Scientific and Clinical Advances Advisory Committee (SCAAC) – minutes

8th February 2021

Teleconference (Zoom meeting)

Authority members of the SCAAC	Present	Yakoub Khalaf (Chair) Gudrun Moore (Deputy Chair) Ermal Kirby Anne Lampe	
	Apologies	Kate Brian	
External advisors of the SCAAC	Present	Richard Anderson Jane Blower Andy Greenfield Robin Lovell-Badge Raj Mathur Kevin McEleny	Daniel Brison Joyce Harper Sheena Lewis Shankar Srinivas
Members of the Executive	Present	Dina Halai (Meeting lead) Matthew Mudford (Meeting secretary) Victoria Askew (Meeting secretary) Laura Riley Clare Ettinghausen Peter Thompson Sally Cheshire Rachel Cutting Paula Robinson Sharon Fensome-Rimmer India Hickey Karen Campbell Sarah Stedman	
Observers	Present	Tim Child (Authority member) Jason Kasraie (Authority member) Georgina Allen (DHSC) Csenge Gal (DHSC)	

1. Annual Review of Committee Effectiveness

1.1. The Annual Review of Committee Effectiveness was led and recorded by the Executive.

2. Welcome, apologies, declarations of interest

2.1. The Chair welcomed members to the meeting.

2.2. The Chair welcomed two new Authority members, Tim Child and Jason Kasraie, who attended the meeting as observers ahead of officially beginning their terms of service in June 2021.

2.3. Declarations of interest were received by Raj Mathur, Joyce Harper, Daniel Brison, Sheena Lewis and Richard Anderson.

3. Matters arising

3.1. Minutes of the meeting held in October 2020 were agreed remotely prior to the meeting.

3.2. The Policy Manager updated the Committee on matters arising:

3.2.1. The Committee has agreed to continue to highlight relevant papers about COVID-19 and the effects on reproduction or early pregnancy to the executive for discussion during a standing agenda item.

3.2.2. It is too early for the Executive to present the effects of COVID-19 and treatment cessation on early pregnancy and live birth data, which requires a two-year delay in reporting. The Committee were instead directed to a published study using HFEA data.

3.2.3. The patient survey of the treatment add-ons webpages had been completed and a summary of results were presented at the November 2020 Authority meeting. In light of feedback from the survey, the October 2020 SCAAC meeting and the November 2020 Authority meeting, the Executive has undertaken a further update to the HFEA treatment add-ons webpages due to be published in February 2021. This update will include refined information on immunological tests and treatments and the traffic light ratings will no longer reflect the safety considerations of each add-on. Instead, safety will be commented on for each treatment add-on outside of the traffic light ratings.

3.3. The Scientific Policy Manager further updated the Committee on progress that had been made in the treatment add-ons project including:

3.3.1. Clarifying that information provided on treatment add-ons is targeted at the general treatment population. There may be circumstances where treatment add-ons are recommended for specific patient groups for justifiable medical reasons other than to increase live birth rate.

3.3.2. Asserting that the treatment add-on traffic light ratings are based on evaluation of the evidence base and are supported by advice from an independent expert in systematic reviews.

3.3.3. Clarifying the definition of green-rated treatment add-ons, such as ICSI for male factor infertility, and that green-rated treatment add-ons may be routinely used in fertility treatments and information on these can be found elsewhere on the HFEA website, therefore will not be included in the HFEA's traffic light rated list of add-ons.

3.4. The Treatment add-ons working Group (TAG) met in November 2020 and one outcome was for the Executive to collaborate with Fertility Network UK (FNUK) to compile a checklist of questions that patients may want their clinician to answer when discussing add-ons. That has been reviewed by patients and will be published on the HFEA website soon.

3.5. The Executive is collating a list of the guidance and information on treatment add-ons already published by professional organisations which will be a resource for clinicians. That will be displayed on the HFEA clinic portal when complete.

3.6. At the November Authority meeting, it was decided that the HFEA should provide information on commonly offered complementary and alternative therapies as a separate item to the treatment add-ons list and that it need not be traffic light rated. This is currently being developed and will be peer-reviewed by external experts and patient feedback will be also be sought before publication.

3.7. Members felt that clarity of communication is key in any information we provide on these contentious subjects.

3.8. A member wished to highlight that a paper has been accepted for publication by RBM Online ~~Society~~ journal related to the advertising of complementary therapies by fertility clinics. It found that provision of professional advice on nutrition (from nutritional therapists, nutritionists, dieticians) was too varied to analyse meaningfully. It looked at the evidence base for three popular therapies- there were no RCTs on reflexology but there are studies on acupuncture, and it concluded that both should be included and rated as add-ons. A systematic review of acupuncture, also for publication, recommended an amber traffic light rating from the HFEA.

3.9. There is also a related RCOG scientific impact paper. The Chair expressed that it may be useful to look at this paper to see if it is current, whether it ~~represents~~ resonates with the views of the Committee and whether it satisfies the framework that we apply to add-ons.

3.10. The Scientific Policy Manager clarified that the HFEA website information on complementary therapies is not in relation to the treatments being add-ons, and will not be traffic light rated, as agreed by the authority. The pages will however be will be peer-reviewed by external experts.

