

## Authority Paper

<b>Committee:</b>	Authority
<b>Meeting Date:</b>	9 December 2009
<b>Agenda Item:</b>	5
<b>Paper Number:</b>	527
<b>Paper Title:</b>	Multiple Births: Moving Towards a Year 2 Target
<b>Author:</b>	Helen Richens (Policy)
<b>For information or decision?</b>	Information
<b>Resource Implications:</b>	Accounted for in business plan
<b>Implementation</b>	December 2009: Authority discussion January 2010: Authority decide Year 2 maximum multiple birth rate Revised General Directions issued to clinics April 2010: Year 2 of policy comes into force
<b>Communication</b>	Outcome of Authority discussion will be communicated to Multiple Births Stakeholder Group in December 2009/January 2010 Year 2 maximum multiple birth rate will be communicated to clinics in January 2010
<b>Organisational Risk</b>	Medium
<b>Recommendation to the Committee:</b>	Members are asked to discuss: - <i>evaluation</i> of Year 1 of the multiple births policy - <i>approach to</i> Year 2 of the multiple births policy
<b>Annexes</b>	Annex A: Timeline of multiple births policy Annex B: Analysis of 2009 data

## 1. Introduction

- 1.1. The single biggest risk of fertility treatment is multiple pregnancy. In November 2007, after a public consultation, the HFEA decided on the following policy to reduce the risk of multiple births from IVF treatment:
  - A maximum multiple birth rate that clinics should not exceed,
  - This will be lowered periodically, with an overall aim of no more than 10% multiple births out of all live births,
  - Clinics should have their own 'multiple births minimisation strategies' setting out how they will not exceed the maximum multiple birth rate for that year, and
  - The policy will be part of a wider national strategy to reduce the risk of multiple births from fertility treatment, managed by an external Multiple Births Stakeholder Group<sup>1</sup>.
  
- 1.2. In May 2008 the Authority decided the first maximum multiple birth rate should be 24% (ie, no more than 24% of a clinic's annual live births from IVF treatment should be multiple births). This came into force in January 2009 in Year 1 of the policy. A timeline of the development and implementation of the multiple births policy is set out in Annex A.
  
- 1.3. In January 2010 Authority members will be asked to decide the second maximum multiple birth rate for clinics for Year 2 of the policy. The aim of this paper is to provide Members with an opportunity to review the first year of the policy and discuss the possible approaches for next year, prior to the January meeting. It presents:
  - the current context around the multiple births policy,
  - an evaluation of Year 1 of the multiple births policy, and
  - strengths and weaknesses of possible approaches to Year 2 of the policy.
  
- 1.4. The key findings of this paper are:
  - All clinics have submitted their multiple births minimisations strategies,
  - Clinics were initially cautious when developing patient selection criteria and implementing their strategies,
  - Though the overall multiple birth rate for 2009 is predicted to be around 24%, there appears to be a decrease in the predicted multiple birth rate for women 35 and under,
  - Embryo quality and grading, embryo freezing policies and consistent patient information are important for an effective strategy,
  - The majority of clinics are now gaining in confidence, revising their strategies and giving stronger messages to patients, and
  - Some clinics are struggling with patient uptake of single embryo transfer, particularly if NHS funding arrangements are unsupportive.

---

<sup>1</sup> For the list of Members and the Group's mission statement see <http://www.oneatatime.org.uk/116.htm>

## 2. What is the current context around the multiple births policy?

- 2.1. The multiple births policy encourages clinics to reduce their multiple birth rate by transferring only one embryo (single embryo transfer) in patients they have identified as most likely to conceive twins at their clinic. Many external factors affect the uptake of single embryo transfer (SET) and the rate of multiple births from fertility treatment, for example NHS funding, professional body guidance and patient information. The HFEA's multiple birth policy is just one strand of work of a national multiple births strategy. The other members of the Multiple Births Stakeholder Group, who represent professional bodies, patients' organisations and NHS Commissioners, work on issues that are outside the HFEA's remit.
- 2.2. Some of the external factors that influence the effectiveness of the multiple births policy are explored below. This section will help Members place the evaluation of the first year of the policy in context in order to have a meaningful discussion about how implementation of the policy will move forward.

### ***NHS fertility commissioning***

- 2.3. Approximately 20 – 25% of fertility treatment is provided by the NHS. NHS funding has a big impact on patients' willingness to have SET. NICE recommends that three full cycles (fresh and subsequent frozen embryo transfers) should be provided to eligible patients. This encourages patients to opt for SET because they will be able to have any frozen embryos transferred at a later date if they are unsuccessful in their first fresh cycle, or go on to have further fresh treatment cycles if necessary. Transferring frozen embryos is a much less invasive procedure for patients as it does not involve ovarian stimulation or egg collection.
- 2.4. The number of cycles and the criteria for treatment varies widely throughout the UK. Figures<sup>2</sup> from the Department of Health show that currently, of the Primary Care Trusts (PCTs) in *England*:
- 30% are funding three cycles (the majority fund full cycles with a very small percentage funding only fresh cycles),
  - 23% are funding two cycles (approximately 4% of these are fresh cycles only),
  - 30% are funding one full cycle, and
  - 15% are funding one fresh cycle only.
- 2.5. The criteria for who is eligible for NHS treatment vary widely across PCTs in England. Provisions around single embryo transfer also vary widely, with some PCTs only allowing patients to have SET cycles (unless it is clinically inappropriate) and others having no requirements around SET. In June 2009 the Expert Group on Commissioning NHS Infertility Provision published a commissioning aid<sup>3</sup> to assist PCTs

<sup>2</sup> Figures as of November 2009 (subject to change). Department of Health are planning to survey PCT provision in early 2010

<sup>3</sup> [http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_101070](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_101070)

in providing fair access to fertility treatment. The report has a dedicated section on multiple births minimisation strategies.

- 2.6. The Department of Health states that there have been improvements in NHS provision of fertility treatment in the last year. However more needs to be done to fund the three full cycles recommended by the NICE guidelines to encourage a move towards SET. It is not known whether additional financial constraints may impact on fertility provision in the future.
- 2.7. The majority of *Scottish* Health Boards fund three cycles of IVF, though some only fund two cycles. The Expert Advisory Group on Infertility Services in Scotland (EAGISS) has recommendations for the criteria Health Boards should use to determine whether patients are eligible for NHS-funded treatment. Many Health Boards have taken these recommendations on board, however a few do not. Waiting lists also vary widely.
- 2.8. The Welsh Health Minister announced in November 2009 that *Wales* will be increasing IVF provision on the NHS from one fresh and frozen cycle to two cycles. It is not clear yet what the new provision will be with regards to frozen embryos. *Northern Ireland* presently funds one fresh cycle. They are hoping to increase this in the near future to one fresh cycle plus one frozen cycle, if funding allows.

