Improving outcomes for fertility patients: **Multiple births**

2011

A statistical report

Human Fertilisation & Embryology Authority

HUMAN FERTILISATION & EMBRYOLOGY AUTHORITY

Contents

Executive Summary

The HFEA collects data about approximately 50,000 fertility treatments performed each year in the UK. We are committed to making as much of this information available as possible to aid and inform patients, researchers and clinicians. This report, focussing on multiple births, is part of that aim.

A multiple birth (twins and triplets) is the single biggest health risk associated with fertility treatment. In order to try to reduce the proportion of multiple births after fertility treatment, the HFEA introduced a series of maximum multiple birth rate targets for clinics to adhere to (see Background section on page 4). For the first time since the initial targets were introduced, we are looking in depth at the national picture of multiple pregnancies and births after fertility treatment.

Decrease in multiple pregnancy and birth rates

The report shows that the multiple pregnancy and multiple birth rates have dropped since the targets were introduced. In 2008, nearly 24% of births after in vitro fertilisation (IVF) or intra-cytoplasmic sperm injection (ICSI) were of two or more babies; but for the first six months of 2009, that had been reduced to 22%.

The change is most dramatic in women aged 18 - 34, who are most at risk of multiple pregnancies. In 2008, 31.2% of pregnancies in women aged 18 to 34 were of two or more fetuses. By the first six months of 2010 this had been reduced to 23.9%.

This reduction has been brought about by marked changes in clinical practice. We have seen an increase in elective single embryo transfers (eSET, where only one embryo is transferred, even if more are available), particularly in women under 35 – those who saw the greatest drop in multiple pregnancies. In 2008, only 6.8% of embryo transfers in women aged 18 to 34 were eSET but by mid 2010 this had reached 22.1%.

Concern had been expressed that a reduction in multiple births, brought about by an increase in eSETs, might negatively impact on pregnancy and live birth rates. However, these rates have broadly been maintained since the introduction of the targets.

Stage of embryo development

This report shows that the risk of conceiving a multiple pregnancy might be affected by the stage of development the embryo has reached when it is transferred. Transferring two blastocyst stage embryos (grown in the laboratory for five to six days after fertilisation) is more likely to result in a multiple pregnancy than transferring two cleavage stage embryos (grown for two to three days). The risk is almost completely reduced by transferring only one embryo.

In April 2011 a new multiple births target of 15% was introduced and we will continue to monitor the results.

► The good news

1. Multiple pregnancies and multiple births have fallen.
2. Elective single embryo transfers have risen.
3. The overall pregnancy and live birth rates have broadly been maintained.

► Room for improvement

1. The proportion of women receiving double embryo transfers is still higher than it should be, meaning women who could be eligible for eSET are at risk of multiple pregnancies.
2. Double blastocyst transfers are resulting in very high multiple pregnancy rates.

Background

The risks of multiple births

A **multiple birth (twins and triplets)** is the single biggest health risk associated with fertility treatment. Multiple births carry risks to both the health of the mother and the babies:

- Mothers have a higher risk of miscarriage and other complications in pregnancy
- The babies are more likely to be premature and to have a low birth weight
- The number of deaths within the first month of life increases from 3 deaths per 1,000 live births for singletons, to 19 deaths per 1,000 live births for multiple babies[1]
- The risk of cerebral palsy increases from 1.7 cases per 1,000 live births for singletons to 6.2 cases per 1,000 live births for twins[2]

The birth of a healthy singleton child, born at full term, is the safest outcome of fertility treatment for both mother and child.

Minimising the risks of multiple births

Multiple births are an *avoidable* risk of IVF. The HFEA restricts the number of embryos that can be transferred in a treatment cycle of IVF to a maximum of two in women aged under 40; and three for women aged 40 and over who are using their own eggs. This has effectively reduced triplet births, but the proportion of twin births remains high.

The only way to reduce the risk of twins is to transfer just one embryo in patients who are most likely to get pregnant and therefore also most at risk of having twins[3]. Replacing one embryo at a time is known as **elective single embryo transfer (eSET)**.

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[1] Office for National Statistics (2009) Mortality Statistics: Childhood, Infant and Perinatal 2007.
[2] Surman, G, *et al*. (2009) Four Counties Database of Cerebral Palsy, Vision Loss, and Hearing Loss in Children: Annual Report University of Oxford/NPEU
[3] 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.pdf

Not all patients are eligible for eSET and every patient needs to be treated as an individual. **However, for good prognosis patients, eSET can maximise the chance of a healthy singleton baby born at term[4] and improve the health outcomes for mother and child[5]**. Careful patient selection, and taking into account fresh and subsequent frozen embryo transfers, can maintain overall live birth rates whilst minimising multiple births[3].

In January 2009 the HFEA introduced a policy to promote eSET and minimise the risk of multiple births from IVF treatment. All clinics must have their own strategy around eSET, which sets out how they will lower their multiple birth rate to within a maximum rate set by the HFEA. The HFEA lowers the maximum multiple birth rate each year, after careful evaluation, towards an ultimate aim of a multiple birth rate of not more than 10% each year.

Year	Target
January – December 2008	No target, acting as a benchmark
January 2009 – March 2010	No more than 24% multiple births
April 2010 – March 2011	No more than 20% multiple births
April 2011 – March 2012	No more than 15% multiple births

Risk based assessment

The HFEA has recently introduced a risk based assessment tool. One function of the tool is to constantly and proactively monitor clinics' multiple pregnancy rates. If it becomes likely that a clinic will not meet the target, the tool will notify an inspector, who will make contact with the clinic to discuss the issue.

Multiple pregnancy rates

The HFEA has based the targets on the multiple *birth* rate of each clinic. But, using multiple *pregnancy* rates provides us with the most up to date indication of a clinic's multiple *birth* rate. Of course, some multiple pregnancies will unfortunately result in miscarriage and the loss of one or more of the babies. It is possible to take this into account to calculate an equivalent multiple *pregnancy* target that gives the HFEA an indication of whether a clinic is likely to meet the overall multiple *birth* rate target.

National strategy: 'One at a Time'

The HFEA policy is part of a wider national strategy to reduce the number of multiple births resulting from fertility treatment, involving representatives from professional bodies, patient groups and NHS-funding bodies. The multi-disciplinary One at a Time campaign (www.oneatatime.org.uk) provides clinics with the tools to change their clinical practice, works to improve NHS funding of fertility treatment and provides information to patients and aims to share best practice across the sector. A wide range of professional bodies and patient organisations signed up to a consensus statement in May 2011 that supports the use of eSET in carefully selected patients to effectively minimise multiple births from fertility treatment.

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[4] McLernon, D J *et al.* (2010) Clinical effectiveness of elective single versus double embryo transfer: meta-analysis of individual patient data from randomised trials. BMJ 2010;341:c6945

[5] Källén B, *et al*. (2010) Trends in delivery and neonatal outcome after in vitro fertilization in Sweden: data for 25 years. Hum Reprod. 25(4):1026-34

About the data

Clinics are required by law to provide information to the HFEA Register about all licensed fertility treatments they carry out. Before publication a validation process is performed on the data and clinics are asked to verify its accuracy, for which they remain responsible. Validation and verification take time, but are necessary to ensure the data is accurate.

In October 2007, the HFEA introduced new data collection forms which clinics started using throughout 2008. The new forms include the requirement for clinics to specify when an embryo transfer was electively of a single embryo, which was not possible before. The new forms may also result in clinics reporting pregnancies earlier than they had before and this may have had an impact on the pregnancy figures; this will be monitored as more data becomes available.

In the past we have published mainly live birth rates, but in response to requests from clinics and patients for more up-to-date data, we have also included *pregnancy* results in this publication. We are able to collect pregnancy information much sooner after the treatment cycle than birth data. Pregnancy rates do not provide the full picture of success that a final live birth rate does, as unfortunately not all clinical pregnancies will end with live births. This information is provided as an additional resource to show how recent changes in clinical practice have affected outcomes. In order to give the most up-to-date figures available, we have also included half year results – births for the first half of 2009, and pregnancies for the first half of 2010. The full year results – which will present the full picture – will be published in our national data publication this Autumn.

This publication focuses on women aged 37 or under as these are the patients identified as being most at risk of multiple births, and therefore are the focus of strategies to reduce this.

Unless otherwise stated, this data covers all IVF and ICSI cycles, both fresh and frozen, which were started with the intention of conceiving immediately and where the woman's own eggs were used.

