

Executive Summary

Multiple birth is the single biggest risk to the health and welfare of children born after in vitro fertilisation (IVF). It can be effectively reduced by transferring only one embryo to those women who are most at risk of having twins. The time has come to make this change to IVF practice in the UK.

This report is the outcome of a series of discussions the Expert Group on Multiple Births after IVF has had since the autumn of 2005. The Human Fertilisation and Embryology Authority (HFEA) set up the independent expert group in response to rising concerns about the incidence of multiple births after IVF/ICSI

(*in vitro* fertilisation and intra-cytoplasmic sperm injection). The group reviewed the available international and national data on multiple births after IVF, health and psychosocial outcomes for twins and their families, and the experience with single embryo transfer gathered in some European countries. It makes recommendations to the HFEA and other organisations that have a role to play in reducing the high incidence of multiple births after IVF.

The most important findings of the group are summarised below.

Incidence of multiple births after IVF/ICSI

- Currently, about 1 in 4 IVF pregnancies leads to the birth of twins. The risk is more than ten times higher than would be expected after spontaneous (natural) conception.
- The number of IVF triplets has decreased significantly since HFEA guidance on two-embryo transfer was tightened.¹
- Although the incidence of identical twinning is also increased after IVF, most IVF twins are non-identical, i.e. they come from two different embryos that were simultaneously transferred to and implanted in the woman's womb.
- Non-IVF fertility treatments (for example IUI – intra uterine insemination) also lead to increased multiple pregnancy rates, but the exact incidence is harder to estimate since these treatments and their outcomes are not registered centrally.

Problems of multiple pregnancy and birth

- Twin pregnancies carry much higher obstetric risks for women: miscarriage, pre-eclampsia, gestational diabetes, haemorrhage and instrumental delivery are all much more common in women carrying twins.
- The biggest risk factor for twins is prematurity and low birth weight, which often necessitates hospitalisation at the beginning of life, and is linked to a significant risk of neonatal death of one or both twins, beside longer term health and cognitive effects. For example twins are at least six times more likely than singletons to suffer from cerebral palsy.

- There are also well-documented problems for families of twins that range from financial hardship to a higher incidence of maternal depression and marital problems.

All these risks are well documented and can no longer be ignored.

Redefining success

- A multiple pregnancy should not be regarded as the ideal outcome of IVF treatment. The problem is not that two healthy babies might be born, but that too often adverse outcomes occur for the mother and one or both of the babies.
- IVF clinicians, embryologists, nurses and counsellors, the professional bodies, patient organisations and IVF patients themselves need to acknowledge that IVF children (like all other children) are entitled to the best possible start in life: their chances of being born as full term singletons with a normal birth weight need to be maximised.

Elective single embryo transfer (eSET) for good-prognosis IVF patients

- The only way to reduce the multiple birth rate after IVF is to transfer only one embryo to those women at most risk of having twins. Overall, eSET needs to be made the norm in IVF treatment.
- International datasets show that single embryo transfer policies can be introduced without significantly reducing pregnancy rates by targeting good prognosis patients (for example relatively young women, women who have not had a number of previous failed IVF attempts), and by ensuring effective embryo freezing programmes.
- The decision as to how many patients should receive one embryo, is a balance between twin rate and success in achieving a pregnancy. Based on large national data sets we conclude that offering eSET to around 50% of IVF patients will lead to a twin rate of less than 10%. This is, for now, an acceptable balance between reducing the number of twins born after IVF and maintaining IVF patients' chances to conceive.
- In order to maintain pregnancy rates it is important that effective cryopreservation programmes accompany eSET, such that good quality additional embryos are frozen and available for transfer should the fresh eSET cycle be unsuccessful.
- Where more than one good quality blastocyst is available for transfer on day 5 or 6 of culture, the case for single blastocyst transfer is overwhelming.

Difficulties for making the transition

We are aware that making this transition is not going to be easy. There are obstacles to progress, but these can and must be overcome in order to make treatments safer for IVF patients and their children.