### ***Promoting best clinical practice***

- 2.9. Clinics need access to up-to-date information about best practice in patient selection for SET, embryo assessment and freezing protocols, so that they can develop a strategy to minimise their multiple birth rates whilst maximising their overall pregnancy rates. In order to address this, the British Fertility Society (BFS) and the Association of Clinical Embryologists (ACE) published joint guidelines on elective single embryo transfer (eSET)<sup>4</sup> before the first maximum multiple births rate came into force. The HFEA also held a series of workshops, in partnership with the BFS, to help clinics develop their multiple births minimisation strategies.
- 2.10. The One at a Time website<sup>5</sup>, launched in June 2008 by the Multiple Births Stakeholder Group, is a dedicated website about the risks and treatment options around multiple births. The website is periodically reviewed by members of an external One at a Time Advisory Board. The website has information on best practice, including the BFS/ACE guidelines, research studies, advice from experts and information from other countries. There will also shortly be an area for clinics to share (anonymously) experiences of introducing their multiple births minimisation strategy in their clinic. We plan to send out a quarterly One at a Time e-newsletter to promote the site and the work of the Multiple Births Stakeholder Group.

<sup>4</sup> <http://www.informaworld.com/smpp/content~content=a902139975~db=all~order=pubdate>

<sup>5</sup> [www.oneatatime.org.uk](http://www.oneatatime.org.uk)

### **Patient information**

- 2.11. The HFEA Code of Practice states that clinics should give all patients information about the risks of multiple births before they begin fertility treatment<sup>6</sup>. Since the introduction of the multiple births policy, the information that clinics give to patients and the way they give this information has become even more important. This is because clinics must be able to convince patients of the benefits of eSET, if their strategy has identified the patient as likely to conceive a multiple pregnancy. Unless patients are willing to have SET, clinics will not be able to reduce the multiple birth rate at their clinic.
- 2.12. The One at a Time website provides information for patients about the risks of multiple births and information about treatment options and SET. We have produced leaflets and other publicity material that clinics can use to direct patients to the One at a Time website. The Department of Health recently provided Infertility Network UK (INUK) with three years' funding to produce patient information on single embryo transfer. INUK is now working jointly with the HFEA and the Multiple Births Foundation to produce a patient information leaflet that can be available at all clinics.

### **Data presentation**

- 2.13. The temptation to construct league tables, based on live births per cycle started, has been thought to dissuade some clinics from carrying out more single embryo transfers. Following a public consultation, we revised the way we publish clinic data on 'Choose a Fertility Clinic' in October 2009. The new data presentation highlights why directly comparing clinics is not meaningful because clinics cannot be compared in a 'like-for-like' way. We explain what the data shows and place more emphasis on singleton births. We also make more comparisons to national data and present live birth per embryo transferred as well as live birth per cycle started.

### **Published research**

- 2.14. When the HFEA policy on multiple births was initially being debated, studies<sup>7</sup> suggested that pregnancy rates for a single fresh cycle are higher when two embryos are transferred (DET) than when SET is carried out. However the studies showed that this difference is minimised or eliminated with careful patient selection for eSET cycles and when subsequent frozen transfers are included to look at *cumulative* live birth rates (ie, the chance of a patient having a live birth over several treatment cycles). Recent studies have emphasised this further and show that cumulative live birth rates for eSET are at least as successful as DET and almost completely minimise the risk of multiple births.

<sup>6</sup> Section 7.5 of the Code of Practice <http://www.hfea.gov.uk/401.html#guidanceBoxLink>

<sup>7</sup> For a summary of studies see Braude, P. (2006) 'One Child at a Time' *Report of the Expert Group on Multiple Births after IVF* [http://www.hfea.gov.uk/docs/MBSET\\_report\\_Final\\_Dec\\_06.pdf](http://www.hfea.gov.uk/docs/MBSET_report_Final_Dec_06.pdf)

- 2.15. Gelbaya *et al.* (2009)<sup>8</sup> carried out a review and meta-analysis of six randomised-controlled trials comparing eSET to DET in cleavage-stage embryos. The study found that, though there was a decrease in the success rate of a single cycle of eSET compared to DET, the cumulative live birth rates of several cycles of eSET (fresh and/or frozen cycles) were similar to that of DET. Multiple birth rates were significantly reduced in eSET cycles. Bechoua *et al.* (2009)<sup>9</sup> looked at the probability of good prognosis couples having at least one live-born baby through repeated eSET cycles using cleavage-stage embryos compared to DET. They concluded that repeated cycles of eSET gave as good a chance of having a baby as DET whilst significantly lowering the multiple birth rate, providing there were appropriate embryo freezing techniques. A study by Veleva *et al.* (2009)<sup>10</sup> from Finland also shows the benefit of a repeated eSET strategy using cleavage-stage embryos in terms of improved cumulative live birth rates and cost-effectiveness of treatment.
- 2.16. Recently published data from Australia and New Zealand<sup>11</sup> has shown a dramatic decrease in their multiple birth rate from 18.7% in 2003 to 10.0% in 2007. This trend has been associated with an increase in the proportion of SET cycles from 32.0% in 2003 to 63.7% in 2007.

### 3. Evaluation of Year 1 of the multiple births policy

#### **Methodology**

- 3.1. In order to evaluate Year 1 of the policy, we looked at clinics' multiple births minimisations strategies, gathered feedback from clinics and patients, and analysed 2009 pregnancy data.
- 3.2. We gathered feedback from clinics in a number of ways:
- HFEA questionnaire sent to all centres in November 2009 (19 responses),
  - questionnaire sent to members of the Senior Infertility Nurses group<sup>12</sup> in October 2009 (13 responses),
  - group discussions and individual interviews with clinicians at a range of stakeholder events from September – November 2009, including Licensed Centres Panel meeting, BFS meeting for persons responsible and senior staff, Fertility Show and the Multiple Births Stakeholder Group (direct feedback from clinic staff at 13 clinics), and
  - feedback from HFEA inspectors.

<sup>8</sup> Gelbaya, T *et al.* (2009) The likelihood of live birth and multiple birth after single versus double embryo transfer as the cleavage stage: a systematic review and meta-analysis. *Fertility and Sterility* 2009 May 14. [Epub ahead of print].

<sup>9</sup> Bechoua, S *et al.* (2009) How to demonstrate that eSET does not compromise the likelihood of having a baby? *Human Reproduction* 24(12): 3073-3081.