The data presented in this publication is based on a snapshot of the HFEA data taken on 14 April 2011. Because clinics may submit data relating to past cycles at any time, the figures published here may differ slightly to those published before or those published in the future.

Our data is presented according to the year the treatment cycle started, not the year a consequent pregnancy or birth occurs in. Most other data providers, including the Office for National Statistics, publish birth rates according to the year of the birth. This, and other differences[6] can make it hard to compare our data to that of other providers.

[6] See data spreadsheet.

Our website, www.hfea.gov.uk, provides information about individual clinics, the fertility treatments available and a full glossary of terms.

Accessing the data

The data in this publication has, except in specific circumstances, been presented as percentages in order to draw comparisons and maintain understanding for lay readers. If you would like to access the absolute figures these are available to download as a spreadsheet from our website.

Revisions policy

No revisions are planned to this publication unless errors are found which will be corrected.

Contact us regarding this publication

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The move to elective Single Embryo Transfer

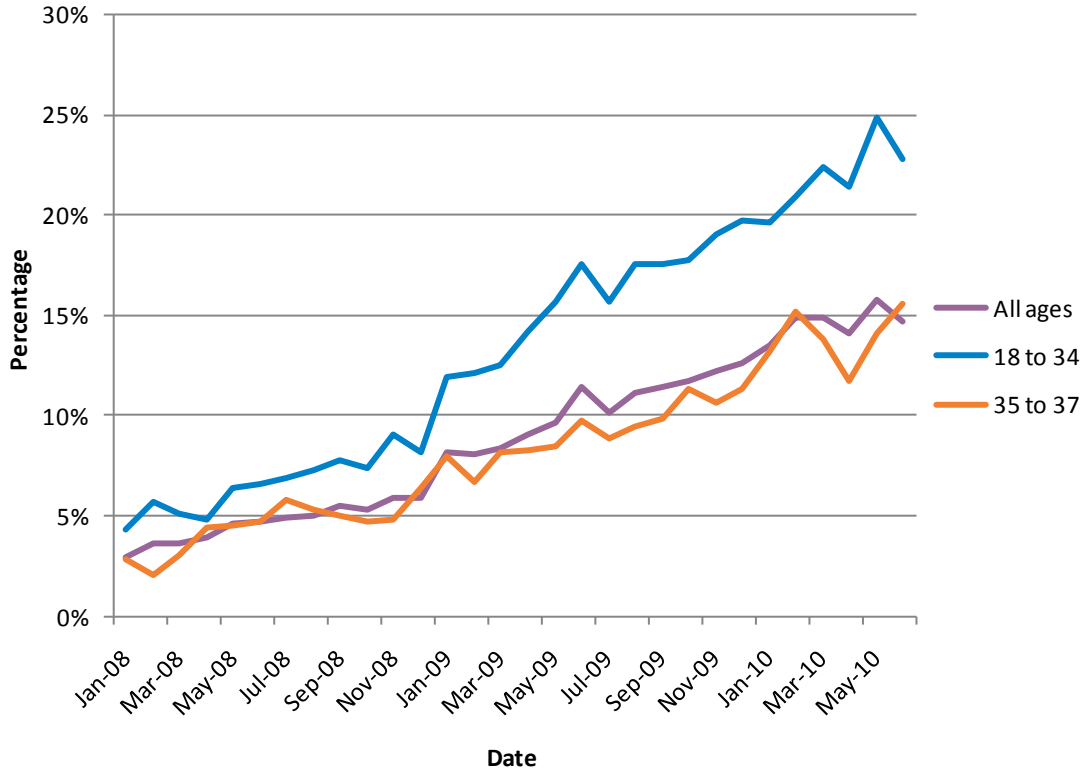
► 1. How has the proportion of elective single embryo transfers changed since January 2008?

The best way to reduce multiple births is to transfer just one embryo in women at risk of multiple pregnancy. For women with more than one embryo available this is known as elective Single Embryo Transfer (eSET) [7].

Since January 2008, the proportion of transfers performed which are eSET has increased across the sector. In 2008, 39,201 embryo transfers were performed, of these 1,862, or 4.8% were eSET. For the first six months of 2010, 22,818 embryo transfers were performed, 3,359, or 14.7%, of which were eSET.

This increase has been greatest in younger women, particularly those aged under 35. The professional bodies recommend that women aged under 37 at the start of treatment (amongst other factors) are best suited to receive eSET[8].

Figure 1: Percentage of embryo transfers which were eSET, January 2008 to June 2010

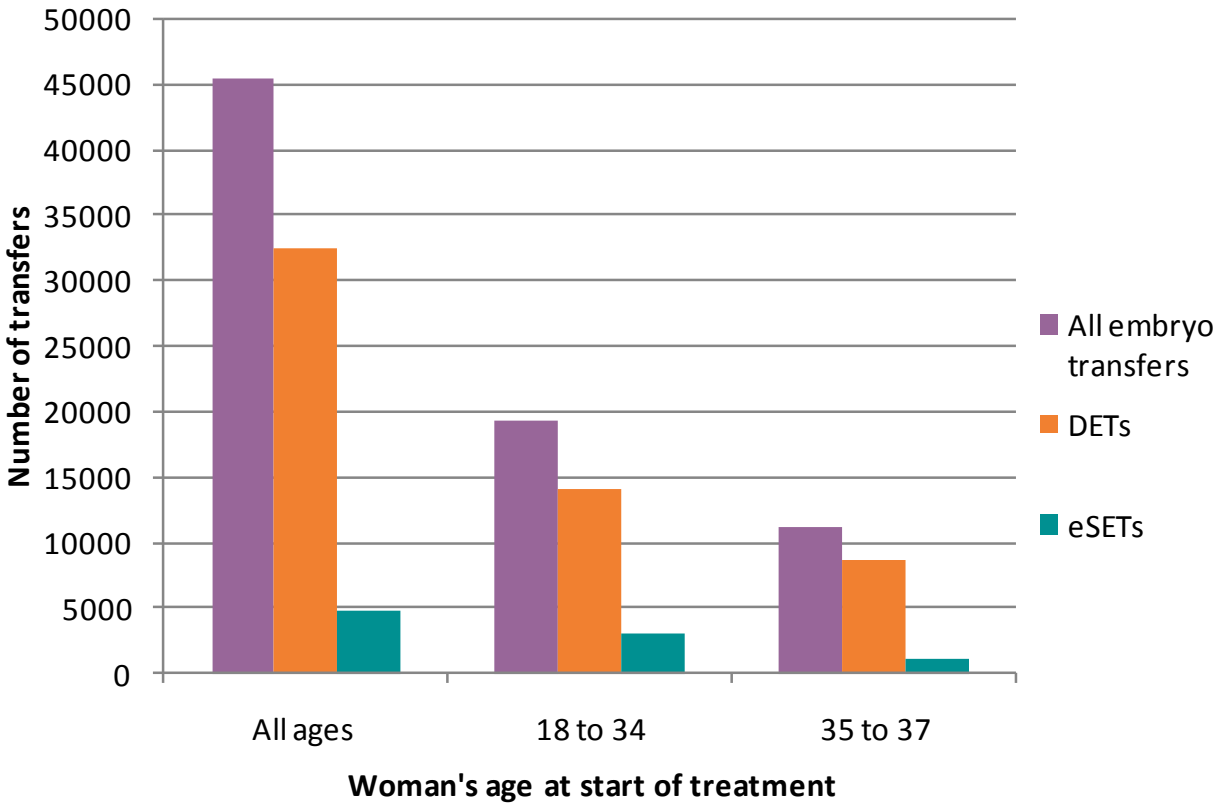


[7] Braude, P (2006) One Child at a Time: Reducing multiple births after IVF *Report of the Expert Group on Multiple Births after IVF* http://www.hfea.gov.uk/docs/MBSET_report.pdf
[8] Cutting, R, *et al* (2008) Elective Single Embryo Transfer: Guidelines for Practice British Fertility Society and Association of Clinical Embryologists. Human Fertility. 1-16

► 2. How does the proportion of eSET transfers compare to other transfers?

The eSET rate as a proportion of all transfers performed is still low, particularly when compared to double embryo transfer (DET). For each age group, DETs formed around three quarters of all transfers.

