

# COULD AN ALGORITHM BOOST YOUR FERTILITY?

Demand for IVF has never been higher, but success has plateaued. Now an unlikely party – big-data analysts – believe AI algorithms could fast-track the process. *WH* reports on the reproductive robotics revolution

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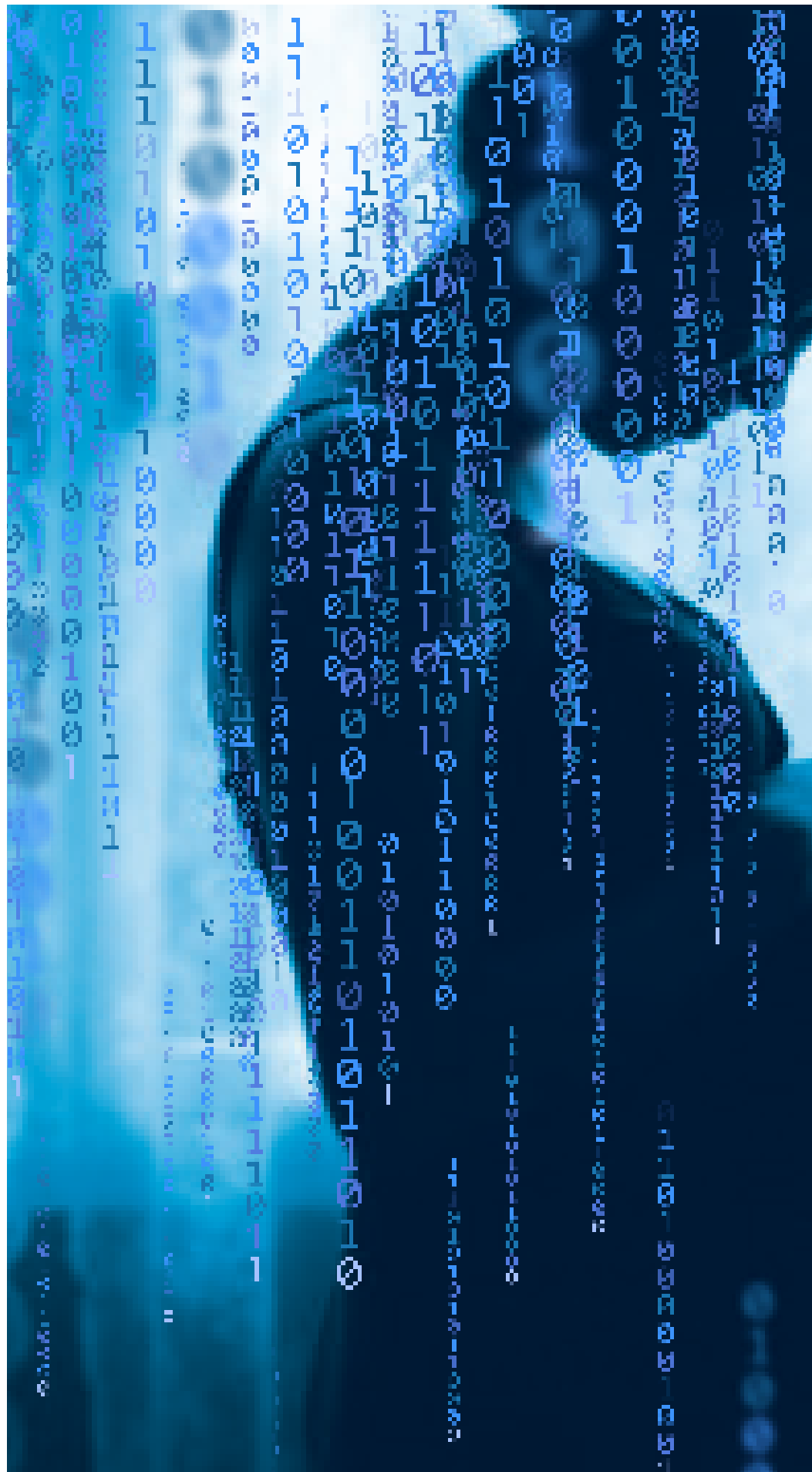




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o the untrained eye, the machine looks like a next-gen Nespresso maker – the kind you'd use to make coffee for a giant. It's the size of a large office printer, with a screen at the front and multiple chambers on top for your outsized coffee capsules. Only at Aria Fertility, your Bianco Doppio is a developing embryo and the strong coffee will be needed in about nine months' time. The machine is a time-lapse incubator, and its embryo-monitoring technology is brewing a rebirth of the fertility industry.