<sup>10</sup> Velaya, Z *et al.* (2009) Elective single embryo transfer with cryopreservation improves the outcome and diminishes the costs of IVF/ICSI *Human Reproduction* 24(7):1632-1639

<sup>11</sup> Wang, Y *et al.* (2009) Assisted reproduction technology series no. 13 Published 24 September 2009; ISSN 1038-7234; ISBN-13 978 1 74024 955 3

<sup>12</sup> Questionnaire designed by Julie Hinks, Nurse Manager at Bristol Centre for Reproductive Medicine

- 3.3. In total, between a third and half of all IVF clinics gave feedback about the first year of the multiple births policy. Feedback came from clinics based throughout the UK, from NHS and private clinics, and from clinics with low, mid and high multiple birth rates. A range of staff members gave feedback, including PRs, nurses, consultants, embryologists and quality managers.
- 3.4. 66 patients responded to an online questionnaire on the HFEA website. The questionnaire was aimed at patients who had IVF or ICSI treatment in 2009. It focused on the information patients had been given about multiple births and SET, and their reasons for having or not having SET.
- 3.5. We talked to approximately 100 visitors at the Fertility Show at Olympia on 6 – 7 November 2009 who approached the ‘One at a Time’ exhibition stand. Most visitors had not yet begun or had recently begun fertility treatment. We discussed their attitudes and understanding of multiple births from fertility treatment. A small number of people also completed an anonymous questionnaire.
- 3.6. We carried out a preliminary analysis of the first eight months of 2009 pregnancy data to see whether it is likely that clinics will meet the 24% maximum multiple birth rate. We compared the 2009 pregnancy data to 2008 data and to data from 2005, as this was the base-line year used to set the 24% maximum multiple birth rate.

***Did clinics comply with the requirements of the General Directions?***

- 3.7. The HFEA issued the Multiple Births General Directions<sup>13</sup> to clinics in September 2008. The Directions came into force on 1 January 2009 and required clinics to:
- develop a multiple births minimisation strategy, which includes:
    - a section identifying cases for eSET on the basis of embryo assessment and patient selection criteria
    - a section identifying how the centre intends to reduce its annual multiple birth rate and to ensure that it does not exceed 24% of its annual live births,
  - submit their strategy to the HFEA by 31 January 2009,
  - keep the outcome of regular audits and evaluations of the progress and effectiveness of the strategy, and
  - keep a summary log of cases in which multiple embryos were transferred to a patient identified as suitable for eSET.
- 3.8. 38% of clinics (27 clinics) submitted their strategy by the deadline of 31 January 2009, with a further 25% (18 clinics) submitting their strategy in February 2009. The HFEA Chief Executive wrote a letter to the clinics who had not submitted their strategies at the beginning of March 2009. 28% (20 clinics) submitted their strategies in March 2009.

<sup>13</sup> [http://www.hfea.gov.uk/docs/2009-06-03\\_GENERAL\\_DIRECTIONS\\_0003\\_Multiple\\_Births\\_-\\_approved.pdf](http://www.hfea.gov.uk/docs/2009-06-03_GENERAL_DIRECTIONS_0003_Multiple_Births_-_approved.pdf)

A remaining 6 clinics (8%) took several months longer to submit theirs. All clinics have now submitted their strategies.

- 3.9. A preliminary analysis of clinics' multiple births minimisation strategies show that 90% of the strategies (64 clinics) include clear selection criteria based on embryo assessment, for example embryo quality grade. 94% (67 clinics) include clear patient selection criteria, for example age and whether this was the patient's first cycle.

***How did clinics develop their multiple births minimisation strategies?***

- 3.10. The majority of clinics (84% of those who gave feedback) used the BFS/ACE guidelines when developing their multiple births minimisation strategies. Whilst clinics clearly found the guidelines useful, most clinics used them in conjunction with an analysis of their own data in order to develop a strategy for selecting patients for eSET that applied to their clinic. A minority of clinics found the BFS/ACE guidelines too imprecise to be helpful.
- 3.11. Several clinics developed their strategies by consulting experts outside their clinic or by creating a uniform strategy across a consortium of clinics. However some clinics who were part of a consortium found that they later needed to revise their strategy to make it work for the individual requirements of their centre.
- 3.12. The strategies submitted by clinics vary widely in depth and length. At a later stage, we recommend that someone with clinical expertise carries out a detailed analysis of the strategies' selection criteria, comparing them against clinics' multiple pregnancy/birth data. This would identify which strategies are the most effective and help share best practice.
- 3.13. This level of analysis cannot be done at present because the 2009 data is not yet complete or robust enough. Many centres have made revisions to their minimisation strategies throughout 2009. The initial version of the strategies that were submitted to the HFEA may therefore not reflect the current version in use by the clinic. The General Directions do not require clinics to submit revised versions of their strategy, though we suggest that this is amended in the next Directions issued in 2010.
- 3.14. However we did a basic analysis of a sample of clinics' strategies to see if there were any themes across clinics that had a low, mid or high multiple birth rate before implementing their strategy. We looked at 15 clinics' strategies, 5 in each category (based on 2007 multiple births data). The strategies of clinics with low multiple birth rates appeared more consistent with each other, whereas strategies from clinics with higher multiple birth rates varied more widely.

Clinic	Embryo assessment criteria	Patient selection criteria
Low multiple birth rate (7 – 20%)	Majority specified at least 2 good quality blastocysts or at least 3 to 4 good quality cleavage stage embryos	All specified women under the age of 37 (the majority under 35) on their first cycle of IVF
Mid multiple birth rate (21 – 27%)	Generally specified at least 2 good quality blastocysts or 4 good quality cleavage stage embryos; less specific about the quality of the embryo	Greater variety in the ages specified: maximum from 30 to 37 (one clinic had no maximum age) on their first cycle of IVF
High multiple birth rate (28 – 35%)	Generally specified at least 2 good quality blastocysts or 2 good quality cleavage stage embryos; quality of embryos specified appeared lower. There was much greater variation in these strategies than in the other two groups	Greater variety in the ages specified: maximum from 30 to 40 (one clinic had no maximum age) on their first cycle of IVF

