transfer. Is it best when the embryo is three days old and comprising four to eight cells or when it is five days old and made up of 70 to 100 cells?

We tested both three and five-day embryo transfers. Overall, comparing nolasiban with placebo, we showed a relative increase in ongoing pregnancy rates of 25 per cent; with day-five transfers, we saw a larger effect of 32 per cent which we consider to be a highly meaningful result. The day-three alone data resulted in a 14 per cent improvement.

### So there may be a strong case for making five-day transfers and nolasiban a routine part of IVF treatment?

We believe so, but before we can answer this question, we await the data from women in the trial giving birth in the final quarter of this year and for the six-month follow-up after birth. We're optimistic that the birth outcomes may be consistent with pregnancy rates because most miscarriages occur within the first 12 weeks of pregnancy.

### Have you a final message for patients and clinicians?

There is a very simple, but critical, message. Nolasiban has the potential to increase pregnancy rates while reducing the number of multiple births. Although single-embryo transfers are now generally recommended, it is still often standard practice in the United States and some European countries to implant two embryos to increase the likelihood of having a baby. But our clinical trial results indicate that a single-embryo transfer plus nolasiban can result in a clinical pregnancy rate that is similar to what has been historically achieved with double-embryo transfer and thereby potentially avoiding risks of multiple pregnancy. This is of major importance both in terms of avoiding the health risks for both mother and baby, and for the considerable financial costs related to multiple births.

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Pablo Heimplatz/Unsplash

# Emotional anguish of infertility

Difficulty conceiving can have a devastating emotional impact and couples should be supported with professional counselling

MARTIN BARROW

Coming to terms with being unable to conceive naturally can be stressful, and can leave you feeling angry, depressed and anxious. It can also put additional stress on relationships, intimacy, and your connection with relatives and friends. The impact can be profound and long lasting.

The process of going through IVF (in vitro fertilisation) for months and even years can take its toll as you may experience hopes and disappointments, while managing the implications on your emotions, your body, your relationship and your finances.

Fertility problems affect between 10 per cent and 15 per cent of the population, according to the World Health Foundation. In the UK, one in six couples are affected and the number seeking medical help to start a family has risen dramatically, with more turning to IVF.

But mental health issues rooted in fertility problems are unlikely to end with a clinical intervention to help create a family. The incidence of depression in couples presenting for fertility treatment is significantly higher than in the general population and poor mental health can itself become an obstacle to a successful outcome through IVF.

Although the stigma of mental health remains, IVF providers are

beginning to give greater priority to the emotional support that is available to couples going through treatment.

Aileen Feeney, chief executive of the charity Fertility Network UK, says women and men who are unable to start a family suffer from stigma, and are likely to suffer from anxiety and stress.

"Society still largely assumes that you will go on to have a family, sooner or later, and so much of what we do revolves around family life," she says. "But it doesn't always work out that way and many people find they cannot conceive naturally. Yet, it can be extremely difficult to come to terms with this, and society gives you constant reminders."

A major survey by Fertility Network UK in 2016 revealed that the emotional and social impact of fertility problems was greater than previously recognised. The survey, conducted in association with Middlesex University London, assessed the impact of failing to conceive and the subsequent impact of fertility treatment on both women and men. Some 90 per cent of respondents reported feeling depressed and 42 per cent experienced suicidal feelings.

Those who had unsuccessful treatment reported greater distress as well as more frequent suicidal thoughts. More than two thirds of respondents (70 per cent) reported some detrimental impact on the relationship with their partner,

while 15 per cent said their relationship ended or was strained as a result of the impact of fertility problems and treatment.

The majority of respondents would have liked to have had counselling if it was free; fewer than half (44 per cent) did have counselling and of these more than half had to pay for some or all of this psychological help. More than half of all respondents reported a lack of local peer support services.

Professor Adam Balen, chair of the British Fertility Society, says: "The survey showed the true picture of living with fertility problems for many people. It can be an incredibly distressing time, and undergoing treatment and facing costs can place a huge amount of stress and pressure on couples and their families."

The National Institute for Health and Care Excellence recommends that counselling should be offered before, during and after IVF treatment, regardless of the outcome. Counselling should be offered by someone not directly involved in the management of a couple's fertility problems. This can help couples to understand the implications of treatment and offer support at a critical time, such as when an IVF cycle has been unsuccessful.