Figure 2: Embryo transfers and the number of embryos transferred, 2009



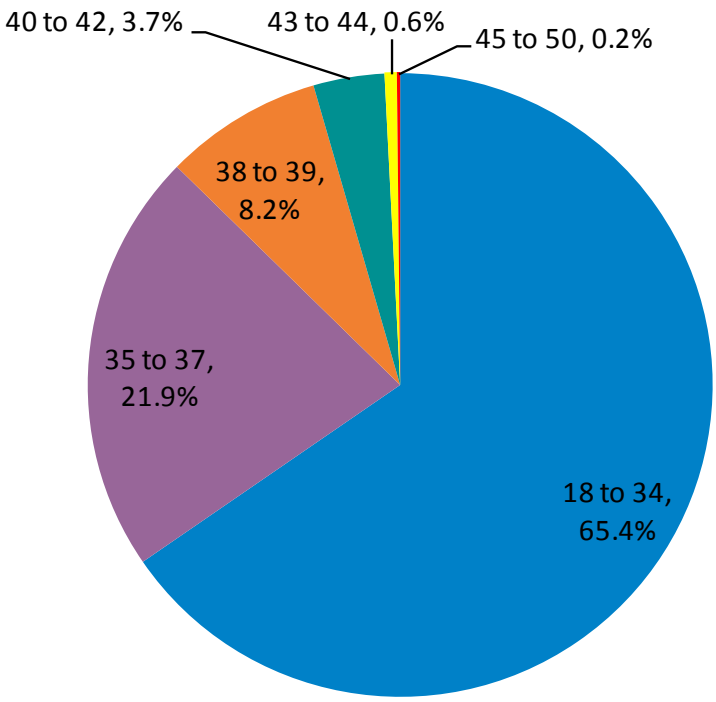
► 3. How old were the women receiving eSET?

The vast majority, 87.3%, of women receiving eSET were aged 37 or under, in line with the professional bodies' guidelines.

Around two thirds of all women having IVF are aged 37 or under.

Women who received eSET tended to be those with a higher likelihood of pregnancy and therefore a higher risk of multiple pregnancy.

Figure 3: Age of women receiving eSET, 2009

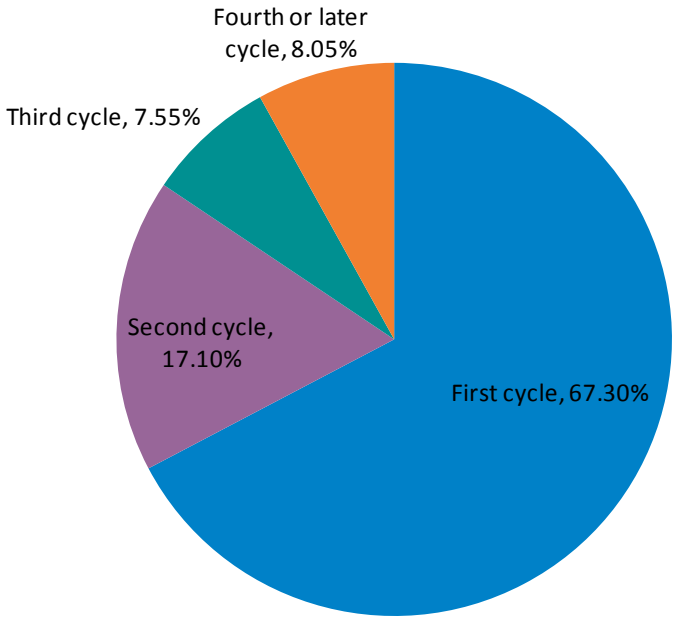


► 4. Which cycle of treatment did women receive eSET on?

Women on their first cycle were more likely to receive eSET than those on subsequent cycles. Two thirds 67.3% of women receiving eSET were on their first cycle, 17.1% on their second and 15.6% on three or more.
Currently, most clinics focus their eSET strategies on the patient's first IVF attempt.

Of the women having eSET on their second or later cycle, 11.2% had already had 1 or more live births through IVF[9].

Figure 4: Number of cycles for women receiving eSET in a fresh IVF cycle, 2009



► 5. How many embryos did women choosing eSET have available?

Women who received eSET in a fresh cycle in 2009, had on average seven embryos available.

► 6. How many women froze embryos after eSET?

Over half (59.6%) of women who received eSET in a fresh cycle in 2009 froze one or more embryos for their own use. The majority of these (85.6%) were able to freeze two or more embryos.

Key points: eSET transfers have increased since 2008, especially in women aged under 35. Most of the women who received eSET were on their first cycle of IVF and were able to freeze embryos for later use. This is in line with professional bodies' guidelines.

[9] For this specific percentage, only data which has been assigned an HFEA ID has been included – the ID number allows the linkage of all of a patient's treatment cycles and has been automatically applied to about 85% of treatment cycles.

The move to blastocyst transfer

Blastocysts are embryos grown in the laboratory incubator for five to six days after fertilisation.

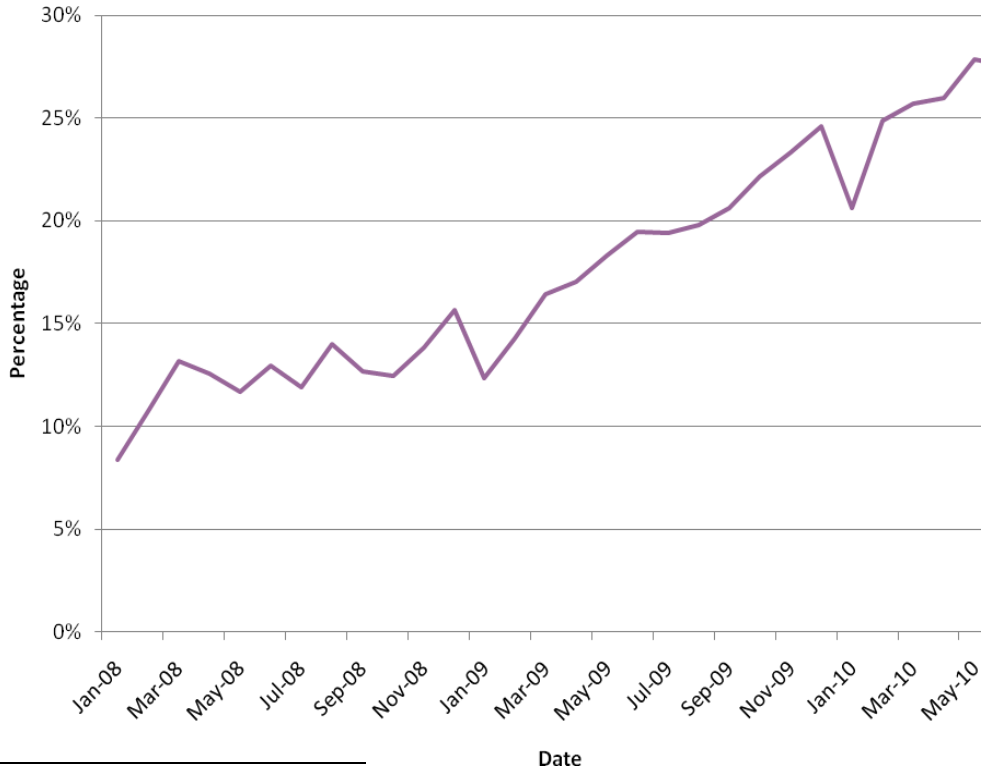
Blastocyst transfer is a relatively new procedure in the UK; previously almost all embryos were transferred two to three days after fertilisation, when they are known as cleavage stage embryos.

Research has shown that transferring blastocyst stage embryos may increase the chance of having a live birth, particularly for patients with a higher likelihood of getting pregnant anyway. This may be because only high quality embryos will be successfully cultured by the embryologist to the blastocyst stage. It may also be easier at this stage for the embryologist to select the best quality embryo[10].

► 7. How has the number of blastocyst transfers changed since January 2008?

Since 2008 there has been a steady increase in the percentage of embryos transferred at the blastocyst stage. Figure 5 shows the percentage of all embryos transferred which were at blastocyst stage. This has increased from 8.4% in January 2008, to 27.6% in June 2010. Figure 5 also shows a 'dip' in January of each year which could be because some laboratories might be closed over the Christmas and New Year period and so fewer embryos are cultured for longer periods.

Figure 5: Blastocyst stage embryo transfers as a percentage of all embryo transfers, January 2008 to June 2009.