### ***Clinics' experience of implementing their strategies***

- 3.15. Clinics have found the first year of the policy has involved a steep learning curve. Some clinics felt daunted by introducing a strategy into their clinic and were often initially cautious in devising their strategy. Clinics commonly set more restrictive criteria for identifying patients for eSET than recommended by BFS/ACE guidelines, for example their strategies identified women aged under 35 instead of the guidelines' recommendation of women aged 37 and under.
- 3.16. Just over half of the clinics that gave us feedback found that their minimisation strategy had reduced their multiple pregnancy rate in 2009. Some clinics had dramatic reductions in their multiple pregnancy rates. For example one clinic's multiple pregnancy rate decreased from 31% to 16% and another from 28% to 10%. Just over a third of clinics found that there had been no change in their multiple pregnancy rate or that there was a reduction in some patient groups but this was balanced out by an increase in others. A minority of clinics found that their multiple pregnancy rates had increased.
- 3.17. Now that clinics have more 2009 pregnancy data available to analyse, many have or are planning to revise their strategies. For example:
- widening the criteria used to select patients for eSET to try and increase the proportion of eSET cycles they carry out,
  - modifying existing selection criteria,

- looking again at their data to identify patients who are particularly at risk of multiple births, and
  - becoming stricter about not letting patients opt out of eSET.
- 3.18. Some clinics are getting very high pregnancy rates from blastocyst transfers and offer eSET to patients with two or more good quality blastocysts. However patients who decide to go against the clinic's recommendation and have two blastocysts transferred have very high multiple pregnancy rates. This has been driving up the overall multiple pregnancy rate in some clinics. Clinics are now recognising that this group of patients are at a high risk of conceiving twins and they need to focus on ensuring they understand the benefits of eSET. Though blastocyst culture appears effective in some clinics, other clinics are getting very good results from cleavage stage embryos. There is also some concern from clinicians that blastocyst transfers may have a higher monozygotic twinning rate.
- 3.19. Embryo quality appears to be more important than patient criteria like age, when predicting which patients are likely to become pregnant or have a multiple pregnancy. Effective and consistent embryo grading is clearly crucially important in maximising pregnancies from SET. Some clinics have found staff training in embryo grading has dramatically increased their pregnancy rates. Other clinics have changed their freezing protocols, for example introducing vitrification and the freezing of single embryos. However, feedback suggested that clinics would like more professional body guidance around effective freezing policies.
- 3.20. Developing an effective strategy to select patients and the best quality embryos for eSET is only one side of the story. Clinics also need to ensure that the patients they have identified through their strategies are deciding to have one embryo transferred.

### ***Patients' response to SET***

- 3.21. 45% of clinics who gave feedback felt that patients were largely positive in accepting single embryo transfer, 18% found patients were negative and 36% had a mixed response from patients. The results appear to be strongly influenced by:
- how patients' treatment cycles are funded, and
  - how clinics inform patients about the risks of multiple births and SET.
- 3.22. Most of the clinics whose patients were positive about eSET had supportive NHS funding arrangements. For example, where PCTs provide two or more cycles, frozen embryo transfers are included, or the PCT enforces SET in certain patients (which takes the pressure off the clinic). One clinic noticed a marked improvement in patients willing to have SET as soon as their PCT increased funding to two full treatment cycles.
- 3.23. Clinics whose patients had a very negative attitude towards eSET generally had unsupportive NHS funding arrangements. Some private clinics found it hard to convince patients to have eSET because patients were paying for their treatment and

were worried that transferring one embryo would reduce their chances of becoming pregnant, when they were already feeling under financial pressure. One patient even questioned whether their clinic used SET to push patients into having to pay more money for treatment.

- 3.24. There was clear feedback that clinics should give information to patients about multiple births and SET from the very beginning of their treatment pathway. Staff members across the clinic need to support the policy and give consistent information to patients. Some clinics admitted they needed to do more staff training around this.
- 3.25. The response from the patient online questionnaire shows that patients were given information about multiple births and SET in a range of ways:
- The most common way of giving information to patients was through face-to-face discussions. Patients found this method the most helpful, though phone conversations, presentations (eg, at patient information evenings) and leaflets were also useful. Patients found information they were directed to on websites less helpful.
  - Clinics gave information to patients at all stages of treatment, most commonly at the initial consultation (60%). 44% of patients were also given information on the day of embryo transfer. Patients who were *only* given information on the day of embryo transfer, or were given information on the day of embryo transfer that differed from previous information they had been given, found it hard to decide how many embryos to transfer and felt confused and upset by the process.
  - 67% of patients looked for more information on SET outside of the information that their clinic gave them, mostly just before or during their treatment. Patients found talking to other patients, discussion forums and support groups the most helpful.
  - 12% of patients said their clinic did not discuss the risk of multiple births.
  - A small proportion of patients found that information was inconsistent between different staff members within a clinic.
- 3.26. 13 patients in the survey said that their clinic recommended they should have SET. Nine patients chose to have SET. The biggest reason that patients chose to have SET was because their clinician recommended it (78% of patients), although how strongly clinics recommended SET varied from clinic to clinic. Only one patient explicitly said they had SET because they were concerned about the risks of multiple pregnancy and only two patients because they were concerned about the emotional and financial burden of twins or triplets.
- 3.27. Clinics that were struggling with patients not wanting to have SET felt that this was because of poor NHS funding, patients paying themselves who could not afford more treatment and fears about lowering success rates. They also held that some patients viewed twins as a positive outcome.
- 3.28. This feedback from clinics was reflected by the response to the patient questionnaire. 39 patients who responded did not have SET in their treatment (33 of these patients said their clinic did not recommend that they have SET):

- The vast majority of these 39 patients (92%) thought that they could increase their chances of getting pregnant by not choosing SET; 41% thought that the risks of multiple pregnancy were acceptable; 21% were influenced by the cost of treatment; 26% because the emotional burden of treatment was so high; and 15% wanted twins.
- When asked what may have changed their minds, 73% said better success rates from SET; 55% said more cycles provided on the NHS (with 15% wanting frozen cycles included); and 30% said less expensive treatment (with 18% wanting frozen cycles included or reduced in price).

### ***How confident are clinics feeling about lowering their multiple birth rate in the future?***

- 3.29. About two thirds of clinics that gave feedback felt confident about lowering their multiple birth rates in the future and were overall positive about the policy. These clinics felt that now they were accumulating data, they were in a stronger position to identify patients most at risk of having a multiple pregnancy and would be able to modify their strategies. Clinics who now have good data to show to patients say that this is a very effective means of encouraging patients to opt for eSET.
- 3.30. Some of these clinics had identified areas of clinical practice to introduce or expand, for example blastocyst culture and more effective freezing policies. However, though clinics appear confident about the policy, they are still cautious about the time it will take to implement an effective strategy in order to reduce the rate of multiple births. They also wanted to know how the HFEA would be taking actions against clinics who were not making any effort to comply with the policy.
- 3.31. A third of clinics that gave feedback were not confident or were neutral about lowering their multiple birth rates and towards the policy in general. The main reason was because of poor patient uptake of SET. As well as being affected by NHS funding, it was noted that it is easier to persuade patients to have eSET if other clinics in the same area have the same or similar eSET policy.