- Those countries that have introduced eSET policies successfully all have fertility sectors that work differently from the UK: generally patients have better access to publicly funded IVF treatments, which directly influences patients' attitudes to eSET, and their patient profile may be different to the UK. Nevertheless, even if the international evidence is not wholly transferable to the UK, the broad trends are helpful in modelling what is likely to happen in the UK context.
- The failure to implement fully the National Institute for Health and Clinical Excellence (NICE) clinical guideline on fertility treatments in England and Wales (and the equivalent rationing of NHS fertility services in Scotland and Northern Ireland), and the consequent lack and inconsistency of NHS funded IVF in the whole of the UK, is the single greatest obstacle to the introduction of eSET policies in the UK.
- The refusal of many Primary Care Trusts (PCTs) to include cryopreservation in a funded cycle (as required by NICE) further exacerbates the problem. Patients and their clinicians are likely to resist even the smallest reduction in pregnancy rates if they believe that this is their sole chance of a pregnancy.

Recommendations for the HFEA

The continuing escalation in twin births means that the status quo is no longer an option. In order to change the practices of the UK fertility sector quickly and consistently, new HFEA guidance on embryo transfers is required urgently. Based on the previous experience of limiting the number of embryos for transfer to two, we do not see that professional guidelines alone can convince the sector of the need for change.

We have identified two main policy options for the HFEA to consider, both are based on the assumption that eSET cycles should be the norm for IVF:

- Setting clinics an overall maximum proportion of twin births that should not be exceeded (for example 5 to 10%), which can be achieved stepwise over time;
- Setting criteria for the group of patients (those with the best prognosis and thus the highest risk of multiple pregnancy) who should be offered eSET cycles in the first instance.

The HFEA collects and publishes information about IVF treatment outcomes ('success rates'). These results are inevitably taken by patient, media and public bodies as league tables. The presence of league tables has a strong effect on the practice of IVF in the UK. Clinics tend to transfer higher numbers of embryos to achieve the highest possible success rates. The flow of patients to both the private and NHS sectors is influenced by the position of clinics in the league table.

Furthermore, the way this data is collected and reported – separating live births per fresh cycle started from frozen follow-on cycles, rather than combining the two into cumulative birth rates per egg collection – does not ease the transition to eSET. League tables do not take regard of the different patient populations clinics might serve, nor do they acknowledge the adverse impact of multiple pregnancies.

- We recommend that the HFEA evaluate how better to collect and publish outcome data for the UK sector in order to represent the incidence of multiple births as a complication, rather than a success, and to reduce incentives for widespread use of double embryo transfer. For example, it could consider publishing cumulative birth rates including frozen follow-on cycles in order to encourage the transition to eSET as the norm.

Recommendations for other organisations

Progress will be difficult if the HFEA acts in isolation. Other key organisations have an important role to play in assisting the transition to safer IVF based on eSET.

Clinicians and IVF professionals

IVF professionals need to acknowledge the problems they create for some IVF children and their families by their continued use of multiple embryo transfer and the subsequent high incidence of twins.

- Clinics should audit their data in order to identify the patients and embryos with the highest chance of conceiving / implantation and thus the highest risk of multiple pregnancy.
- They should develop good patient and embryo selection protocols for eSET cycles and need to offer effective cryopreservation programmes.
- They should educate themselves about the incidence and significant risks of multiple pregnancy, and need to communicate these risks clearly to their patients.

The NHS

NHS commissioners need to address the inconsistencies and overall lack of access to the recommended three full (fresh and frozen) cycles of IVF in order to take the pressures out of the UK fertility sector that distort best practice and limit patient choice.

- Since the public health burden of multiple birth falls on the NHS and then other publicly funded services, commissioners should consider the potential savings (for example in neonatal intensive care – a notoriously overstretched service) that could be realised were more IVF patients offered eSET cycles.
- The twin rate of clinics should be taken into account when the NHS commissions fertility services.
- A statement from the Department of Health about the public health benefits of eSET and subsequent lower twin rates, and clarity on the priority to be ascribed to NHS funded IVF services, would help to raise awareness and a sense of urgency amongst local commissioners.

The professional bodies and patient groups

- The professional bodies (British Fertility Society, Association of Clinical Embryologists, Royal College of Obstetricians and Gynaecologists) should work together to provide guidelines that would help clinics identify which patients and which embryos are most appropriate for eSET.
- Clinicians, counsellors, Royal College of Nursing fertility nurses, the Multiple Births Foundation, patient groups like Infertility Network UK and the HFEA itself need to evaluate and improve patient information about the risks of multiple pregnancy and birth.