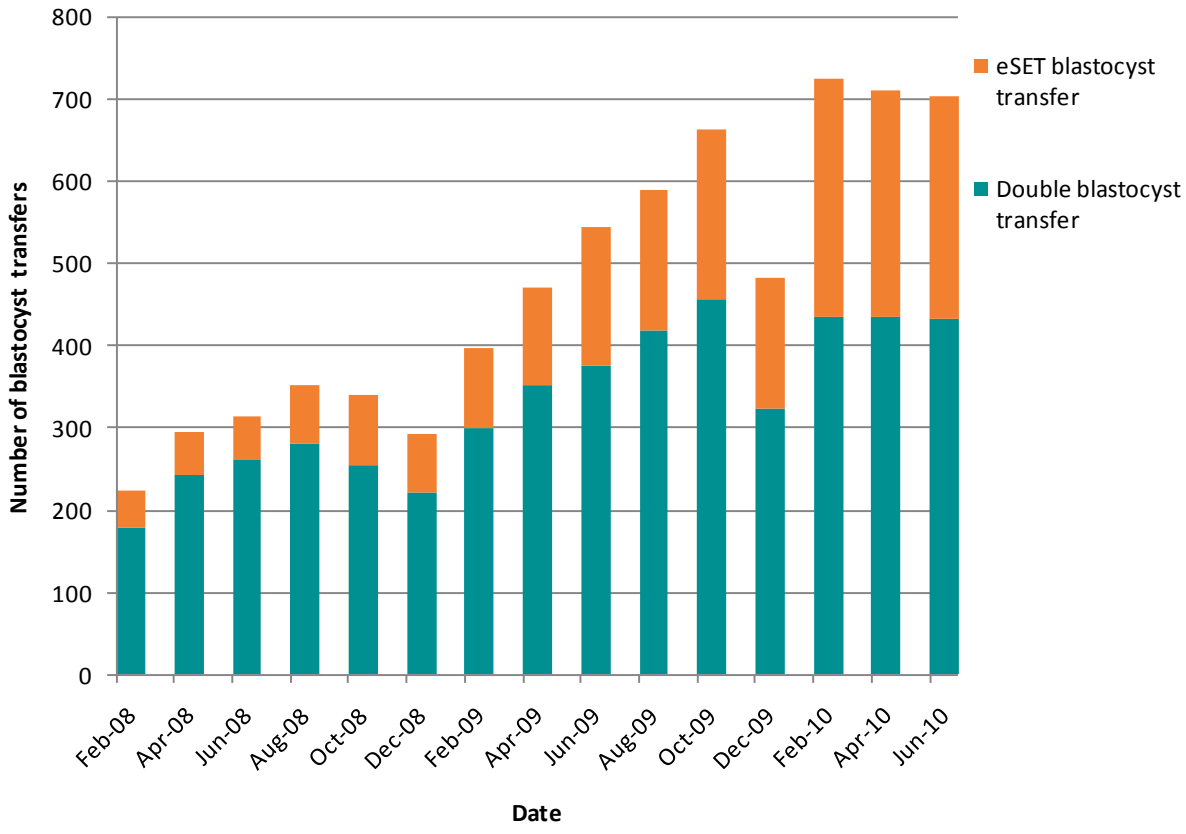
[10] Blake D, Farquhar C, Johnson N, Proctor M. Cleavage stage versus blastocyst stage embryo transfer in assisted reproductive technology. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No.: CD002118. DOI: 10.1002/14651858.CD002118.pub3.

► 8. Has the number of embryos transferred in each fresh blastocyst transfer changed recently?

When clinics in the UK were introducing blastocyst transfer, in early 2008, doctors tended to transfer two blastocysts at a time.

Figure 6 shows that as the technique has become more widespread, the proportion of these which are eSET has increased. Generally, fewer embryos are transferred in January and December of each year, and this is noticeable in this graph.

Figure 6: Proportion of fresh blastocyst transfers which were eSET or DET, January 2008 to June 2010 (plotted every two months)

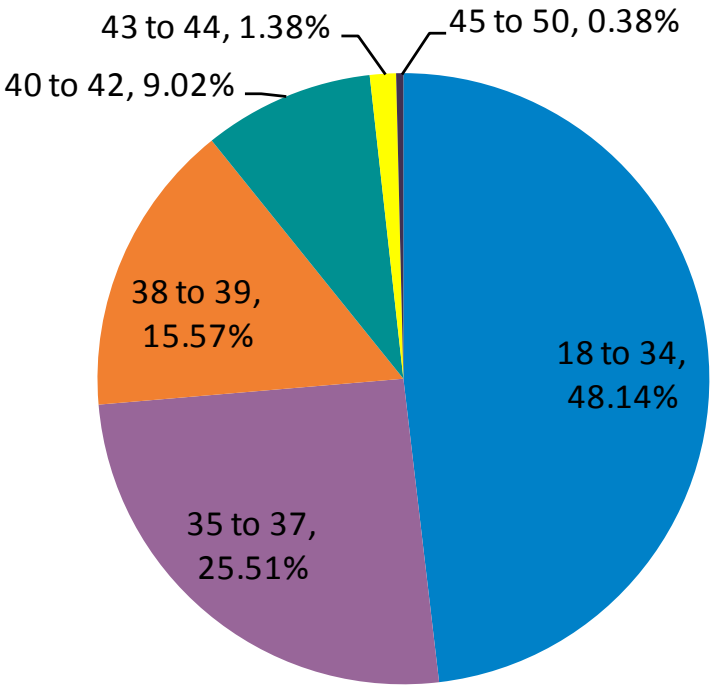


► 9. How old are the women having blastocyst transfers?

Nearly three quarters (73.7%) of women having blastocysts tranferred were aged 37 or under.

Around two thirds of all women having IVF are aged 37 or under.

Figure 7: Age of women receiving blastocyst stage embryo transfer, 2009



Key points: Blastocyst transfers have increased since January 2008 and the most recent data shows about a quarter of all embryo transfers are of blastocysts. Over this time, the number of these transfers which were of just one embryo has increased. Women who had blastocysts transferred tended to be slightly younger than the IVF population as a whole.

Fresh and Frozen Transfers

In the majority of treatment cycles (82.1%) the woman's own freshly collected eggs are used. A smaller number use embryos which have been frozen previously and then thawed just before transfer. This is known as a frozen cycle, or a frozen transfer.

► 10. Is there a difference between the eSET and DET rate in fresh and frozen transfers?

Women are more likely to receive eSET if they are having a fresh cycle than if they are having a frozen one (Table 1). Overall, they are also more likely to receive DET when having a fresh cycle. This is because it seems that women having frozen cycles may be more likely to have a non-elective SET (where they only have one embryo available to transfer) than when having a fresh cycle.

Table 1: Embryos transferred, as a percentage of all transfers, by age and whether the embryo is fresh or had been frozen, 2009[11]

		Fresh transfers		Frozen transfers	
	Transfer type:	eSET	Double	eSET	Double
Age	**18 to 34**	17.9	72.1	7.4	74.7
	35 – 37	9.8	79.7	6.9	69.5
	All ages	11.3	72.0	6.5	69.8

► 11. Is there a difference between the eSET and DET rate based on the stage of the embryo thawed?

Women receiving thawed blastocysts are more likely to have eSET than women receiving thawed cleavage stage embryos. Only a small proportion of thawed cleavage stage embryos are transferred as eSETs (Table 2).

Table 2: Embryos transferred, as a percentage of all frozen transfers, by age and whether the embryo is cleavage or blastocyst stage, 2009[11]

	Stage of thaw:	Cleavage		Blastocyst	
	Transfer type:	eSET	Double	eSET	Double
Age	**18 to 34**	6.3	79.3	11.3	60.3
	35 – 37	6.8	73.9	7.1	55.8
	All ages	5.9	76.0	9.1	56.7

Key points: Most treatment cycles use the woman's own fresh eggs to create embryos but some use embryos which were frozen, and then thawed just before transfer. These frozen cycles were more likely to involve the transfer of two embryos than fresh cycles; this was most pronounced where a cleavage stage embryo was transferred.

[11] Although the numbers in the table are percentages, they do not add up to 100% because some transfers are non-elective SET and a few are of three embryos.

Pregnancies

► 12. What is the pregnancy rate?

