Human Fertilisation & Embryology Authority

Scientific and Clinical Advances Advisory Committee - minutes

17 October 2016

Conwy Room, 10 Spring Gardens, London SW1A 2BU

Committee members		Yacoub Khalaf (Chair) Kate Brian Andy Greenfield Anne Lampe Tony Rutherford	
Members of executive		Anna Rajakumar (lead) Anna Quinn (secretary) Juliet Tizzard Nick Jones Nadia Huq	Polly Todd Dee Knoyle Anjeli Kara
External advisor	Present	Daniel Brison Robin Lovell-Badge Gudrun Moore Melanie Davies Joyce Harper	Sheena Lewis
	Apologies	Raj Mathur Jane Blower	
Invited Speakers		Azim Surani	
Observers		Steve Pugh (DH)	

1. Welcome, apologies and declarations of interest

1.1. The Chair welcomed committee members to the meeting and conveyed apologies on behalf of Raj Mathur and Jane Blower.

1.2. In relation to the meeting agenda, interests were declared by Kate Brain and Melanie Davies, who were members of the NICE IUI guidelines committee. Melanie Davies also declared a conflict in relation to multiple births as she sits on the Multiple Births Stakeholder group on behalf of the Royal College of Obstetrics and Gynaecology.

2. Matters Arising

2.1. Minutes of the meeting held on 13 June were agreed remotely prior to the meeting.

3. Chair's Business

3.1. The Chair noted that the Nuffield Council on Bioethics has recently issued an ethical review on genome editing. Two priority areas were identified by Nuffield: human reproduction and livestock. Working groups have been formed to consider these areas further. One member of the committee noted that no policy recommendations have been made by either group as yet.

3.2. The Chair of the mitochondrial donation expert panel informed the committee that their review of the safety and efficacy of mitochondrial donation techniques is ongoing.

3.3. The dates for the 2017 committee meetings were agreed as:

6 February 2017
19 June 2017
16 October 2017

4. Committee work plan

4.1. The committee discussed potential speakers to invite to a focussed meeting on embryo testing in February and highlighted the importance of having a balance of opinions.

4.2. The committee agreed to postpone inviting a speaker on the topic of in vitro maturation as members did not think the use of this technique is widespread in the UK. Members agreed that they could consider this topic if horizon scanning identified it as high priority.

4.3. Some committee members requested that culture media be considered at the meeting in February 2017 due to recent developments in this area.

Action

4.4. The Scientific Policy Manager will invite speakers to the February 2017 for a focussed discussion about embryo testing.

5. Reinvigorating the multiple births policy

5.1. The Regulatory Policy Manager gave a presentation on the topic of reinvigorating the HFEA's multiple births policy which was initially launched in 2009. The current average multiple births rate following fertility treatment is around 14%, and the current target is 10%. The natural twinning rate is between 1-2% of all pregnancies. The Regulatory Policy Manager asked for feedback from the committee on the impact of double blastocyst transfer and what can be done to help clinics achieve the multiple birth rate target. Some suggested:

- making single embryo transfer a focus for inspections with a tougher approach being taken for clinics doing double embryo transfer
- developing further patient information to educate patients on the potential risks of double embryo transfer and multiple births

- focussing on clinics who carry out double blastocyst transfer and ensuring clinicians are educated on the associated risk of multiple births.

5.2. The committee were in agreement that impressive progress has already been made in reducing multiple births and stressed that further reduction will require extra work by the sector and the regulator.

5.3. The committee noted that there has been a rise in blastocyst transfer, without a concurrent rise in single embryo transfer. This implies that some clinics are transferring two blastocysts during a single treatment cycle, which raises issues for multiple pregnancies and births.

5.4. One committee member asked how many clinics have multiple birth rates significantly higher than the target rate, and if data for these clinics were removed from the analysis, would the average multiple births rate change? The Executive noted that there are a small number of clinics who tend to repeatedly miss the target multiple births rate and agreed to carry out the analysis without these clinics to assess their impact on the overall average. The committee also discussed the limitations of low numbers in statistical analyses and the possibility of looking at data over two year periods to increase the sample size and generate a more reliable indication of whether clinics are meeting the multiple births target.

5.5. One member noted that single embryo transfer is more common in NHS clinics compared with private clinics, partly due to NHS commissioning policies. The committee considered whether patients at private clinics could be more demanding in asking for double embryo transfer as they are paying for their treatment. The committee agreed that it will be important to educate patients as well as clinics on the risks of multiple pregnancies and births as some patients still believe that a multiple pregnancy is an especially desirable outcome of fertility treatment. The committee were in agreement that displaying success rates 'per embryo transfer' will help people to consider single embryo transfer.