Since the first IVF baby was born in Oldham in 1978, most fertility clinics have monitored embryos by hand. 'Once a day, you'd remove an embryo from the incubator, have one look under a microscope and base all your decisions [about how healthily the embryo was developing] on that,' explains Robert Smith, embryologist and clinic director at Aria Fertility. Introducing time-lapse incubators – smart incubators with cameras that record images of multiple embryos every 10 minutes – to his clinic around eight years ago was like getting embryo CCTV. Embryos never have to leave the optimally controlled comfort of their faux womb, and scientists like Smith suddenly found themselves with masses of digital images and videos detailing exactly which embryos had made successful pregnancies and which hadn't. And so the reproduction industry has quickly become fertile ground for some serious number crunching.



technology in medical, robotics and AI spaces, including an American fertility start-up called Alife. She sees the recent change of tack not only as a consequence of a surge in big data and demand, but a broadening of perspective. The Society for Assisted Reproductive Technology now reports that 40% of infertility cases are in fact due to male factors; a 2022 report in *Human Reproduction Update* showed that sperm count has declined a hefty 62% since 1973. 'Fertility is a *human* health issue, not a women's health issue,' she adds. 'With fertility in crisis, new technology will be evermore critical to the continued sustainability of the population.'

### Birth of an idea

It has echoes of an end-of-days sci-fi film, but reproductive robotics is already here. Venture capital funding for fertility start-ups has grown steadily since

### Maybe, baby

It was smart timing, because the global population was making fewer babies. In 1950, globally, women had an average of 4.7 children. By 2017, that had almost halved to 2.4 and it's predicted to drop below 1.7 by 2100, according to analysis by the University of Washington's Institute for Health Metrics and Evaluation. The reasons aren't all bad – more women in education and work, some choosing to be child-free – but among those who do want to start a family, the NHS expects one in seven couples will have trouble conceiving.

Cruelly, but undeniably, trying for a baby later in life is a factor. You're born with your lifetime stash of eggs, so as you age, your eggs age with you. And older eggs have glitches. Put simply, they are less adept at following the steps needed to form a healthy embryo: that is, making copies of your 23 chromosomes and inserting them into cells. 'If there's one small mistake – for example, three copies of chromosome 21 accidentally get put into one cell – then

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the most likely outcome is an embryo that can't ever form a pregnancy.'

This is where IVF comes in – to assist in selecting embryos with the right number of chromosomes. But while demand for IVF has increased (births via IVF were three times higher in 2019 than 1991), IVF birth rates still fall short of demand. For under-35s, the average odds of a successful pregnancy are 32% per embryo transferred, dropping to less than 5% per transfer if you're 43 or older. With the IVF process still largely manual, analogue and dependent on a specialist clinician at every stage (the labour-intensive nature of which creates fees of around £5,000 per cycle if you fall outside the NHS criteria in your local area), success has plateaued.

Cue: the birth of a business opportunity for tech start-ups. 'Historically, women's health has been overlooked and underfunded, and because fertility care was regarded as a "women's issue", research and innovation did not always get the attention it should have,' argues Melissa Teran, a systems engineer who develops new

2017, but it exploded by a whopping 89% between 2020 and 2021, according to intel from business insights provider Crunchbase. Companies proposed digital advancement in everything from egg freezing to artificial wombs for premature babies, but the biggest growth area was applying machine learning to embryo selection in IVF; harnessing the data that time-lapse incubators have recorded of developing embryos, then letting computers – rather than embryologists – spot patterns that could lead to successful pregnancies.

Today, several research groups from around the world are analysing thousands of anonymised videos to create algorithms to finesse embryo

## Fertile ground

selection for IVF patients. ‘There’s a lot going on in an embryo that’s invisible to the human eye but might not be to a computer,’ says Andrew Thomson, director of embryology at the IVF Scientific Advisory Service. While this technology is new to IVF, he adds, AI pattern-spotting is already used in cancer diagnosis and to predict conditions such as heart attacks. ‘The AI will assess each of the patient’s embryos and compare these against embryos that it knows have gone on to achieve pregnancy, and against those that developed in an abnormal way. It [the AI] will give each embryo a score (usually out of 10) and rank them in order [of which embryo is most likely to form a pregnancy and which is least likely].’

The hope is that transferring the algorithm’s top-ranked embryos first will speed up the time to conception, as well as helping scientists more accurately predict how effective an implantation will be and base decisions on a huge set of historical data rather than human subjectivity. All embryos will still be reviewed, selected and implanted by a highly trained (human) embryologist, who can override any AI decision. Currently, this AI tech is available in most UK clinics that offer the option of time-lapse incubators, either included for free as part of the time-lapse add-on, or for a fee of around £1,000.

### Labour of love

So, if you’re adding a grand on to your fertility journey, can you expect to up your odds of expecting? Clinical data is beginning to trickle in – particularly from Israel, a global med-tech hub in the fertility space. Fairtility, one of its leading players, has an AI product called Chloe – a cutesy acronym for the more cyborg-sounding ‘Cultivating Human Life through Optimal Embryos’. Chloe’s algorithms are trained on a data set of over 200,000 videos from time-lapse incubators, which it can break down to a pixel level to quantify variables such as embryo size, shape and symmetry.