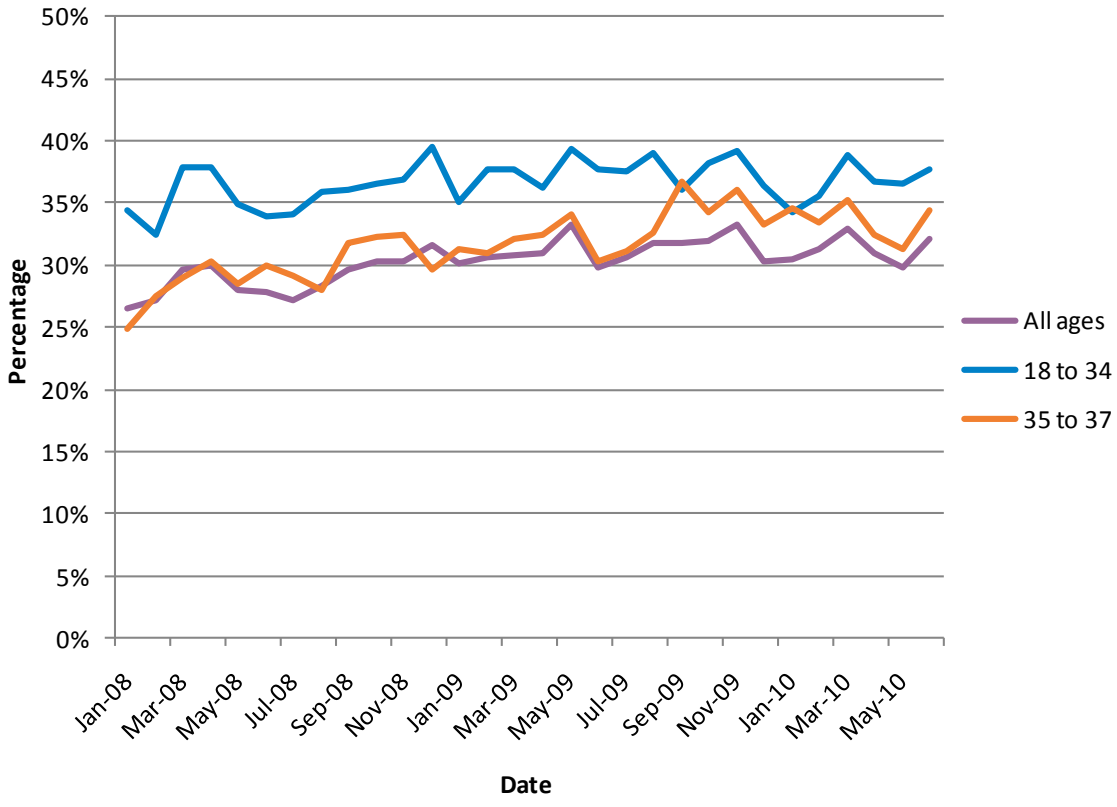
The pregnancy rate is the number of women who were subsequently confirmed pregnant with an ultrasound scan expressed as a percentage of those who had embryos transferred. There have been concerns that increasing the eSET rate would lead to a drop in overall pregnancy rates for patients, however, the pregnancy rate increased from 2008 to 2009 and remained steady in the early part of 2010.

Table 3: Pregnancy rate, per embryo transfer

	Year of treatment:	2008	2009	2010 (Jan to Jun)
Age	**18 to 34**	35.9	37.6	36.8
	35 – 37	29.7	33.0	33.5
	All ages	29.0[12]	31.4	31.3

Figure 8 shows how the pregnancy rate has changed, month by month, since January 2008. The general trend for all ages from January 2008 is upwards, which is reflected in the overall annual figures above, but it does vary each month and pregnancy rates seem to have levelled out for the younger patients.

Figure 8: Pregnancy rate, per embryo transfer, January 2008 to June 2010



[12] Note that this figure was updated from 26.5% to 29.0% in December 2001 after re-analysis

► 13. What is the multiple pregnancy rate?

A multiple pregnancy is a pregnancy where two or more fetuses develop at one time in the womb. The multiple pregnancy rate is the percentage of pregnancies confirmed by ultrasound to which were multiple pregnancies.

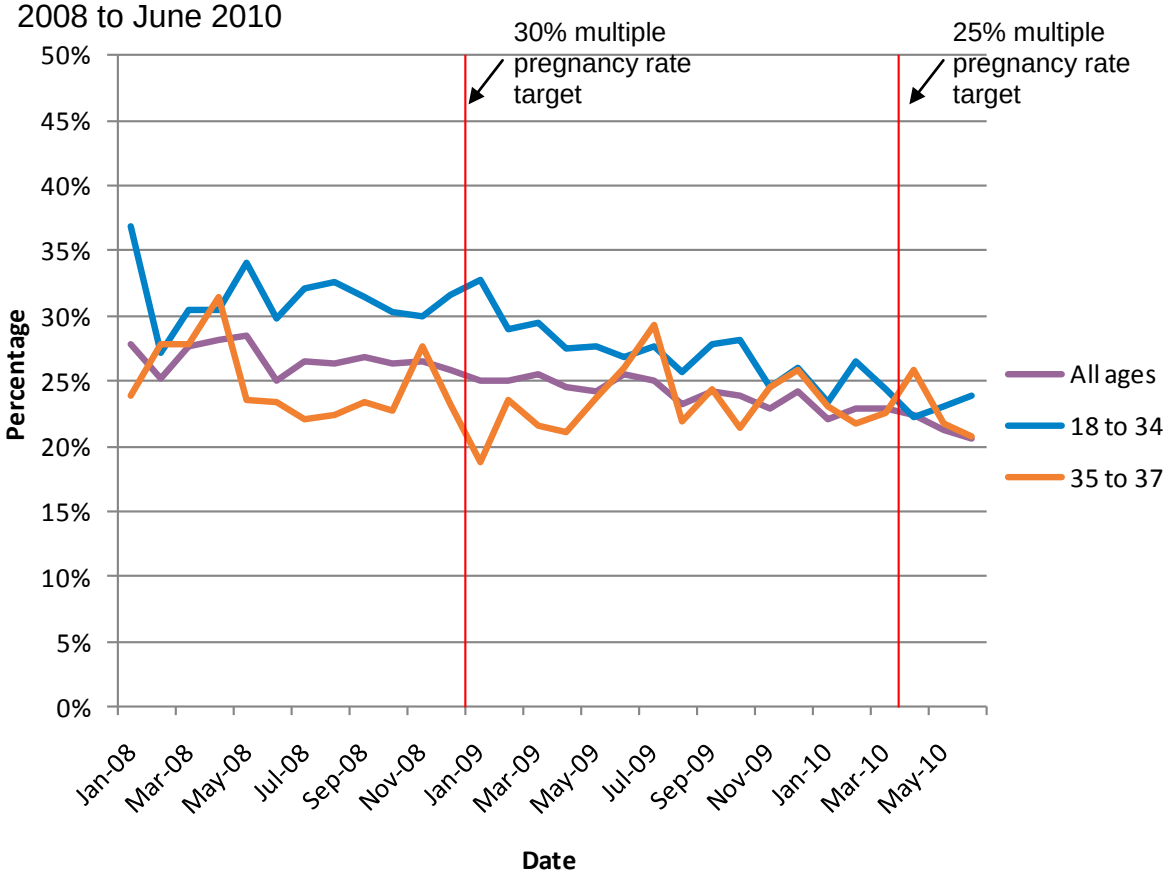
The multiple pregnancy rate has decreased between 2008 and the beginning of 2010 (Table 4). The decrease is most pronounced in women aged under 35, who saw the greatest increase in eSET (figure 1).

Table 4: Multiple pregnancy rate, per pregnancy

	Year of treatment:	2008	2009	2010 (Jan to Jun)
Age	**18 to 34**	31.2	27.6	23.9
	35 – 37	25.0	23.5	22.6
	All ages	26.7	24.4	22.0

Figure 9 shows the decline in the multiple pregnancy rate since January 2008. We can see variability from month to month, but overall the trend is downwards. The vertical lines on the graph show when the equivalent maximum multiple pregnancy rates were introduced by the HFEA.

Figure 9: Multiple pregnancies as a percentage of all pregnancies, January 2008 to June 2010



Key points: Concerns that the pregnancy rate would drop due to the increase of eSET were not confirmed. The multiple pregnancy rate dropped, dramatically in the case of the younger patients, while the overall pregnancy rate was maintained.

► 14. Does the multiple pregnancy rate differ when one or two cleavage or blastocyst embryos were transferred?

Multiple pregnancies following single embryo transfer are rare and happen when the embryo splits in two, resulting in identical (monozygotic) twins.

After a double cleavage stage embryo transfer between a quarter and a third (depending on the woman's age) of pregnancies confirmed by ultrasound were of two or more babies. By receiving eSET, the risk of a multiple pregnancies is similar to that of all conceptions, which is 1.64%[13].