### ***Lessons learnt***

- 3.32. The first year of the policy has been about clinics developing their strategies and setting up the processes in their clinic to effectively implement them. It has been a steep learning curve and clinics have needed to gain a better understanding and more confidence over the year. Clinics are now in better position to revise their strategies to make them more effective. They also now have better data to share with patients, which will make it easier for patients to confidently choose eSET.
- 3.33. Key points from feedback:
- Initial multiple births minimisation strategies often set cautious criteria,
  - Embryo quality, consistent embryo grading techniques and effective embryo freezing policies are very important and may need more staff training or professional body guidance,

- Some clinics have been getting high pregnancy results from single blastocyst transfers and high multiple pregnancy rates when two blastocysts are transferred,
- Some clinics are struggling with patient uptake of SET, especially where patients cannot afford more than one cycle of treatment or where NHS funding arrangements are unsupportive,
- Information to patients needs to be given clearly and consistently throughout the whole treatment pathway, and
- Patients need to be more aware of the benefits of SET and of frozen embryo transfers.

***Will clinics meet the Year 1 maximum multiple birth rate of 24%?***

- 3.34. The multiple birth rate has stayed around 23 – 24% over the last few years. In 2005, 24% of all live births across all clinics were multiple births. This was the figure the HFEA based the first maximum multiple birth rate on. In 2006, the multiple birth rate was 22.7% and in 2007 (the latest complete year's worth of live births data) it was 23.0%.
- 3.35. We carried out a preliminary analysis of the 2009 pregnancy data submitted by clinics. This analysis should only be used to give a rough indication of how clinics are performing. The data set is not yet complete or robust enough to carry out a detailed analysis or make firm conclusions. Pregnancy rates appear lower than they are for 2009 because clinics have not submitted 25% of their early outcome forms (forms that indicate whether a cycle resulted in a pregnancy) and 4% of the early outcome forms that have been submitted have not been completed correctly.
- 3.36. From the available 2009 data (treatment cycles started between January – August 2009) we predicted the proportion of pregnancies likely to lead to either a singleton or multiple birth. We needed to do this because the policy sets 24% as the maximum multiple *birth* rate, not the multiple *pregnancy* rate. We then forecast the likely multiple birth rate for the complete year. Because of the time it takes to predict and forecast data, most of the analysis has been carried out on fresh, stimulated IVF and ICSI cycles that use the patient's own eggs. This represents the majority (78%) of cycles.
- 3.37. We analysed the proportion of eSET cycles, the overall pregnancy rates and the multiple pregnancy rates. Annex B explains how we analysed the data and presents a series of graphs. Key points to note are:
- The proportion of eSET cycles is increasing, with the fastest increase appearing to be in women aged under 35.
  - It is not yet possible to say what effect this has had on the overall pregnancy rates for 2009. The pregnancy rates are underestimated because clinics have not submitted a quarter of the early outcome forms that they should have done.
  - The multiple pregnancy rate and predicted multiple birth rate for patients aged under 35 appears to have decreased in 2009 compared to 2008 and the 2005 base rate.

- However this decrease has largely been negated by an increase in the multiple pregnancy and birth rate in patients aged 35 – 37 and 38 – 39 during the first half of the year.
  - The predicted overall multiple birth rate for all patients has remained largely the same as the 2005 figure.
- 3.38. What will the overall multiple birth rate be for the whole of 2009?
- The average *predicted* multiple birth rate for treatment in the first eight months of 2009 is 24.4%, for all patients having fresh, stimulated cycles using their own eggs.
  - For the whole of 2009, we can forecast that the multiple birth rate for these patients is likely to be around 24.9%.
  - From looking at the data we know that the multiple birth rate for patients having fresh, stimulated IVF and ICSI treatment cycles using their own eggs is about 1% higher than for all patients receiving all types of IVF and ICSI treatment.
  - Therefore we can estimate that **the overall multiple live birth rate for patients having IVF and ICSI treatment for the whole of 2009 is likely to be around 24%**, in effect no change from the 2005 level.
- 3.39. Though the data analysis shows that it is unlikely that the first year of the policy will decrease the overall multiple birth rate, we should not necessarily expect that it would have done so. The majority of clinics have used the first year of the policy to develop their multiple births minimisation strategy and get systems in place to monitor, implement and improve it. They have now gathered data, built up confidence and are in a better position to revise their strategy to make it more effective.
- 3.40. Feedback suggests that clinics have been cautious in setting their criteria for identifying patients for eSET and have focused on younger women (ie, under 35). There appears to be a decrease in the multiple pregnancy rate for patients under 35 years old, and the proportion of eSET cycles appears to have increased more in the under 35 age group than the older categories of patients. It is the multiple pregnancy rate in older women that appears to be increasing the overall multiple pregnancy rate. Transferring two blastocysts in older women may have had an impact. We are aware that some clinics are now planning to widen their criteria for who should be offered eSET. Embryo quality may also have a greater impact on pregnancy and multiple pregnancy rates than patient criteria such as age. If clinics carry out more eSET cycles in older women with good quality embryos, this may help reduce the overall multiple birth rate in the future.
- 3.41. This analysis shows what is happening at a national level. However, it does not tell us if the predicted national average of 24% is because all clinics are around 24%, or because some clinics with very low multiple birth rates are balancing out others with very high multiple birth rates. The policy's maximum multiple birth rate of 24% applies to all clinics. For individual clinics we predict that just over two thirds of clinics will meet this and just under a third will exceed it:

Predicted multiple birth rate for 2009	Number of clinics*	Proportion of clinics	Proportion of all cycles** carried out
24% and below	47	68%	67%
25 – 30%	14	20%	26%
Over 30%	8	12%	11%

\*1 clinic has been excluded from the analysis because the number of cycles is too small to be meaningful

\*\* Cycles that reach embryo transfer stage

3.42. Clinics that carry out a large number of treatment cycles each year will have a disproportionate effect on the overall multiple birth rate. We looked at the ten largest clinics in 2007, which carried out 35% of all treatment cycles reaching embryo transfer stage. In 2007, seven of these ten clinics had a multiple birth rate of 24% and below, and three had a multiple birth rate of 25 – 30%. In 2009, we predict that six of these clinics will have a multiple birth rate of 24% and below, two clinics will have a multiple birth rate of 25 – 30% and two clinics will have increased their multiple birth rate to over 30%. Therefore some of the larger clinics appear to have a slightly *higher* multiple birth rate since the policy was introduced.