A recent study by the start-up, published in *Nature’s* Scientific Reports section, pitted Chloe’s embryo-grading system against manual embryo grading and found that Chloe’s accuracy was 70% compared with 63% for human judgement. ‘In other words, the algorithm performed almost 10% better than an expert embryologist,’ says Dr Assaf Ben-Meir, Fairtility’s chief medical officer and director of the fertility

and IVF unit at Hadassah Hebrew University Medical Center. Fairtility also claims its AI automation can reduce an IVF cycle by 30 hours, with embryologists spending 33% less time on admin alone (Chloe automatically annotates embryologists’ notes on to digital medical records, for example, instead of the old pen-and-paper approach).

At AIVF, another Israeli start-up automating embryo selection and IVF workflow processes, co-founder Daniella Gilboa’s goal is for AI to reduce the number of IVF cycles it takes to have a child. She hopes for one or two cycles – instead of the current average, an emotionally and financially gruelling, five. Both AIVF and Fairtility have the European conformity CE mark, which means they’re being rolled out commercially across Europe, and are now targeting FDA clearance for the US.

### The poster child

But, to put a pregnant pause on proceedings, there are limitations. With so few studies focusing on the real barometer of success – live births – sceptics argue the tech is yet to prove itself. In fact, there’s debate about the merit of time-lapse incubators altogether. On its traffic light system of cost-effectiveness, industry regulator the UK Human Fertilisation and Embryology Authority (HFEA), places them on its amber list – which means there’s limited or conflicting evidence that they improve the chances of having a baby sufficiently to warrant the fee. For AI specifically, HFEA director of strategy and corporate affairs Clare Ettinghausen tells *WH* that the

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regulator’s reservations surround the fact that it’s not always possible to explain how machine-learning models make the decisions they do. She’s also vigilant about the importance of obtaining informed consent to share patients’ personal data.

Perhaps the most important limitation, however, is an emotional one – expectation. AI is merely a selection tool; it cannot improve the quality of your eggs or embryos. ‘AI or no AI, it’s still the same eggs and the



same sperm,’ says Smith. The bigger issue is that beyond the known impact of age and egg count, 70% of infertility causes remain a mystery. ‘You can have a 32-year-old woman whose fallopian tubes aren’t blocked, she’s got a brilliant ovarian reserve (the number of healthy eggs in the ovaries), her fertility hormones are exactly where you’d want them to be and the partner sperm is brilliant. Why isn’t she getting pregnant? We just don’t know,’ says Smith. ‘You’ve got more



chemical messages in your body than you could spend your life counting, so which ones are important for this individual to get pregnant? That is the challenge.' If the underlying factor preventing pregnancy is identified, Smith believes the patient's fertility rate would rise to around 80%. And that, he hopes, is where computer-learning of the future can take us.

Theoretically, it would involve a bigger-picture approach to fertility, and could appeal to women as young as their twenties – which is a better time to harvest eggs for freezing than late thirties. A patient would share their demographics with a doctor to compute: blood tests, ovarian reserve, lifestyle factors that may influence egg quality, ultrasound scans. This data would be compared against a huge dataset of similar patients, and the computer would pitch an optimal treatment strategy. 'At the minute, all we can do as experts is look at

what we have on a bit of paper: the medical history of a patient, blood test and scan results. Whereas if AI develops to a radical extent and we were able to put all of these factors into a computer, it could point us to look at things we maybe hadn't thought about,' Smith ponders. At the moment, the AI technology involved in fertility is very much in its infancy. But no one could knock the promise of increased visibility – and efficiency – around your pregnancy prospects. The algorithm might be your nemesis on Instagram, but for baby-making, it's definitely one to follow. **WH**

## Conception store

Other birth-tech names to know



### For smart swimmers: Mojo

Launched in April, Mojo – a £150 home test – will courier a semen sample to its lab where a smart microscope will count the number of sperm cells and analyse their movement, morphology and DNA integrity. It's nothing a skilled lab technician can't do, but Mojo's AI robot will do the analysis in four minutes instead of 30, and for at least half the price.



### For cracking eggs: Future Fertility

This Canadian start-up is the first company to use AI-powered tools to measure and evaluate egg quality. Designed for women freezing their eggs, its program, Violet, will give objective analysis about how successful future fertilisation is likely to be. Useful info to know when you're deciding how many eggs to bank.



### For storage hacks: TMRW

Amy Schumer recently invested in New York-based TMRW, which automates IVF storage. Its robotic platform automatically tags the vials that store eggs and embryos with radio-frequency ID chips, then places them in precision-monitored cryo-storage. Voted *Fast Company's* most innovative biotech company, TMRW plans to enter the UK in 2023.