3.11. Members expressed that the pages should be evidence-based and should not be seen to promote these therapies.

3.12. Members felt that there needs to be clarity as to whether general well-being improves outcomes of fertility treatment. If that were to be so, then a treatment that improves well-being could also be seen to be increasing chances of improving the outcome of treatment.

Action:

3.13. The Executive to check what was agreed at the November Authority meeting in relation to the brief of the complementary therapies information.

4. Update from Fertility 2021

4.1. The Chair invited members to share learning points from the Fertility 2021 conference.

4.2. A member highlighted talks given by Prof Darren Griffith about how the recommendations of SCAAC are perceived and how add-ons are presented. It included data from the HFEA register which he requested under the FOI Act.

5. Monitoring the effects of COVID on fertility, assisted conception and early pregnancy

5.1. The Chair acknowledged the papers that had been submitted and shared with the Committee prior to the meeting.

5.2. As a response to the widespread misinformation and lack of clarity regarding vaccines and their use in fertility patients, the British Fertility Society (BFS) and the Association of Reproductive and Clinical Scientists (ARCS) have developed a public-facing set of FAQs. Members felt that it was important to maintain a pro-vaccination stance to overcome the vaccine hesitancy caused by earlier messaging. The HFEA website displays an FAQ that includes advice on vaccinations and is regularly updated with the latest guidance from government and professional bodies.

5.3. Members agreed it was important to monitor the research closely, particularly with how frequently outcome studies are being published. It has been confirmed that oocytes and embryos have the receptors and signalling pathways for the virus and in one study SARS-CoV-2 was found in human oocytes.

5.4. It is important to differentiate what effects, such as the effect on sperm function, are related to the virus specifically and which are caused by the illness, by fever for example.

Action:

5.5. The Executive will update their website in line with the BFS and ARCS guidance when it becomes available.

Action:

5.6. The Committee will continue to monitor and share relevant literature.

Action

5.7. The Executive will add a section to the clinic portal website which will include all papers related to COVID-19 that have been discussed at SCAAC meetings.

6. Prioritisation of the issues identified through the horizon scanning process

6.1. The Policy Manager presented a summary of the HFEA's horizon scanning process and the topics for consideration by members.

6.2. The horizon scanning process is an annual cycle that takes information from journal articles, conferences and the Executive's Annual Horizon Scanning meetings.

6.3. The purpose is to identify issues that could have an impact on the field of assisted reproduction or embryo research. This feeds into the business planning for the Executive, SCAAC and the Authority so the latter are aware of potential licence applications and can prepare, if necessary, a policy position or develop relevant patient information.

6.4. It was noted that although it is a high-priority issue, treatment add-ons were not included in this horizon scanning process as they are discussed in detail at the October SCAAC meetings. The effects of COVID on fertility, assisted conception and early pregnancy is a standing item on the SCAAC agenda and so was also not included.

6.5. The horizon scanning process has highlighted that there are a number of treatments available to patients that may fit the criteria to be included in the HFEA's traffic light rated list of treatment add-ons. These are outlined in the horizon scanning paper.

6.6. Members were asked to:

- note the issues identified as high and medium priority through the horizon scanning process;
- consider the high and medium priority issues and work recommendations; and
- consider whether advice from additional external advisors would help in achieving the work recommendations.

Action:

6.7. Update the committee's 2021/22 workplan as follows:

- The SCAAC discussion on Artificial Intelligence (AI)/Machine Learning should take place in 2021 because it has already begun to be used in clinical practice.
- Synthetic human entities with embryo-like features, "SHEEFs", are so far in the future that there is less value in discussing them now and can be pushed back in the workplan to 2022.
- Consider replacing the term 'Synthetic human entities with embryo-like features, "SHEEFs" with the terms used in the ISSCR guidelines when available.
- 'New technologies in embryo testing including PGT-M and PGT-A' is a high priority issue but is not scheduled for discussion by the Committee for two years. They suggested more closely following this issue by including it on the Committee Workplan for 2021-22, inviting a speaker and discussing it.

6.8. The Scientific Policy Manager clarified that all issues are discussed every two years and the workplan presented only covers the next year.

6.9. One member suggested that SCAAC should invite a speaker from one of the organisations featured in the paper, the Victorian Assisted Reproduction Authority (VARTA) or Monash IVF, to present to SCAAC.

6.10. One member highlighted that the horizon scanning paper identifies surgical sperm retrieval (SSR) for use in ICSI as a potential future add-on for the treatment of high DNA fragmentation rates. Although there is little work being done scientifically on the subject, it is currently being offered in the UK and so they would welcome the Committee's opinion on this.

6.11. It was suggested that Mary Herbert, in Newcastle, would be an appropriate speaker for the discussion of mitochondrial donation, although there may be some conflict of interest.

6.12. One member wished to make an amendment to what PRISM data is being recorded in particular what is being asked to be recorded for testicular biopsies for sperm retrieval. The data the HFEA are requesting is not meaningful as it does not distinguish between obstructive and non-

obstructive causes so it would be helpful if the HFEA could change that so that the reason for the retrieval would be listed.