3.43. We also looked at the ten clinics that had the highest multiple birth rates in 2007. These clinics carried out 11% of all treatment cycles reaching embryo transfer stage in 2007. In 2007, five of these clinics had a multiple birth rate of 25 – 30% and five had a multiple birth rate of over 30%. In 2009, we predict that five of these clinics will have lowered their multiple birth rate to 24% and below, three will have a multiple birth rate of 25 – 30% and two will have a multiple birth rate of over 30%. Therefore some of the clinics who had a very high multiple birth rate in 2007 appear to have *lowered* their multiple birth rates since the policy was introduced.

#### 4. What will happen to clinics who do not comply with the multiple births policy?

4.1. We are committed to reducing the risk of multiple births from IVF treatment and ensuring compliance with the multiple births policy across all clinics. We currently monitor clinics' multiple birth rates as part of our routine inspection and compliance cycle, and multiple births will be one of the focused themes of inspection in the new compliance cycle.

4.2. From 2010, we are aiming to closely monitor clinics' pregnancy rates and multiple pregnancy rates in 'real-time', taking into account the statistical variation of each clinic's data. This will feed into a consistent compliance and enforcement process on multiple births that will set out:

- what information and data we will analyse to assess how a clinic has complied with Year 1 of the multiple births policy,

- how inspectors will use this information and when they should request more information to identify whether a clinic is complying, trying to comply or not making any effort to comply with the policy, and
  - appropriate enforcement action steps we will take and how these will be escalated as necessary. This may include informal discussions with the clinic, external peer review, written action plans, management review or referral to Licence Committee.
- 4.3. It is important that those centres who are trying to reduce the risks of multiple births for their patients, are confident that the HFEA will take action against other centres that are unwilling or unable to do the same. Consistency of enforcement will be a central factor in keeping the HFEA's multiple births policy credible and coherent. Joined-up enforcement will allow us to provide support to clinics that need it, help share best practice across the sector and demonstrate our commitment to enforcing the multiple births policy. The compliance and enforcement process will be presented at the January 2010 Authority meeting.

## 5. How should the HFEA approach the Year 2 target?

- 5.1. In January 2010 members will be asked to decide on the maximum multiple birth rate for Year 2 of the policy. This paper is not asking members to make this decision and does not present options. However it does set out two broad possible approaches to the next year of the policy to help prepare members for the January meeting. Members may find it useful to keep these approaches in mind when discussing the evaluation of Year 1 of the policy.

- 5.2. Potential approaches for Year 2 of the multiple births policy:

<b>Gradual reduction in maximum multiple birth rate</b>		<b>Steep reduction in maximum multiple birth rate</b>	
<b>Pros</b>	<b>Cons</b>	<b>Pros</b>	<b>Cons</b>
<ul style="list-style-type: none"> <li>- Allows clinics more time to revise strategies and get systems in place to implement strategies eg, staff training, embryo grading, patient information</li> <li>- More support from centres, which might help build confidence</li> <li>- More clinics might meet target</li> </ul>	<ul style="list-style-type: none"> <li>- Might lose momentum</li> <li>- May be seen as not taking the policy seriously</li> </ul>	<ul style="list-style-type: none"> <li>- Keep momentum</li> <li>- Will be making a firm commitment to reducing multiple births</li> <li>- Might encourage clinics to take definite action in their strategies</li> </ul>	<ul style="list-style-type: none"> <li>- Clinics might struggle to implement an effective strategy and lose confidence in the policy</li> <li>- Patient uptake of SET may limit effectiveness</li> <li>- Resentment from clinics</li> <li>- More clinics might not meet target</li> </ul>

- 5.3. Views from the Multiple Births Stakeholder Group at their October 2009 meeting:
- Members thought that the Year 2 maximum multiple birth rate needs to maintain momentum but not be too steep a reduction that it discourages clinics,
  - Clinics have been on a steep learning curve since the policy was introduced and the HFEA needs to be aware of how much is possible or feasible to expect clinics to reduce their multiple birth rates, and
  - Members thought the HFEA should adopt a reasonably gradual approach to the next multiple birth rate.

## 6. Next steps

17 December 2009:	Corporate Management Group to consider the multiple births compliance and enforcement process
6 January 2010:	Multiple births stakeholder meeting to discuss the HFEA Year 2 target
20 January 2010:	Authority meeting to decide the Year 2 target, sign off the General Directions to clinics and approve the process for monitoring and enforcing compliance with the multiple births policy
Late January 2010:	Communicate Authority decision to centres and issue General Directions
April 2010:	Year 2 target comes into force

## 7. Recommendations

- 7.1. Members are invited to:
- discuss and review the evaluation of Year 1 of the multiple births policy,
  - discuss possible approaches to Year 2 of the multiple births policy, in light of this evaluation, and
  - note the enclosed timeline for the next steps, in particular that Members will be asked to decide the Year 2 maximum multiple birth rate and approve the process for monitoring and enforcing the multiple births policy at the January 2010 Authority meeting.

## Annex A: Timeline of multiple births policy

<b>August 2005</b>	The HFEA launches the multiple births and single embryo transfer review and forms an Expert Group chaired by Professor Peter Braude from the Royal College of Obstetricians and Gynaecologists.
<b>October 2006</b>	The Expert Group publishes its recommendations <sup>14</sup> for the HFEA and other stakeholders. The group concludes that the risks associated with multiple births are significant and that steps should be taken to reduce the incidence of multiple births following IVF in order to minimise these risks to women and their babies.
<b>April to July 2007</b>	The HFEA holds a public consultation <sup>15</sup> about the policy options recommended by the Expert Group's report.
<b>May 2007</b>	A 'Consensus statement' is published by professional bodies, patient groups and other stakeholders.
<b>October and November 2007</b>	<b>Initial policy decision</b> - The Authority decides the HFEA should lead a 'National Strategy' involving key stakeholders to reduce the risks of multiple births from IVF. The Authority agrees on a phased approach to reduce clinics' multiple births rate. This will involve setting a maximum multiple birth rate for clinics, which will be progressively lowered. Clinics will be required to have their own multiple births minimisation strategy.
<b>December 2007</b>	Policy decision announced at BFS winter conference and in a letter to then-Public Health Minister, Dawn Primarolo. First meeting of the Multiple Births Stakeholder Group decides the scope and aims of the 'National Strategy' to minimise multiple births from fertility treatment.
<b>January 2008</b>	Alan Doran writes to NHS Directors of Public Health to outline the public health challenge of multiple births.
<b>February 2008</b>	The Authority clarifies various policy details, including a January 2009 start date and that interim targets should operate as an 'upper limit' that will apply to all clinics. The Authority approves plans for a 'root and branch' review of how the HFEA collects and presents data from clinics.
<b>April and May 2008</b>	<b>Year 1 target</b> - The Authority agrees that the first maximum multiple births rate should be 24%. This will be regulated through General Directions, Code of Practice guidance and through the risk tool and inspection process.
<b>June 2008</b>	Official launch of the multiple births 'National Strategy' and the One at a Time website <sup>16</sup> . BFS/ACE 'Elective Single Embryo Transfer: Guidelines for Practice' are published in Human Reproduction <sup>17</sup> .