In the UK, the Human Fertilisation and Embryology Authority (HFEA) is responsible for the regulation of clinics providing IVF treatment. All clinics licensed by the HFEA must offer couples an opportunity to talk to a counsellor before treatment begins. This helps them to think about their treatment in advance, and how it might affect them and those close to them, in the short term and in the future.

Some clinics offer free counselling, but others charge. Couples researching clinics are advised to ask about this, and whether clinics offer support groups or the opportunity to meet other patients who are undergoing similar treatment.

In addition to the counselling couples may receive from their clinic, the HFEA advises couples to consider seeking counselling on the NHS or privately. This provides an opportunity to explore feelings around fertility more generally and can be done individually or as a couple. GPs provide a gateway to NHS counselling.

For private counselling, the British Infertility Counselling Association has a directory of accredited therapists, with options including telephone and Skype counselling. The HFEA website also lists other support organisations,

**IVF providers are beginning to give greater priority to the emotional support that is available to couples going through treatment**

## More than half of men would not be open to discussing fertility with their partner

including the Donor Conception Network and Fertility Friends.

Research shows that more than half of men would not be open to discussing fertility with their partner, yet they are just as at risk of experiencing feelings of sadness, shame, anger, depression or inadequacy. Sadly, there are fewer dedicated support options for men than there are for women. One option is the *Men's Health Forum*, which has information about men's health as well as an online community where men can chat anonymously.

Many support groups welcome individuals and couples so this could be a good place to meet other men with similar experiences, either alone or with a partner. Some men also find it easier to speak to a counsellor who has experience working with men with fertility problems, and can be a trusted and impartial "outsider".

Getting news that you are not pregnant after a round of IVF treatment can be devastating. Experts advise that it is important to take the time to come to terms with this outcome and give your body and mind time to recover. When you're ready, talk to your doctor about whether you should try again and what the chance of conceiving might be if you did. Health professionals may suggest a different treatment or discuss any other options for maximising your chances of conceiving. It is also important to consider the financial implications of your decision.

