

## A Perfect Storm

*Non-evidence-Based Medicine in the Fertility Clinic**Emily Jackson*

## 38.1 INTRODUCTION

*In vitro* fertilisation (IVF) did not start with the birth of Louise Brown on 25 July 1978. Nine years earlier, Robert Edwards and others had reported the first *in vitro* fertilisation of human eggs,<sup>1</sup> and before Joy Brown's treatment worked, 282 other women had undergone 457 unsuccessful IVF cycles.<sup>2</sup> None of these cycles was part of a randomised controlled trial (RCT), however. After decades of clinical use, it is now widely accepted that IVF is a safe and effective fertility treatment, but it is worth noting that there have been studies that have suggested that the live birth rate among couples who use IVF after a year of failing to conceive naturally is not, in fact, any higher than the live birth rate among those who simply carry on having unprotected sexual intercourse for another year.<sup>3</sup>

Reproductive medicine is not limited to the relatively simple practice of fertilising an egg *in vitro*, and then transferring one or two embryos to the woman's uterus. Rather, there are now multiple additional interventions that are intended to improve the success rates of IVF. Culturing embryos to the blastocyst stage before transfer, for example, appears to have increased success rates because by the five-day stage, it is easier to tell whether the embryo is developing normally.<sup>4</sup>

Whenever a new practice or technique is introduced in the fertility clinic, in an ideal world, it would have been preceded by a sufficiently statistically powered RCT that demonstrated its safety and efficacy. In practice, large-scale RCTs are the exception rather than the norm in reproductive medicine.<sup>5</sup> There have been some large trials, and meta-analyses of smaller trials,

<sup>1</sup> R. G. Edwards et al., 'Early Stages of Fertilization In Vitro of Human Oocytes Matured In Vitro', (1969) *Nature*, 221, 632–635.

<sup>2</sup> S. Franklin, 'Louise Brown: My Life as the World's First Test-Tube Baby by Louise Brown and Martin Powell, Bristol Books (2015)', (2016) *Reproductive Biomedicine and Society Online*, 3, 142–144.

<sup>3</sup> H. K. Snick et al., 'The Spontaneous Pregnancy Prognosis in Untreated Subfertile Couples: The Walcheren Primary Care Study', (1997) *Human Reproduction*, 12(7), 1582–1588; E. R. te Velde et al., 'Variation in Couple Fecundity and Time to Pregnancy: an Essential Concept in Human Reproduction', (2000) *Lancet*, 355(9219), 1928–1929.

<sup>4</sup> E. G. Papanikolaou et al., 'Live Birth Rate Is Significantly Higher after Blastocyst Transfer than after Cleavage-Stage Embryo Transfer When at Least Four Embryos Are Available on Day 3 of Embryo Culture. A Randomized Prospective Study', (2005) *Human Reproduction*, 20(11), 3198–3203.

<sup>5</sup> K. Stocking et al., 'Are Interventions in Reproductive Medicine Assessed for Plausible and Clinically Relevant Effects? A Systematic Review of Power and Precision in Trials and Meta-Analyses', (2019) *Human Reproduction*, 34(4), 659–665.

but it would not be unreasonable to describe treatment for infertility as one of the least evidence-based branches of medicine.<sup>6</sup>

In addition to an absence of evidence, another important feature of reproductive medicine is patients' willingness to 'try anything'. Inadequate NHS funding means that most fertility treatment is provided in the private sector, with patients paying 'out of pocket' for every aspect of their IVF cycle, from the initial consultation to scans, drugs and an ever-increasing list of 'add-on' services, such as assisted hatching; preimplantation genetic screening; endometrial scratch; time-lapse imaging; embryo glue and reproductive immunology. The combination of a poor evidence base, commercialisation and patients' enthusiasm for anything that might improve their chance of success, results in a 'perfect storm' in which dubious and sometimes positively harmful treatments are routinely both under-researched and oversold.