<sup>14</sup> Braude, P. (2006) One child at a time: Reducing multiple births after IVF *Report of the Expert Group on Multiple Births after IVF* [http://www.hfea.gov.uk/docs/MBSET\\_report\\_Final\\_Dec\\_06.pdf](http://www.hfea.gov.uk/docs/MBSET_report_Final_Dec_06.pdf)

<sup>15</sup>

[http://www.hfea.gov.uk/docs/The\\_best\\_possible\\_start\\_to\\_life\\_HFEA\\_public\\_consultation\\_paper\\_April\\_2007.pdf](http://www.hfea.gov.uk/docs/The_best_possible_start_to_life_HFEA_public_consultation_paper_April_2007.pdf)

<sup>16</sup> <http://www.oneatatime.org.uk/>

<b>July to August 2008</b>	Training workshops for clinic staff based on the BFS/ACE guidelines held in London, Glasgow, Leeds and Birmingham.
<b>September 2008</b>	Chair's letter, General Directions and update to Code of Practice guidance sent out to clinics about the policy. The General Directions require clinics to have a Multiple Births Minimisation Strategy, to record the outcome of regular audits of the effectiveness of their strategy and to keep a log of cases in which multiple embryos are transferred to a patient who meets the criteria for single embryo transfer in the clinic's strategy.
<b>November 2008 to February 2009</b>	Public consultation on how we should present treatment data in the Choose a Fertility Clinic section of the website <sup>18</sup> .
<b>January 2009</b>	<b>Year 1 of Policy</b> - General Directions setting the first maximum multiple birth rate of 24% come into force on 1st January. Clinics are required to submit their strategies to the HFEA by 31st January.
<b>February 2009</b>	Alan Doran writes to NHS Directors of Public Health to outline the importance of ensuring that commissioning strategies are consistent with the HFEA's new multiple births policy.
<b>May 2009</b>	Authority decisions about how to present data in Choose a Fertility Clinic, including how to present data about multiple births to support the multiple births policy
<b>June 2009</b>	Expert Group on Commissioning NHS Infertility Provision publishes a commissioning aid <sup>19</sup> .
<b>September 2009</b>	INUK, Department of Health and One at a Time members start work on producing patient information leaflets
<b>December 2009</b>	Authority discuss evaluation of Year 1 of the multiple births policy

<sup>17</sup> <http://www.informaworld.com/smpp/content~content=a902139975~db=all~order=pubdate>

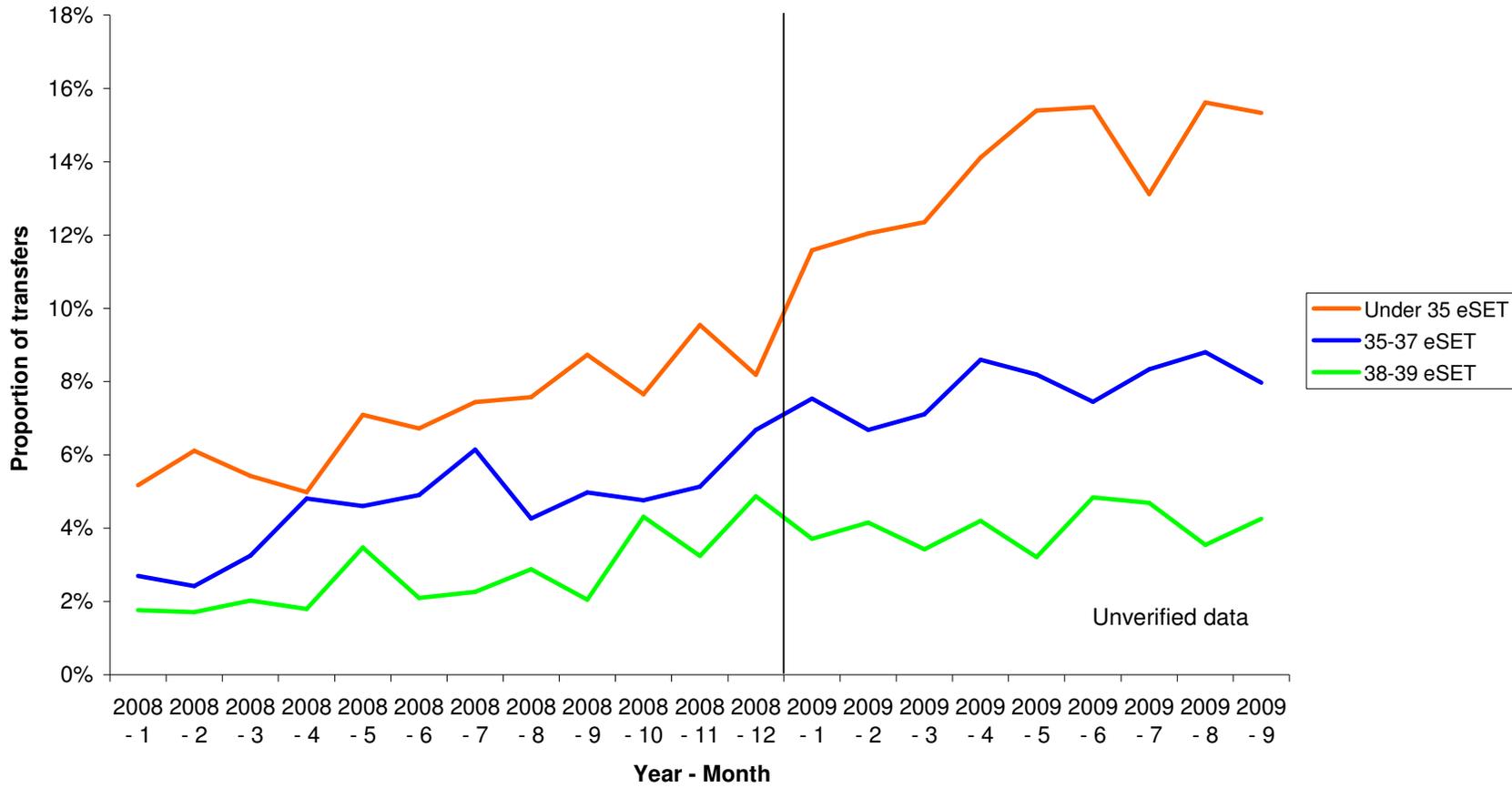
<sup>18</sup> <http://www.hfea.gov.uk/512.html>