After a double blastocyst stage embryo transfer a much higher percentage of pregnancies confirmed by ultrasound were of two or more babies, almost half in women aged under 35. Again, by receiving eSET this risk is reduced to a similar level to all conceptions.

Table 5: Multiple pregnancy rate, per pregnancy by stage and number of embryos transferred, 2009

	Stage:	Cleavage stage embryo		Blastocyst stage embryo	
	Transfer type:	eSET[14]	Double	eSET	Double
Age	**18 - 34**	<1.0	33.2	<2.0	44.0
	35 – 37		25.4		37.6
	All ages	<1.0	27.6	<2.0	39.4

Key points: Transferring two blastocysts at a time leads to a very high multiple pregnancy rate.

► 15. How does the pregnancy rate differ for fresh and frozen transfers?

Table 6 contains data for both cleavage and blastocyst stage embryos. It is clear that the pregnancy rate is higher following fresh embryos compared to frozen embryos transfer. In frozen transfers there is very little difference between the pregnancy rates for eSET and DET, but the risk of multiples is of course reduced considerably by having eSET.

Table 6: Pregnancy rate, by type and number of embryos transferred, 2009

	Fresh/Frozen:	Fresh		Frozen	
	Transfer type:	eSET	Double	eSET	Double
Age	**18 - 34**	39.4	43.2	25.7	25.8
	35 – 37	37.0	37.3	22.2	25.9
	All ages	37.2	36.3	22.7	25.0

[13] Office for National Statistics, 2010, Statistical Bulletin: Live births in England and Wales by characteristics of birth www.statistics.gov.uk/pdfdir/birth1110.pdf. The ONS figures will contain multiple births after fertility treatment, as well as natural conceptions as they cover all recorded births in England and Wales.

[14] Figures for 18 – 34 and 35 – 37 are aggregated due to the very small numbers involved, to protect patient identity.

► 16. What is the pregnancy rate if a woman aged under 38 (with spare embryos to freeze) transfers either two embryos at the same time (DET) or first one fresh and then another frozen embryo at a later stage (eSET)?

The professional bodies recommend that younger women with three or more good quality embryos qualify for eSET. The HFEA does not hold data about how the quality of an embryo used in treatment was graded by the IVF lab. So to study outcomes for women who qualified for eSET, but went on to have DET, we used the fact embryos were frozen in the same cycle as an indication that these women had more than two good quality embryos.

The group of women who elected to have only one embryo put back, didn't get pregnant, and then went back to the clinic to have another treatment attempt with a frozen embryo, is still quite small (269), so these figures need to be considered as part of a preliminary analysis. We will follow up this question again at a later stage, when we have a larger number of women to base the analysis on. Research in other countries has shown that, after the introduction of an eSET policy, the pregnancy and live birth rate can be maintained with the addition of subsequent frozen cycles[15].

Comparing outcomes for these good prognosis women shows that, overall, women who qualify for eSET have slightly higher pregnancy rates if they have two embryos put back in the first instance, than if you put back first one fresh, and then the other frozen embryo at a later stage. The pregnancy rate for fresh DET in women under 38 is 52.1% per cycle. The pregnancy rate for fresh eSET in women under 38 is 42.6% per cycle, this increases to 43.7% when the subsequent frozen eSET cycle is included.

However, it is important to read these results in conjunction with the respective multiple pregnancy rates: the multiple pregnancy rate for eSET patients is close to the level occurring naturally, whereas the multiple pregnancy rate for good prognosis women (i.e. those under 38 that had additional embryos to freeze) who went on to have DET is very high (40.9%).

[15] 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.pdf

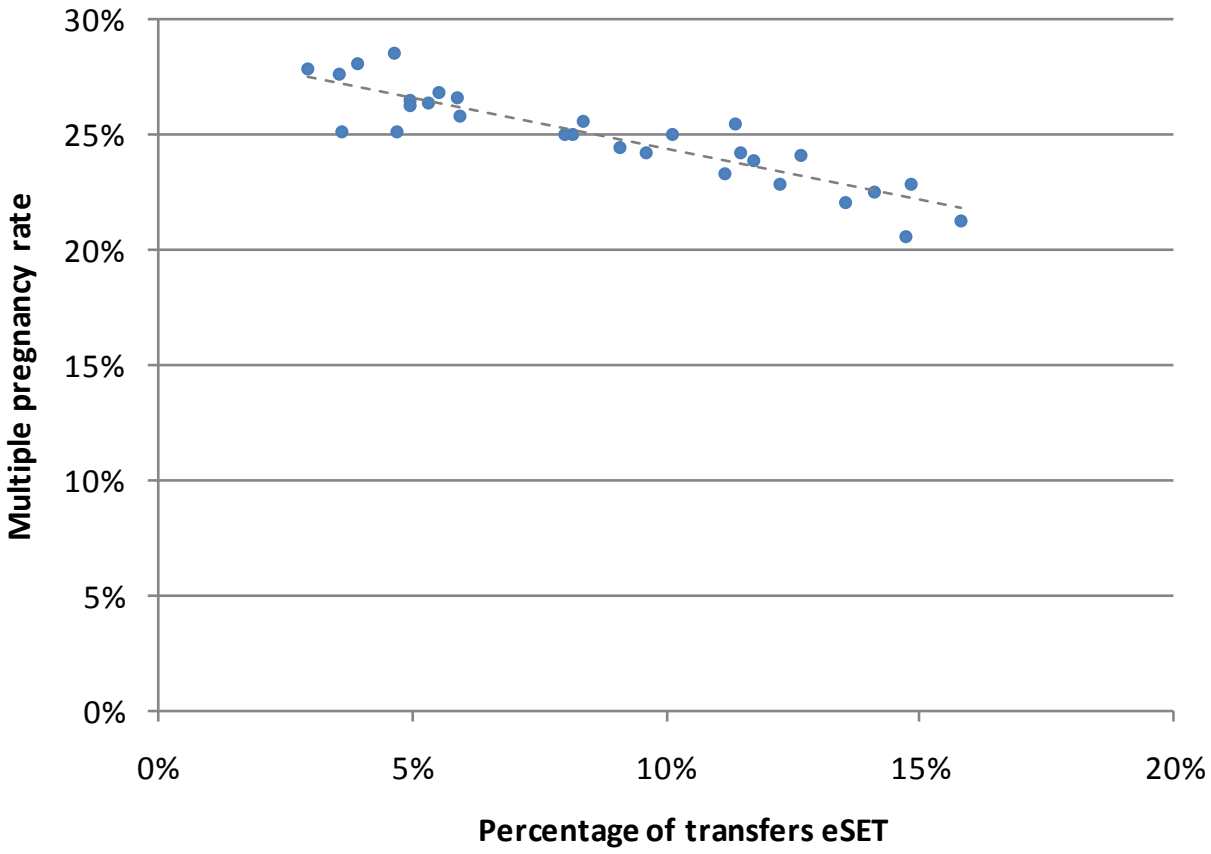
► 17. How does the multiple pregnancy rate vary with the eSET rate?

We know that the proportion of embryo transfers which were eSET in January 2008 was 2.9%, and the multiple pregnancy rate in cycles started in that month was 27.9%. A year later these figures were 8.2% (an increase) and 25.0% (a decrease) respectively. It is possible to plot these figures, the eSET rate and the multiple pregnancy rate, against each other on a graph to see whether, in general, they vary together in the same way.

Figure 10 shows that there is an association between the overall eSET rate (along the horizontal line) and the overall multiple pregnancy rate (along the vertical line).

The multiple pregnancy rate decreases as the eSET rate increases. This association has been seen in the results published by other countries too[16]. The dashed line has been added by a computer program to highlight the trend.

Figure 10: Sector wide early multiple pregnancy rate plotted against the corresponding sector wide eSET rate for that month, January 2008 – June 2010.



[16] 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.pdf

Live births

► 18. What is the live birth rate?

The live birth rate is the number of live birth events achieved from every 100 treatment cycles started.

As with pregnancies (Table 3), on average, women aged under 35 when their treatment starts are more likely to have a baby than women who are older. The live birth rate remained steady overall between 2008 and the first six months of 2009, but declined very slightly for women aged under 38.

Table 7: Live birth rate, per cycle started, by woman's age

	Year of treatment:	2008	2009 (Jan to Jun)
Age	**18 - 34**	31.7	30.1
	35 – 37	25.6	24.6
	All ages	24.4[17]	23.6

► 19. What is the multiple birth rate?