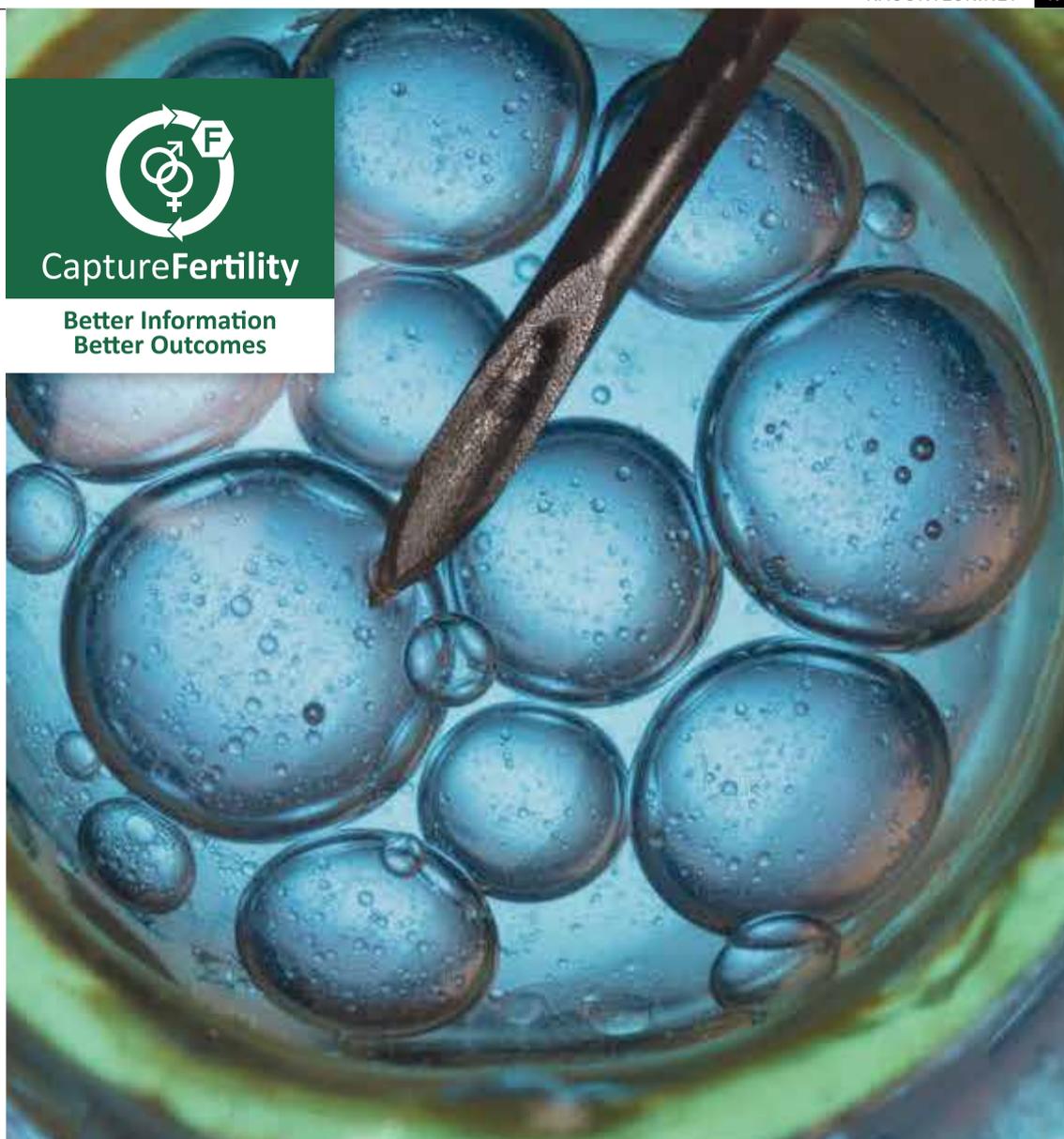
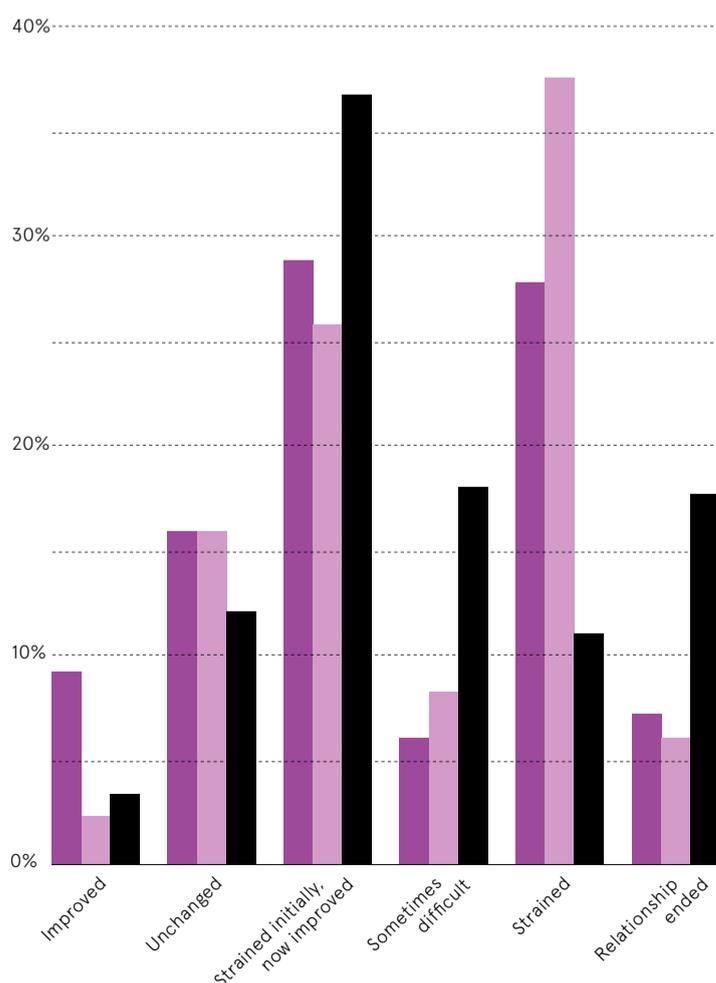
If you're unable to have more treatment, or you're not sure if you want to go through treatment again, you may find it helpful to talk your feelings through with a counsellor. Some couples have different opinions on whether to continue with treatment; talking to an impartial professional may help you to think through the issues together and come to an agreement about how to move forward.

IVF treatment continues to make great progress, with new techniques and products bringing real hope to more couples who are unable to conceive naturally. But while pushing these boundaries, the IVF industry must also accept its responsibility to support its clients' emotional wellbeing as well as their fertility problems. ♦

### Impact of fertility problems and/or treatment on relationships

Changes to relationships

◆ Friends ◆ Family ◆ Partner



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