<sup>19</sup> [http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_101070](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_101070)

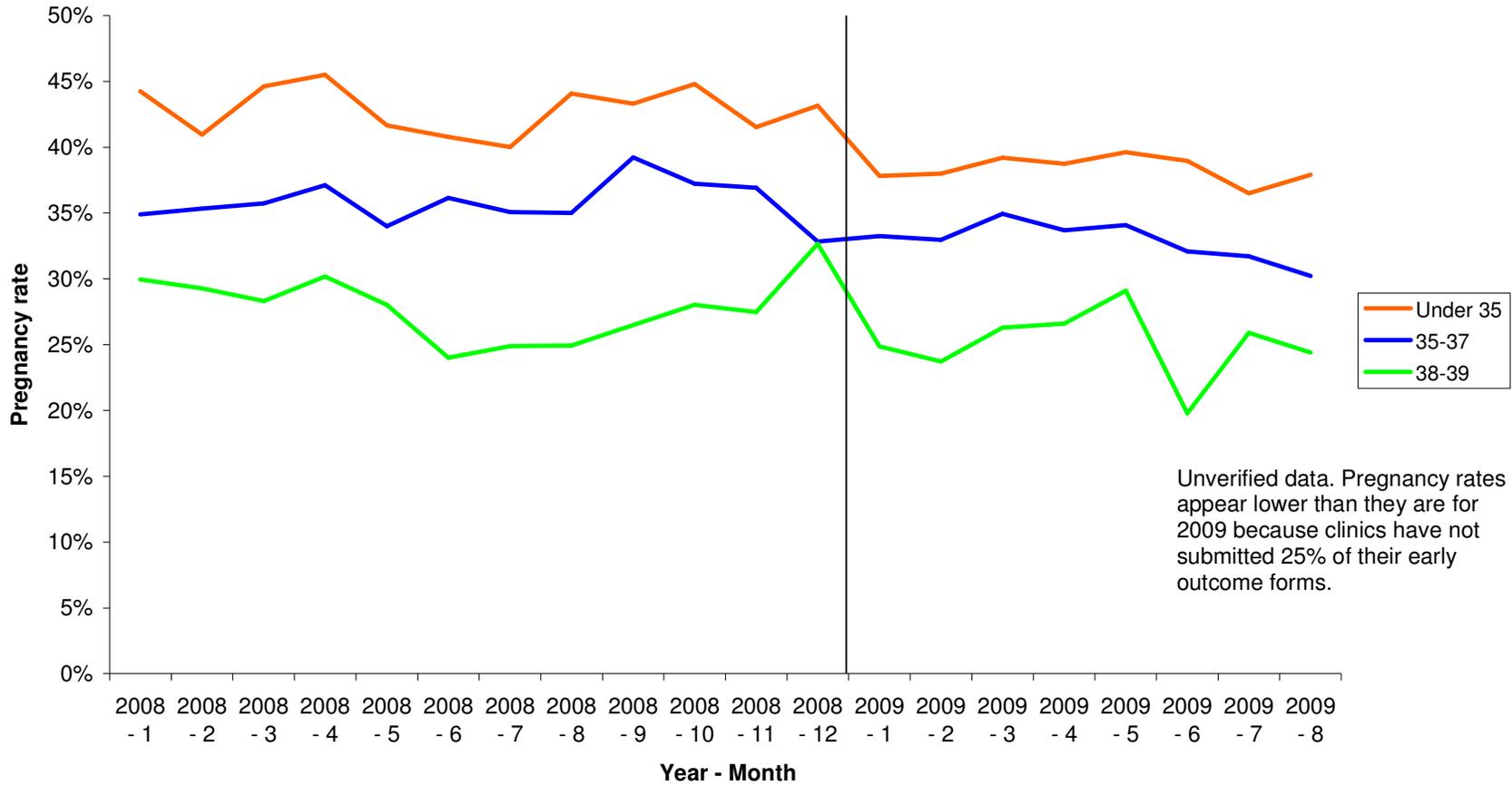
## Annex B: Analysis of 2009 data

- 1.1. We have pregnancy data from treatments started between January and August 2009. This data has not been verified by clinics. Because of the time it takes to analyse the data to predict live births from pregnancy data, we only analysed pregnancy data from fresh, stimulated, own egg (FSO) cycles. These form the majority of treatment cycles (78%).
- 1.2. We predicted the number of live births and multiple live births by directly comparing pregnancy and live birth data from 2007, (the most recently verified year). We obtained basic conversion factors by partitioning the treatment data by:
  - age category of patient,
  - number of embryos transferred, and
  - whether blastocysts (defined as 5-7 days incubation) were transferred, and looking at how many singleton and multiple births resulted from singleton and multiple pregnancies in each category.
- 1.3. We applied the conversion factors to the eight months of available 2009 pregnancy data to estimate the number of singleton and multiple live births from FSO cycles in 2009. We carried out a time series analysis to forecast the likely multiple birth rate for FSO cycles for the whole of 2009.
- 1.4. The multiple birth rate for FSO cycles in 2005 (the reference year that set the Year 1 maximum multiple birth rate) was 25%. The multiple birth rate for all treatment cycles was 1% lower, at 24%. We therefore estimate that the predicted multiple birth rate for all treatment cycles for 2009 will be approximately 1% lower than the predicted multiple birth rate from FSO cycles.
- 1.5. 25% of the early outcome forms, which indicate whether a cycle resulted in a pregnancy, have not been submitted by clinics for treatment cycles started in 2009. 4% of submitted early outcome forms that have been submitted do not have the number of gestational sacs recorded. This means the overall pregnancy rates shown for 2009 will be underestimated. It should not affect the multiple pregnancy rates shown for 2009, providing that the pregnancies in the missing early outcome forms show the same proportion of multiples to singletons as in the submitted early outcome forms.
- 1.6. When looking at individual clinics, the basic conversion factors indicate that clinics' multiple live birth rates are about 2.5% below clinics' multiple pregnancy rates.

**Figure 1. Proportion of fresh, stimulated, own egg IVF & ICSI embryo transfers by patient age that are elective single embryo transfers (eSET)**



**Figure 2. Pregnancy rate per transfer for fresh, stimulated, own egg IVF & ICSI embryo transfers by patient age**



**Figure 3. Multiple pregnancy rate per pregnancy for fresh, stimulated, own egg IVF & ICSI embryo transfers by patient age**