The multiple birth rate is the number of multiple births from every 100 live birth events.

The multiple birth rate decreased from 2008 to the first six months of 2009, most noticeably in the group aged under 35 (Table 8). We expect the multiple birth rate to follow the multiple pregnancy rate and continue to drop.

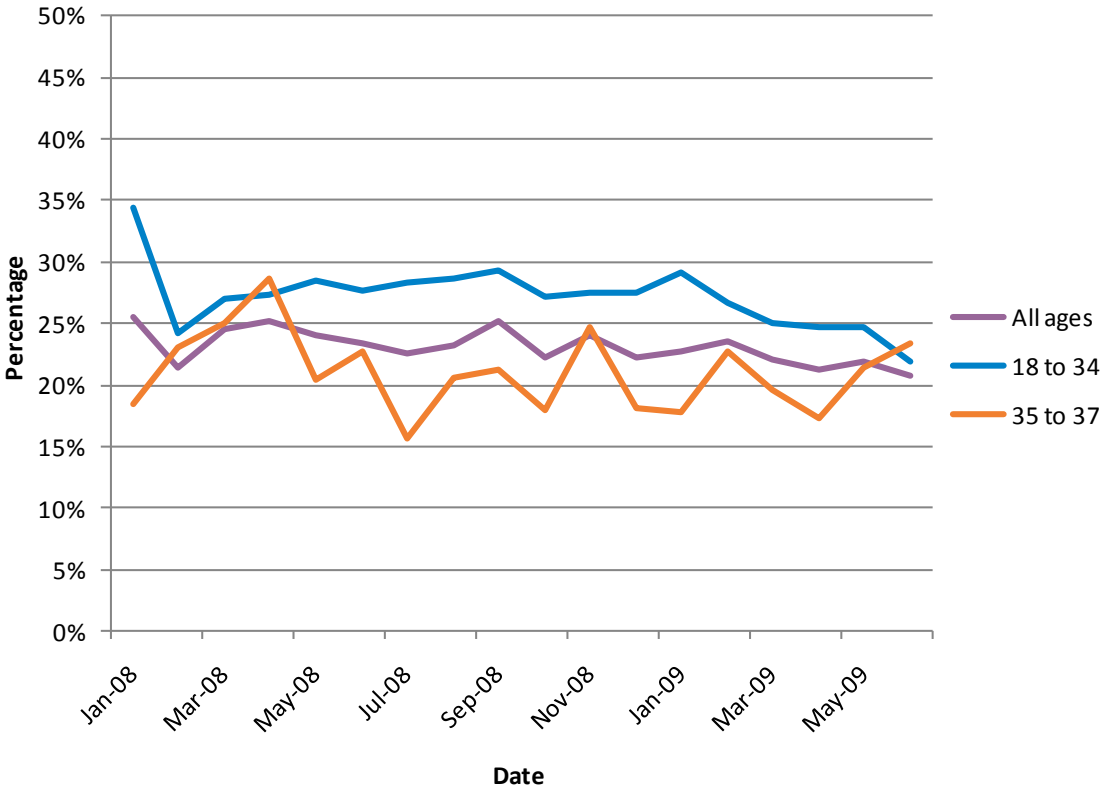
Table 8: Multiple birth rate, per live birth event, by woman's age

	Year of treatment:	2008	2009 (Jan to Jun)
Age	**18 - 34**	27.9	25.1
	35 – 37	21.5	20.4
	All ages	23.6	22.0

Figure 11 is on the next page.

[17] Note that this figure was updated in December 2011 from 23.7% to 24.4% after re-analysis.

Figure 11: Multiple births, as a proportion of all live births, January 2008 to June 2009.



► 20. Does the multiple *birth* rate differ when one or two cleavage or blastocyst embryos were transferred?

As seen in table 6 (pregnancies), there is a substantial increase in the percentage of multiples when blastocyst stage embryos are transferred (Table 9). As with pregnancies, after eSET, the risk of multiples is greatly reduced in both cleavage and blastocyst transfers.

Table 9: Multiple birth rate by stage and number of embryos transferred, 2008

	Stage:	Cleavage stage embryo		Blastocyst stage embryo	
	Transfer type:	eSET[18]	Double	eSET	Double
Age	**18 - 34**	<0.5	29.6%	<1.5	41.2%
	35 – 37		23.2%		28.5%
	All ages	<0.5	25.2%	<1.5	33.8%

[18] Figures for 18 – 34 and 35 – 37 are aggregated due to the very small numbers involved, to protect patient identity

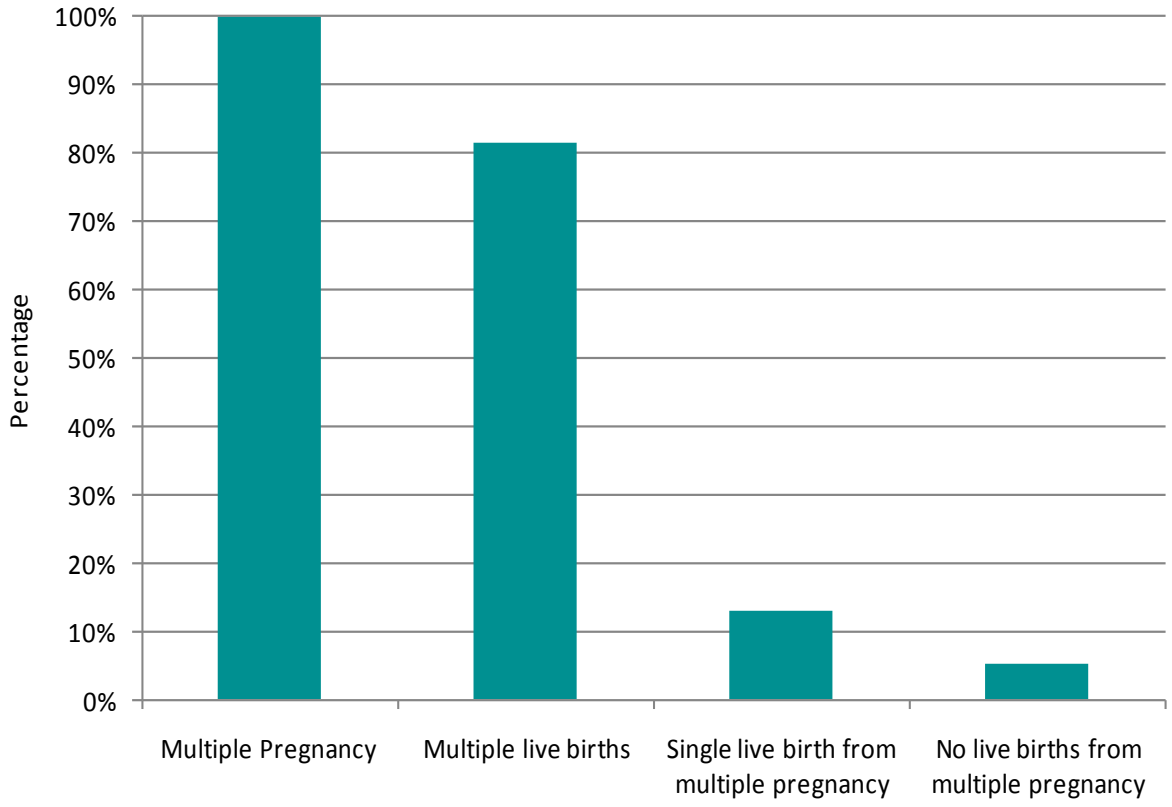
► 21. Do all multiple pregnancies result in a multiple birth?

The majority 81.5% of women who had an early multiple pregnancy (where two or more fetal heartbeats are seen on the ultrasound) went on to deliver multiple live births. A minority, but almost a fifth, 18.5% lost one or more fetuses and gave birth to only one live baby or none.

Of the women with an early multiple pregnancy who suffered a miscarriage, around a third of them lost all of the fetuses, resulting in no live births.

In the graph below, all reported multiple pregnancies are shown as the bar touching 100%, the resulting multiple live births, singleton live births and no live births are shown as a percentage of this starting point.

Figure 12: Outcomes of multiple pregnancies, 2008.