Added to this, although clinics must have a licence from the Human Fertilisation and Embryology Authority (HFEA) before they can offer IVF, the HFEA does not have the power to license, or refuse to license the use of add-on treatments. Its powers are limited to ensuring that, before a patient receives treatment in a licensed centre, patients are provided with 'such relevant information as is proper', and that 'the individual under whose supervision the activities authorised by a licence are carried on' (referred to as the Person Responsible), ensures that 'suitable practices' are used in the clinic.<sup>7</sup> In this chapter, I will argue that, although giving patients information about the inadequacy of the evidence-base behind add-on treatments is important and necessary, this should not be regarded as a mechanism through which their inappropriate use can be controlled. Instead, it may be necessary for the HFEA to categorise non-evidence-based and potentially harmful treatments as 'unsuitable' practices, which should not be provided at all, rather than as treatments that simply need to be accompanied by a health warning.

### 38.2 A PERFECT STORM?

In order to be appropriately statistically powered, it has been estimated that a trial of a new fertility intervention should recruit at least 2610 women.<sup>8</sup> Trials of this size are exceptional, however, and it is much more common for smaller statistically underpowered trials to be carried out. Nor does meta-analysis of these smaller trials necessarily offer a solution, in part because their outcomes are not always reported consistently, and the meta-analyses themselves may not be sufficiently large to overcome the limitations of the smaller studies.<sup>9</sup>

Fertility patients are often keen to 'try something new', even if it has not been proven to be safe and effective in a large-scale RCT.<sup>10</sup> IVF patients are often in a hurry. Most people take their fertility for granted, and after years of trying to prevent conception, they assume that conception

<sup>6</sup> Archie Cochrane famously said that obstetrics deserved 'the wooden spoon' for being the least scientific medical speciality. A. L. Cochrane, '1931–1971: A Critical Review with Particular Reference to the Medical Profession' in G. Teeling-Smith and N. E. J. Wells (eds), *Medicines for the Year 2000* (London: Office of Health Economics, 1979), pp. 2–12.

<sup>7</sup> Human Fertilisation and Embryology Act 1990, sections 13(6), 17(1) and 17(1)(d).

<sup>8</sup> J. Wilkinson et al., 'Reproductive Medicine: Still More ART than Science?', (2019) *British Journal of Obstetrics and Gynaecology*, 126(2), 138–141.

<sup>9</sup> Stocking et al., 'Interventions in Reproductive Medicine'; J. M. N. Duffy et al., 'Core Outcome Sets in Women's and Newborn Health: A Systematic Review', (2017) *British Journal of Obstetrics and Gynaecology*, 124(10), 1481–1489.

<sup>10</sup> J. Rayner et al., 'Australian Women's Use of Complementary and Alternative Medicines to Enhance Fertility: Exploring the Experiences of Women and Practitioners', (2009) *BMC Complementary and Alternative Medicine*, 9 (1), 52.

will happen soon after they stop using contraception. By the time a woman realises that she may need medical assistance in order to conceive, her plan to start a family will already have been delayed for a year or more. At the same time, women's age-related fertility decline means that they are often acutely aware of their need to start treatment as soon as possible.

Although, in theory, fertility treatment is available within the NHS, it is certainly not available to everyone who needs it. The National Institute for Health and Care Excellence's (NICE) 2013 clinical guideline recommended that the NHS should fund three full cycles of IVF (i.e. a fresh cycle followed by further cycles using the frozen embryos) for women under 40 years old, and one full cycle for women aged 40–42, who must additionally not have received IVF treatment before and not have low ovarian reserve.<sup>11</sup> Implementation of this NICE guideline is not mandatory, however, and in 2018 it was reported that only 13 per cent of Clinical Commissioning Groups (CCGs) provide three full cycles of IVF to eligible women; 60 per cent offer one NHS-funded cycle – most of which fund only one fresh cycle – and 4 per cent provide no cycles at all.<sup>12</sup>

The majority of IVF cycles in the UK are self-funded,<sup>13</sup> and although the average cycle costs around £3350,<sup>14</sup> costs of more than £5000 per cycle are not uncommon. As well as simply wanting to have a baby, IVF patients are therefore commonly also under considerable financial pressure to ensure that each IVF cycle has the best possible chance of success. In these circumstances, it is not surprising that patients are keen to do whatever they can to increase the odds that a single cycle of IVF will lead to a pregnancy and birth.