5.6. The committee discussed the One at a Time website and members of the Executive confirmed that the website will be decommissioned and the content incorporated into the new HFEA website. The Executive anticipate that this will increase views of content related to multiple pregnancies and births.

5.7. One member suggested changing the target measure from percentage multiples births to a percentage of single embryo transfer. Another member questioned whether the HFEA has powers to sanction clinics who are meeting the multiple births target, who would not be meeting a new single embryo transfer target.

5.8. The committee discussed lowering the current 10% multiple births target and it was raised that this might act as a disincentive to clinics who are not meeting the current target as the new figure may feel out of reach. Members agreed that a decision about lowering the target should be made after the reaction to displaying statistics per embryo transfer has been assessed.

5.9. The committee agreed that they would like to see statistics on the number of babies admitted to neonatal units to determine if this has reduced in line with a reduction in average multiple births rates.

6. In vitro derived gametes

6.1. The Scientific Policy Officer introduced a paper on in vitro derived gametes, highlighting that it has been several years since the committee last considered this topic and significant progress has been made during this time.

6.2. One member asked to what extent the mouse model is an accurate model for human development. The committee discussed the benefits of using mice as a model for human development as it is possible to study multiple generations in a shorter time by deriving embryonic stem cells. Using mice also avoids potential ethical issues relating to deriving and culturing human embryos in vitro.

6.3. The committee discussed the need for transplanting in vitro derived gametes back into the ovary to develop, and that ideally when culturing in vitro derived gametes the supporting somatic cells would also be derived in vitro.

7. Biology of human development

7.1. The Chair welcomed Professor Azim Surani to the meeting to give a presentation on the biology of human development. Prof Surani spoke to the committee about transmission of genetic and epigenetic information via the germline and successes in deriving primordial germ cells from embryonic stem (ES) cells and induced pluripotent stem (iPS) cells.

7.2. Prof Surani addressed the issue that in order to derive germ cells from primordial germ cell-like cells (PGCLCs), the cells have previously had to be implanted into the ovaries or testes as this is where imprinting occurs. He noted that progress in research in 2016 has been able to bypass this stage and derive germ cells without implantation into ovaries or testes. Prof Surani also highlighted the importance of reproducing these results.

7.3. Members of the committee asked Prof Surani about the limitations of using the mouse as a model for human development. Prof Surani explained that there are differences in regulation of the pluripotency network between mice and human, as well as differences between the germ cell transcriptome and post implantation development.

7.4. Prof Surani explained that animal models are also required as in the UK, human embryos cannot be cultured for more than 14 days after fertilisation. He noted that the pig is an affordable and accessible model for human development which allows detailed epigenetic research to be carried out. Prof Surani explained that slaughterhouse material can be used to obtain animal tissues for research as it is readily available and raises few ethical concerns.

7.5. The committee discussed the possibility of deriving germ cells directly from somatic cells such as fibroblasts and agreed that research is still progressing in this area and robust methodology for deriving germ cells is this way is yet to be developed.

7.6. One member asked Prof Surani how long he anticipates it will be before human germ cells which are high enough quality to be used in treatment could be developed. Prof Surani highlighted the difficulty in predicting the progress of future research but suggested that successful derivation of high quality cells in humans is still a number of years away. The committee also noted that in vitro derived gametes cannot legally be used in treatment in the UK.

8. Treatment add-ons

8.1. The Communications Manager provided an update to the committee on the HFEA's treatment add-ons work and confirmed that the Executive will shortly be commissioning an independent systematic review of the evidence supporting the use of the agreed treatment add-ons. Members agreed that the relevant Cochrane group should also be approached to provide an assessment of the evidence base for each treatment add-on.

8.2. The committee requested that a clinician be involved in the assessment of the evidence in order to assess the relevance of the evidence and to put the evidence into context.

8.3. One committee member requested that additional treatment add-ons are added to the material: DNA fragmentation, intracytoplasmic morphological sperm injection (IMSI) and physiological ICSI (PICSI).

8.4. The Communications Manager presented a table showing the range of prices for different treatment add-ons at different clinics. The table was produced by a review of all clinic websites and presented an estimate rather than a comprehensive list of prices The committee agreed that it would be useful for patients to see the variable costs of these treatments and questioned whether cost effectiveness could be incorporated into the traffic light system proposed for the new HFEA website. Some members argued that it would be too complicated to include cost effectiveness as this would vary from patient to patient, they suggested including some indication of cost alongside the traffic light. The committee discussed whether the HFEA should publish the cost to the clinic for providing an add-on instead or a range of charges for the patient.