Prematurity, birth weight and Complications

► 22. Prematurity and low birth weight

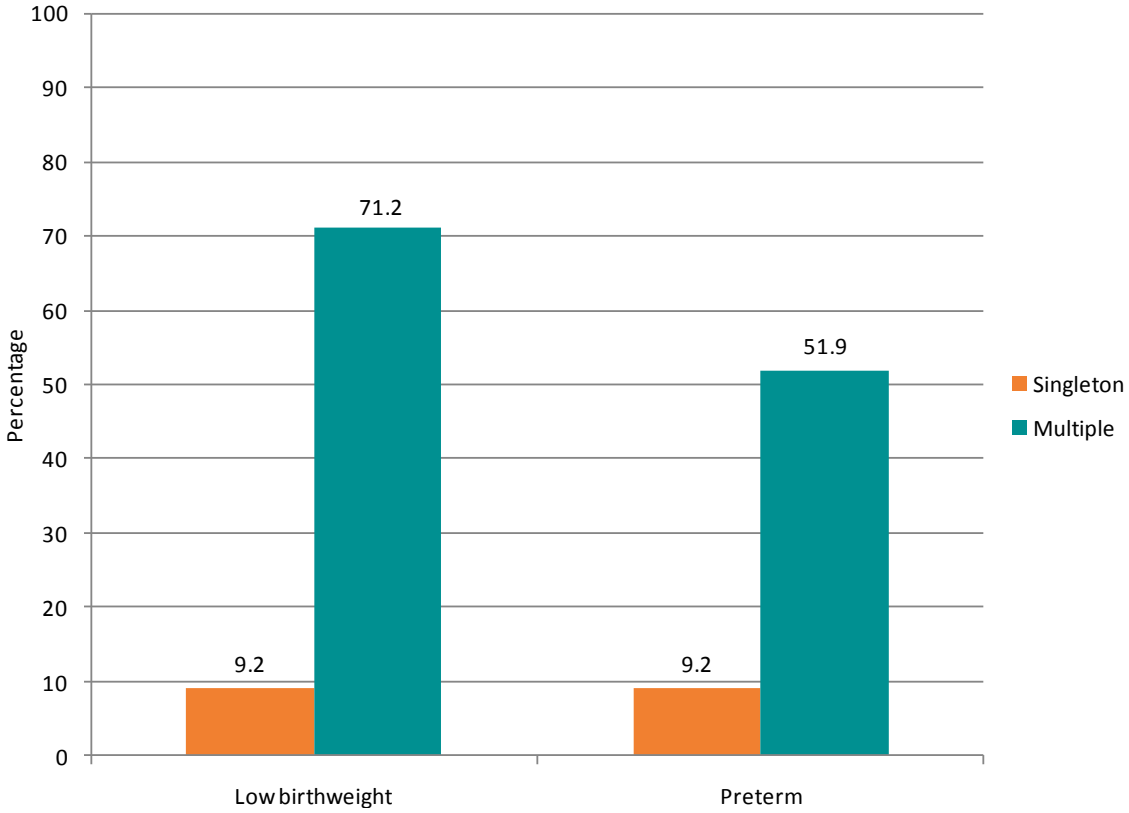
Most babies born as a result fertility treatment are full term and of a normal birthweight. That is 37 weeks gestation or more, and more than 2500g, or 5½ pounds in weight.

Preterm babies, and those of a low birthweight (including full term babies) have an increased risk of developing health problems during the first days and weeks of life.

Twins born after IVF typically are not identical, as they are the result of two embryos being transferred, rather than one embryo splitting (which has more health risks associated) and so tend to do better than multiples in the wider population where a higher proportion of twins are identical.

The graph below shows that babies born as part of a multiple are much more likely to be born prematurely and with at least one baby of a low birth weight than babies born as a singleton.

Figure 13: Preterm and low birth weight rate for babies born as singletons and multiples*, 2008



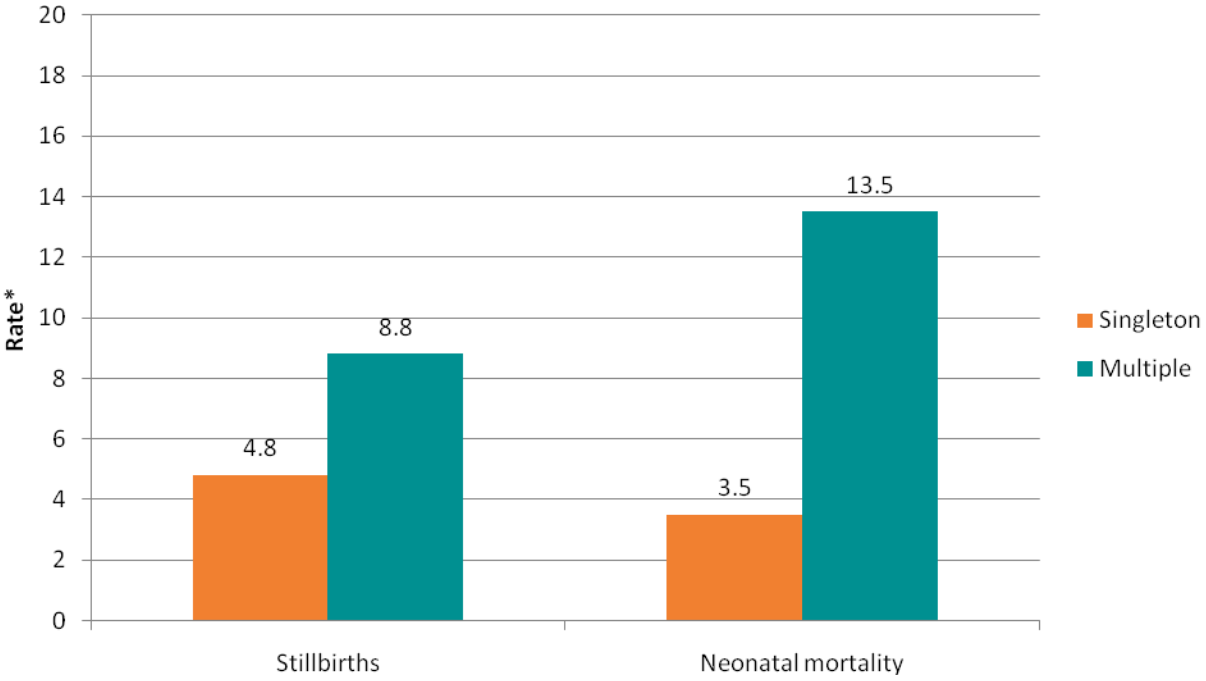
*Where at least one baby born as part of a multiple was low birthweight
Low birthweight less than 2.5kg, preterm less than 37 weeks gestation

► 23. Still births and neonatal deaths.

As with any pregnancy, a small number of IVF pregnancies sadly end with the delivery of a baby who is stillborn, that is, born after 24 weeks showing no sign of life. And, as with any baby born, a small number of IVF babies sadly die within their first month of life, these are called neonatal deaths.

Because the numbers are very small, these results are presented per 1,000 live births. This is not the same as a percentage, where results are expressed per 100 live births.

Figure 14: Stillbirth rate (per 1,000 total births) and neonatal mortality rate (per 1,000 live births) for babies born as singletons and multiples, 2008



*Rate – per 1,000 total births (babies born alive and still born) for still births and 1,000 live births for neonatal deaths

Key points: Still births and neonatal deaths are rare events. The likelihood is increased in multiple pregnancies.

Conclusions

This report aims to understand better what happened with pregnancy and multiple births rates during a time when efforts were made to make IVF safer, by increasing the number of full term singleton births.

In terms of reducing the risks associated with multiple pregnancies and births, the strategies pursued by clinics, in line with HFEA policy, have been a clear success.

Elective single embryo transfers (eSET) have increased, especially in younger women – those for whom it is generally most appropriate.

Multiple pregnancies have decreased; again especially in younger women – those who are generally most at risk of multiple pregnancy.

Overall, live birth rates appear to be maintained. However, pregnancy rates in younger women do seem to have levelled out between 2009 and the first half of 2010. Other countries' experiences suggest this is to be expected and it highlights the importance of subsequent frozen transfers to maintain pregnancy rates overall. It is early days for understanding the impact of eSET plus subsequent frozen transfers, so pregnancy rates will continue to be monitored closely.

It is clear from the analysis published here, the first for the UK sector, that it is possible to make IVF safer, and to maintain success rates. It is also clear that further efforts need to be made to select the right patients for eSET treatment, so that women's chances of getting pregnant aren't damaged in the process.

The HFEA is extremely grateful to the work of the professional bodies, of patient groups and many committed clinicians and embryologists who have made the progress so far possible. We are all united behind our one goal: to give IVF children the best possible start to life.