One of the principal obstacles to making single embryo transfer the norm was that, for many patients, the birth of twins was regarded as an ideal outcome.<sup>15</sup> Most patients want to have more than one child, so if one cycle of treatment could create a two-child family, this appeared to be a 'buy one, get one free' bargain. In order to persuade women of the merits of the 'one at a time' approach, it was not enough to tell them about the risks of multiple pregnancy and multiple birth, both for them and their offspring. Many women are prepared to undergo considerable risks in pursuit of a much-wanted family. Instead, the 'one at a time' campaign emphasised the fact that a properly implemented 'elective single embryo transfer' policy did not reduce birth rates, and tried to persuade NHS funders that a full cycle of IVF was not just one embryo transfer, but that it should include the subsequent frozen embryo transfers.<sup>16</sup>

Not only are patients understandably keen to try anything that might improve their chance of success, they are also paying for these extra services out of pocket. As consumers, we are used to paying more to upgrade to a better service, so this additional expense can appear to be a 'sign of quality'.<sup>17</sup> Rather than putting patients off, charging them several hundred pounds for endometrial scratch and assisted hatching may make these additional services appear even more desirable. New techniques often generate extensive media coverage, leading patients actively to seek

<sup>11</sup> National Institute for Health and Care Excellence, 'Fertility: Assessment and Treatment for People with Fertility Problems', (NICE, 2013).

<sup>12</sup> See further [www.fertilityfairness.co.uk](http://www.fertilityfairness.co.uk).

<sup>13</sup> Human Fertilisation and Embryology Authority, 'State of the Fertility Sector 2016–7', (HFEA, 2017).

<sup>14</sup> S. Howard, 'The Hidden Costs of Infertility Treatment', (2018) *British Medical Journal*, 361.

<sup>15</sup> G. M. Hartshorne and R. J. Lilford, 'Different Perspectives of Patients and Health Care Professionals on the Potential Benefits and Risks of Blastocyst Culture and Multiple Embryo Transfer', (2002) *Human Reproduction*, 17(4), 1023–1030.

<sup>16</sup> P. Braude, 'One Child at a Time: Reducing Multiple Births through IVF, Report of the Expert Group on Multiple Births after IVF', (Expert Group on Multiple Births after IVF, 2006).

<sup>17</sup> Wilkinson et al., 'Reproductive Medicine'.

out clinics that offer the new treatment.<sup>18</sup> Clinics that offer the non-evidence-based new intervention are therefore able to say that they are simply responding to patient demand.

As well as the appeal of expensive high-tech interventions, patients are also attracted to simple and apparently plausible explanations for IVF failure. If an IVF cycle does not lead to a pregnancy because the embryo fails to attach to the lining of the woman's uterus, it is easy to understand why patients might be persuaded of the benefits of 'embryo glue', in order to increase adhesion rates. Alternative therapists have also flourished in this market: acupuncturists are said to be able to 'remove blocks to conception'; and hypnotherapists treat women 'with a subconscious fear of pregnancy'.<sup>19</sup> In practice, however, the evidence indicates not only that complementary and alternative medicine (CAM) does not work, but that live birth rates are lower for patients who use CAM services.<sup>20</sup>

Perhaps the most egregious example of an apparently simple and plausible explanation for IVF failure being used to market a non-evidence-based and potentially harmful intervention is reproductive immunology. The existence of the unfortunately named 'natural killer cells' in the uterus has helped to persuade patients that these cells might – unless identified by expensive tests and suppressed by expensive medications – 'attack' the embryo and prevent it from implanting. News stories with headlines like 'The Killer Cells That Robbed Me of Four Babies'<sup>21</sup> and 'My Body Tried to Kill My Baby'<sup>22</sup> suggest a very direct link between NK cells and IVF failure. The idea that the embryo is a genetically 'foreign' body that the woman's uterine cells will attack, unless their immune response is suppressed, sounds plausible,<sup>23</sup> and as Datta et al. point out, 'couples seeking a reason for IVF failure find the rationale of immune rejection very appealing'. It has no basis in fact, however.<sup>24</sup>