6.13. Regarding ooplasm transfer for treatment of infertility, one member wished the Committee to consider a trial published in ELife Costa-Borges et al. (2020) where maternal spindle transfer was used to rescue failure of embryo development in mice and they did reciprocal transfer. There is a clinic in the Ukraine that has reported 'success' in treating infertile women with these techniques. This work has mainly gone unpublished so far. One member stated that while looking at the evidence it is important to establish why these techniques work, whether it is the mitochondrial donation that has made the difference in these patients and not another factor in the cytoplasm that has led to failure of the early embryos to develop. There may be a simpler process than spindle transfer. One member also wished to clarify that microfluidic sperm sorting does not allow separation of X and Y variant sperm.

6.14. Several members suggested that the horizon scanning process should be a literature review of all journals, not just from a selected list. The Scientific Policy manager clarified that the list of journals used for the scanning process is based on a list that was decided by SCAAC but that the Executive will do a broader search in future if that is preferred by SCAAC.

Action:

6.15. In future, the horizon scanning will be based on a more open (but informed) PubMed search.

6.16. One member wished to include that along with prime editing genome editing techniques there have also been significant developments in base editing which is promising in that it is improving accuracy. Kathy Niakan could be a good guest speaker on this topic and someone who is actively using these techniques on early embryos.

7. Embryo culture media

7.1. The Scientific Policy Manager summarised the paper, highlighting that SCAAC has been concerned about embryo culture media for some time, particularly that the components and make-up of the media frequently changed, meaning research quickly went out of date. SCAAC have had concerns about the impact of culture media on embryo development and the long-term effects on children conceived by Assisted Reproductive Technology (ART).

7.2. The paper focuses on studies published since embryo culture media was last discussed by SCAAC in 2019.

7.3. The Scientific Policy Manager highlighted that embryo culture media is legally out of the remit of the HFEA and is under that of the MHRA. For instance, if a lab became concerned about CE-marked product, it would be up to them to raise it with the MHRA through the yellow card process. If the product was not marked with CE, ie used for research, it would be the responsibility of the researchers to raise it with the manufacturer directly.

7.4. Issues are considered by the HFEA to be a medium priority if they are within the HFEA remit but meet at least two other criteria, as defined in the paper. Low priority issues are those outside of HFEA's remit and unlikely to impact on research or treatment in the near future. As embryo culture media is outside of the HFEA remit but could impact on research or treatment it should be considered should be considered as medium/low priority for SCAAC.

7.5. One member argued that this topic is closely related to a high priority issue, 'health outcomes of children conceived by ART' and should not be considered as low priority for SCAAC. The composition of the embryo culture media and the effect it has on birthweight could be considered one of the most significant mechanisms in the altered health outcomes of children conceived by ART. Randomised Controlled Trials have shown that the choice of culture media used affects birthweights and in turn, differences in birthweight are associated with long-term health outcomes. Therefore, the composition of culture medium, the disclosure of the components and the ability to track the effects of them on outcome should be considered a high priority for SCAAC. MHRA do not track long-term health outcomes, neither do the European Commission, so it is down to SCAAC to consider such outcomes and make recommendations accordingly.

7.6. For the HFEA, high priority issues must fall within the HFEA remit so at present embryo culture media will remain as a medium priority and embryo culture media shall continue to be included as part of the SCAAC horizon scanning process.

7.7. A member noted that several members of SCAAC were asked to be external advisors to the MHRA on embryo culture media compositions, approximately 5 years ago, but have not been asked for advice by them since.

8. Any other business

8.1. The Executive will keep members informed of progress on the information we provide to patients relating to treatment add-ons. That work includes defining and detailing 'routine' IVF to draw attention to the success without add-ons.

8.2. The Chair thanked Kate Brian for her valuable contributions to SCAAC and for representing patients so well.

8.3. The Chair was delighted to report that Raj Mathur and Robin Lovell-Badge have accepted their invitation to continue on the Committee for a term of three years.

8.4. The Chair has also gratefully accepted an invitation to remain as an HFEA Authority member and Chair of SCAAC until the end of 2021.

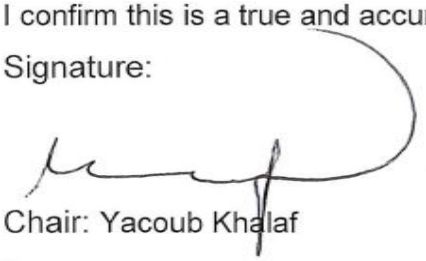
8.5. On behalf of the Committee, the Chair expressed his gratitude to Sally Cheshire for her longstanding support of the meeting and for her valuable contributions. The impact that she has had will leave a lasting legacy for the role of SCAAC and for the HFEA. Sally Cheshire thanked the Chair and showed her appreciation for the work of SCAAC members.

8.6. The Chair summarised the meeting and thanked the Committee.

9. Chair's signature

I confirm this is a true and accurate record of the meeting.

Signature:



Chair: Yacoub Khalaf

Date: 24/03/2021