8.5. The Executive explained that the tone of the website will not be to advertise or endorse treatment add-ons. Rather, the tone will be to inform patients that they may be offered an add-on and to provide information that may help the patient to decide whether they wish to pay for it. The committee were in agreement with this approach but highlighted that careful user testing of the information will be required to ensure that the correct message is being conveyed.

8.6. The committee discussed whether labelling some treatment add-ons as 'experimental' could be confusing to patients and suggested that 'early stage research' may be more appropriate. In general, members preferred the current suggested categories of 'experimental', 'limited evidence' and 'backed up by clinical trials'.

8.7. The committee agreed that intrauterine culture should be categorised as red and suggested that the independent systematic reviewers also comment on the suggested categories to determine if they agree with the proposed categories.

Action

8.8. The Scientific Policy Manager will circulate the costs table to the committee for their information.

8.9. The Executive will share the results of the independent systematic review with the committee once the process is complete.

8.10. The Executive will aim to publish the new treatment add-ons information when the new website is launched in early 2017.

9. NICE IUI Guidelines

9.1. The Scientific Policy Manager informed the committee of consideration by NICE of the evidence for intrauterine insemination (IUI) versus expectant management where NICE's recommendations excluded the use of IUI.

9.2. One member noted that IUI is quite an unsuccessful treatment, however they disagreed with the notion that this treatment option should not be recommended to any patients. The committee questioned the decision to compare IUI with expectant management and some members of the committee were in agreement that a more relevant question would be to compare IUI with IVF. It was also noted that removing NHS commissioning of IUI would disadvantage couples living in areas where funding for IVF cycles is limited to one cycle.

9.3. Another member suggested that based on the limited evidence available regarding IUI versus expectant management, a clinic trial comparing the two approaches would be of value in deciding whether IUI is a worthwhile intervention.

9.4. The committee discussed issues with commissioning of fertility treatment, where CCGs do not follow NICE guidance. It was noted that NICE have made a recommendation based on the false assumption that CCGs are funding fertility treatment according to their current guidance.

9.5. One committee member highlighted that NICE may look at IUI versus IVF in the future. However, another member noted that there are no studies directly comparing these two treatments. Rather, a study may compare the strategy of IUI with a single cycle of IVF, which may not be a meaningful comparison.

9.6. The committee were in agreement of the importance of research into fertility treatments but noted the difficulties in obtaining funding for these studies.

9.7. The committee discussed what advice the HFEA can give alongside NICE guidelines. It was noted that it would be difficult to contradict NICE guidelines but that the HFEA could highlight the need for more evidence. The HFEA could also highlight that the guidance says 'do not routinely recommend'.

10. Any other business

10.1. One member raised the issue of clinic websites overstating their success rates and questioned whether the HFEA can regulate websites. It was noted that the HFEA can question clinics about information that may be misleading on their websites, however they do not audit websites. The committee discussed the variety in reporting of statistics by clinics and descriptions of treatment add-ons. An HFEA Inspector informed the committee of a pre-inspection audit tool which is used prior to inspection. The committee requested a more systematic review of clinic websites be carried out and suggested that the HFEA provides a standard format for clinics to display statistics on their websites.

10.2. One committee member updated the group on current active clinical trials funded by the National Institute for Health Research (NIHR). eFreeze recruitment is currently slow and not meeting milestones. It was questioned whether the HFEA could encourage centres to recruit to clinical trials. It was noted for the eFreeze trial that whilst consent rates are good, a patient must have three or more good quality embryos in order to be randomised and the number of patients meeting this criterion is lower than expected. A study looking at endometrial scratching is in the early stages of recruitment. The possibility of a trial looking into PGS is being explored in order to determine is this technique can improve live birth rates. The committee highlighted that slow recruitment can hinder future trials receiving funding, which makes completing trials even more important in this sector. The committee agreed that the new HFEA website should promote participation in clinical trials and highlight the importance of research.

Action

10.3. The Scientific Policy Manager will ask the Chief Inspector to follow up on the request for a more detailed review of clinic websites.

11. Next meeting:

11.1. Monday 6 February 2017, Etc. Venues, One Drummond Gate, Victoria, London SW1V 2QQ

Signature

Name Yacoub Khalaf

Committee chair

Date 2/03/17