There is no evidence that natural killer cells have any role in causing miscarriage; rather despite their name, they may simply help to regulate the formation of the placenta. As Moffett and Shreeve explain, regardless of this lack of evidence, 'a large industry has grown up to treat women deemed to have excessively potent uterine "killers"'.<sup>25</sup> In addition to the absence of RCTs establishing that reproductive immunology increases success rates, the medicines used – which include intravenous immunoglobulins, TNF- $\alpha$  inhibitors, granulocyte-colony stimulating factor, lymphocyte immune therapy, leukaemia inhibitory factor, peripheral blood mononuclear cells, intralipids, glucocorticoids, vitamin D supplementation and steroids – may pose a risk of significant harm to women.<sup>26</sup>

The lack of evidence for reproductive immunology, and the existence of significant risks, has been known for some time. In 2005, Rai and others described reproductive immunology as

<sup>18</sup> A. K. Datta et al., 'Add-Ons in IVF Programme – Hype or Hope?', (2015) *Facts, Views & Vision in ObGyn*, 7(4), 241–250.

<sup>19</sup> C. N. M. Renckens, 'Alternative Treatments in Reproductive Medicine: Much Ado About Nothing: "The Fact That Millions of People Do Not Master Arithmetic Does Not Prove That Two Times Two Is Anything Else than Four": W. F. Hermans', (2002) *Human Reproduction*, 17(3), 528–533.

<sup>20</sup> J. Boivin and L. Schmidt, 'Use of Complementary and Alternative Medicines Associated with a 30% Lower Ongoing Pregnancy/Live Birth Rate during 12 Months of Fertility Treatment', (2009) *Human Reproduction*, 24(7), 1626–1631.

<sup>21</sup> R. Barber, 'The Killer Cells That Robbed Me of Four Babies', *Daily Mail* (2 January 2011).

<sup>22</sup> J. Fricker, 'My Body Tried to Kill My Baby', *Daily Mail* (2 July 2007).

<sup>23</sup> See, for example, H. Shehata, quoted in BBC News, 'Baby Born to Woman Who Suffered 20 Miscarriages', *BBC News* (17 January 2014): 'We found that some women's natural killer cells are so aggressive they attack the pregnancy, thinking the foetus is a foreign body'.

<sup>24</sup> Datta et al., 'Add-Ons in IVF Programme'.

<sup>25</sup> A. Moffett and N. Shreeve, 'First Do No Harm: Uterine Natural Killer (NK) Cells in Assisted Reproduction', (2015) *Human Reproduction*, 30(7), 1519–1525.

<sup>26</sup> Datta et al., 'Add-Ons in IVF Programme'.

‘pseudo-science’, pointing out that ‘Not only is there no evidence base for these interventions, which are potentially associated with significant morbidity, the rationale for their use may be false’.<sup>27</sup> The HFEA’s most recent advice to patients is also clear and unequivocal:

There is no convincing evidence that a woman’s immune system will fail to accept an embryo due to differences in their genetic codes. In fact, scientists now know that during pregnancy the mother’s immune system works with the embryo to support its development. Not only will reproductive immunology treatments not improve your chances of getting pregnant, there are risks attached to these treatments, some of which are very serious.<sup>28</sup>

Despite this, patients continue to be persuaded by a simple, albeit false, explanation for IVF failure, and by ‘evidence’ from fertility clinics that is better described as anecdote. The Zita West fertility clinic blog, for example, contains accounts from satisfied ex-patients with headlines like ‘I Was Born to Be a Mum and Couldn’t Have Done It Without Reproductive Immunology’.<sup>29</sup> It is not uncommon for clinics’ websites to ‘speak of “dreams” and “miracles”, rather than RCTs’<sup>30</sup> Spencer and others analysed 74 fertility centre websites, and found 276 claims of benefit relating to 41 different fertility interventions, but with only 16 published references to support these, of which only five were high level systematic reviews.<sup>31</sup>

From the point of view of a for-profit company selling fertility services, why bother to do expensive large-scale RCTs, when it is possible to sell a new therapy to patients in the absence of such trials? If patients do not care about the lack of evidence, and are happy to rely upon a clinician’s anecdotal report that X therapy has had some success in their clinic, the clinic has no incentive to carry out trials, which may indicate that X therapy does not increase live birth rates.

A free market in goods and services relies upon consumers choosing not to buy useless products. If a mobile phone company were to produce a high-tech new phone that does not work, then after an initial flurry of interest in a shiny new product, its failings would become apparent and the market for it would disappear. Because there can be no guarantee that any cycle of IVF will lead to the birth of a baby, and almost every cycle is more likely to fail than it is to work, it is much harder for consumers of fertility services to tell whether an add-on service is worth purchasing. Rather than relying on individual patients ‘voting with their feet’ in order to crowd out useless interventions, it may be important instead for an expert regulator to choose for them.

### 38.3 REGULATING ADD-ON SERVICES

There are three mechanisms through which the provision of add-on services in the fertility clinic is regulated. First, if it involves the use of a medicinal product, that product must have a product licence from the European Medicines Agency or the Medicines and Healthcare products Regulatory Agency. The Human Medicines Regulations 2012 specify that, before a new medicine can receive a product licence, the licensing authority must be satisfied that ‘the applicant

<sup>27</sup> R. Rai et al., ‘Natural Killer Cells and Reproductive Failure – Theory, Practice and Prejudice’, (2005) *Human Reproduction*, 20(5), 1123–1126.

<sup>28</sup> HFEA, ‘Treatment Add-On’, (HFEA, 2019).

<sup>29</sup> ‘I was Born to Be a Mum – And Couldn’t Have Done It without Reproductive Immunology’, (Zita West), [www.zitawest.com/i-was-born-to-be-a-mum-and-couldnt-have-done-it-without-reproductive-immunology/](http://www.zitawest.com/i-was-born-to-be-a-mum-and-couldnt-have-done-it-without-reproductive-immunology/).

<sup>30</sup> J. Hawkins, ‘Selling ART: An Empirical Assessment of Advertising on Fertility Clinics’ Websites’, (2013) *Indiana Law Journal*, 88(4), 1147–1179.

<sup>31</sup> E. A. Spencer et al., ‘Claims for Fertility Interventions: A Systematic Assessment of Statements on UK Fertility Centre Websites’, (2016) *BMJ Open*, 6(11).

has established the therapeutic efficacy of the product to which the application relates', and 'the positive therapeutic effects of the product outweigh the risks to the health of patients or of the public associated with the product'.<sup>32</sup> In short, it must be established that the product works for the indication for which the product licence is sought, and that its benefits outweigh its risks.

In practice, however, the use of medicines as add-ons to fertility treatment generally involves their 'off-label' use. Reproductive immunology, for example, may involve the use of steroids, anticoagulants and monoclonal antibodies. Although efficacy and a positive risk–benefit profile may exist for these medicines' licensed use, this is not the same as establishing that they work or are safe for their off-label use in the fertility clinic. There are comparatively few controls over doctors' freedom to prescribe drugs off-label, even though, when there has not been any assessment of the safety or efficacy of a drug's off-label use, it may pose an unknown and unjustifiable risk of harm to patients.

The General Medical Council (GMC) has issued guidance to doctors on the off-label prescription of medicines which states that:

You should usually prescribe licensed medicines in accordance with the terms of their licence. However, you may prescribe unlicensed medicines where, on the basis of an assessment of the individual patient, you conclude, for medical reasons, that it is *necessary* to do so to meet the specific needs of the patient (my emphasis).<sup>33</sup>

The guidance goes on to set out when prescribing unlicensed medicines could be said to be 'necessary':

- a. There is no suitably licensed medicine that will meet the patient's need . . .
- b. Or where a suitably licensed medicine that would meet the patient's need is not available. This may arise where, for example, there is a temporary shortage in supply; or
- c. The prescribing forms part of a properly approved research project.<sup>34</sup>

Doctors must also be satisfied that be 'there is sufficient evidence or experience of using the medicine to demonstrate its safety and efficacy', and patients must be given sufficient information to allow them to make an informed decision.<sup>35</sup> It is possible that a doctor who prescribed medications off-label could have his fitness to practise called into account, although, in practice, it seems likely that clinicians will simply maintain that these medicines 'meet the patient's need', and that they have sufficient experience within their own clinic to 'demonstrate safety and efficacy'.

Second, before receiving treatment services in a licensed centre, section 13(6) of the Human Fertilisation and Embryology Act 1990 specifies that patients must be provided with 'such relevant information as is proper', and that they must give consent in writing.<sup>36</sup> Although add-ons are not licensable treatments, it could be said that the clinician's statutory duty to give patients clear and accurate information extends to the whole course of treatment they receive in the clinic, not just to the treatment for which an HFEA licence is necessary. Indeed, the HFEA's Code of Practice specifies that:

<sup>32</sup> Human Medicines Regulations 2012, 58(4)(a) and 58(4)(b).

<sup>33</sup> General Medicine Council, 'Good Practice in Prescribing and Managing Medicines and Devices', (GMC, 2013), para 68.

<sup>34</sup> *Ibid.*, para 69.

<sup>35</sup> *Ibid.*, paras 70(a) and 71.

<sup>36</sup> Human Fertilisation and Embryology Act 1990, Schedule 3, para 1.

Before treatment is offered, the centre should give the woman seeking treatment and her partner, if applicable, information about . . . fertility treatments available, including any treatment add ons which may be offered and the evidence supporting their use; any information should explain that treatment add ons refers to the technologies and treatments listed on the treatment add ons page of the HFEA website.<sup>37</sup>

The Code of Practice also requires centres to give patients ‘a personalised costed treatment plan’, which should ‘detail the main elements of the treatment proposed – including investigations and tests – the cost of that treatment and any possible changes to the plan, including their cost implications’.<sup>38</sup> Before offering patient an add-on treatment, clinics should therefore be open and honest with patients about the risks, benefits and costs of the intervention.

In practice, however, patients will not necessarily be put off by underpowered trial data, especially when more optimistic anecdotal accounts of success are readily available online. In order to try to counter the circulation of misinformation about treatment add-ons, the HFEA has recently instituted a ‘traffic light’ system that is intended to provide clear and unambiguous advice to patients. At the time of writing, no add-on is green. Most are either amber (that is, ‘there is a small or conflicting body of evidence, which means further research is still required and the technique cannot be recommended for routine use’), or red (that is, ‘there is no evidence to show that it is effective and safe’). The HFEA further recommends that patients who want more detailed information ‘may want to contact a clinic to discuss this further with a specialist’.<sup>39</sup>

It is, however, unsatisfactory to rely upon informed patient choice as a mechanism to control the over-selling of unproven add-on treatments. The fertility industry has ‘a pronounced predilection for over-diagnosis, over-use and over-treatment’, and the widespread adoption of a ‘right to try’ philosophy in practice translates into clinics profiting from the sale of unproven treatments.<sup>40</sup> For example, the HFEA gives intrauterine culture – in which newly fertilised eggs are placed in a device inside the woman’s womb – an amber rating, and informs prospective patients:

There’s currently no evidence to show that intrauterine culture improves birth rates and is safe. This is something you may wish to consider if you are offered intrauterine culture at an additional cost.

It could instead be argued that the fact that a treatment is expensive and is not known to be either safe or effective is not merely something that patient should ‘consider’ when deciding whether to purchase it, but rather is a reason not to make that treatment available outside of a clinical trial.

Third, while the HFEA does not license add-on services, Persons Responsible are under a duty to ensure that only ‘suitable practices are used in the course of the activities’.<sup>41</sup> If the HFEA were to decide that those add-on services that it ranks as red are not suitable practices, then clinicians should not use them in the clinic. It has not (yet) done this.

<sup>37</sup> HFEA, ‘9th Code of Practice’, (HFEA, 2019), para 4.5.

<sup>38</sup> *Ibid.*, para 4(9).

<sup>39</sup> HFEA, ‘Treatment Add-Ons’.

<sup>40</sup> Wilkinson et al., ‘Reproductive Medicine’.

<sup>41</sup> Human Fertilisation and Embryology Act 1990, section 17(1)(d).

### 38.4 WON'T PATIENTS GO ELSEWHERE?

Given patients' interest in add-on services, many of the 70 per cent of UK clinics that offer at least one of these treatments claim to be responding to patient choice.<sup>42</sup> Reputable clinicians maintain that if they cease to offer add-on services, patients are likely to go instead to clinics that do provide these treatments, either within the UK – where a clinic does not need a licence from the HFEA if it is only providing add-on services – or overseas.<sup>43</sup> If patients are going to pay for these treatments elsewhere anyway, then, so the argument goes, it is better to provide them in safe, hygienic, regulated clinics, rather than abandoning patients to the wild west of unregulated fertility services.

The easiest way to see why this argument should be dismissed is to imagine that it is being made about a different sort of non-evidence based treatment, such as stem cell therapies for the treatment of spinal injury. Although stem cell therapies hold very great promise for the treatment of a wide range of conditions, most are still at the experimental stage. That does not stop unregulated clinics overseas from marketing stem cell therapies for the treatment of a wide range of conditions, and as a miraculous cure for ageing.<sup>44</sup>

If a UK doctor was to justify injecting stem cells into a patient's spinal column, on the grounds that, if he did not do so, the patient would be likely to travel to China for unproven stem cell treatment, it could be predicted that the GMC might be likely to investigate his fitness to practise. The argument that, if he did not offer unproven and unsafe treatment in the UK, patients might choose to undergo the same unsafe treatment in a foreign clinic, would be likely to be given short shrift.

### 38.5 CONCLUSION

It is important to remember that add-on treatments are not simply a waste of patients' money, though they are often that as well. Many add-on treatments are also risky. Despite this, patients are enthusiastic purchasers of additional services for which there is little or no good evidence. In such circumstances, where the lack of robust clinical trial data does not appear to dent patients' willingness to buy add-on treatments, there is little 'bottom-up' incentive to carry out large-scale RCTs.

The HFEA's information for patients is clear and authoritative, but it is not the only information that patients will see before deciding whether to pay for additional treatment services. Patients embarking upon fertility treatment also seek out information from other patients and from a wide variety of online sources. It is increasingly common for ill-informed 'discourses of hope' about unproven treatments to circulate in blogs and in Facebook groups, coexisting and competing with evidence-based information from scientists and regulators.<sup>45</sup> Fertility patients often report doing their own 'research' before embarking on treatment, and this generally means

<sup>42</sup> A. J. Rutherford, 'Should the HFEA Be Regulating the Add-On treatments for IVF/ICSI in the UK? FOR: Regulation of the Fertility Add-On Treatments for IVF', (2017) *British Journal of Obstetrics & Gynaecology*, 124(12), 1848.

<sup>43</sup> W. L. Ledger, 'The HFEA Should Be Regulating Add-On Treatments for IVF/ICSI', (2017) *British Journal of Obstetrics & Gynaecology*, 124(12), 1850–1850.

<sup>44</sup> D. Archard, 'Ethics of Regenerative Medicine and Innovative Treatments', (Nuffield Council of Bioethics, 13 October 2017), [www.nuffieldbioethics.org/blog/ethics-regenerative-medicine-innovative-stem-cell-treatment](http://www.nuffieldbioethics.org/blog/ethics-regenerative-medicine-innovative-stem-cell-treatment).

<sup>45</sup> A. Petersen et al., 'Stem Cell Miracles or Russian Roulette?: Patients' Use of Digital Media to Campaign for Access to Clinically Unproven Treatments', (2016) *Health, Risk and Society*, 17(7–8), 592–604.



gathering material online, from sources where the quality and accuracy of information may be distinctly variable.<sup>46</sup>

In this perfect storm, it is unreasonable to expect patients to be able to protect themselves from exploitation through the application of the principle of *caveat emptor*.<sup>47</sup> On the contrary, what is needed instead is a clear message from the regulator that the routine selling of unproven treatments should not just prompt patients to ask additional questions, but that these treatments should not be sold in the first place. Of course, it is important that reproductive medicine does not stand still, and that new interventions to improve the chance of success are developed. But these should first be tried in the clinic as part of an adequately powered clinical trial. Trial participants must be properly informed that the treatment is still at the experimental stage, and they should not be charged to participate. The GMC also has a role to play in investigating the fitness to practise of doctors who routinely sell, for profit, treatments that are known to be risky and ineffective. As Moffett and Sheeve put it: 'it is surely no longer acceptable for licensed medical practitioners to continue to administer and profit from potentially unsafe and unproven treatments, based on belief and not scientific rationale'.<sup>48</sup>

<sup>46</sup> E. Jackson et al., 'Learning from Cross-Border Reproduction', (2017) *Medical Law Review*, 25(1), 23–46.

<sup>47</sup> Ledger, 'HFEA Should Be Regulating Add-On Treatments'.

<sup>48</sup> Moffett and Shreeve, 'First Do No Harm'.