Scientific and Clinical Advances Advisory Committee (SCAAC) – Minutes

Monday 3rd February 2025, 10:00am – 3:00pm

Wandle room, 2nd floor, 2 Redman Place, London, E20 1JQ & Microsoft Teams (hybrid meeting)

Authority members	Present	Tim Child (Chair) Frances Flinter Christine Watson (virtual) Stephen Troup Geeta Nargund
	Apologies	Zeynep Gurtin
External advisers	Present	Anthony Perry Scott Nelson (virtual) Kevin McEleny (virtual) Richard Anderson (virtual) Alison Campbell Peter Rugg-Gunn Veronique Berman (virtual) Ying Cheong
Speakers	Present	Andy Vail (Expert Statistician, University of Manchester) for item 9 (virtual)
Executive	Present	Julia Chain (Chair of Authority) Peter Thompson (Chief Executive) Clare Ettinghausen (Director of Strategy and Corporate Affairs) Rachel Cutting (Director of Compliance and Information – virtual) Dina Halai (Head of Policy, Scientific) Rebecca Taylor (Scientific Policy Manager) Molly Davies (Policy Manager, Scientific) Dharmi Deugi (Scientific Policy Officer; Committee Secretariat)
Observers	Present	Several HFEA staff observed the meeting as relevant to their role or induction into the organisation.

1. Welcome, apologies, declarations of interest

1.1. The Chair welcomed the Committee and introduced two Authority Members who have joined the SCAAC:

- Stephen Troup brings expertise in Clinical Embryology.
- Geeta Nargund brings expertise on Reproductive Medicine.

1.2. Dharmi Deugi was introduced as the Executives' new Scientific Policy Officer and Secretariat for SCAAC.

1.3. Apologies were received from Zeynep Gurtin.

1.4. The Chair reminded members of the advisory role of the SCAAC, highlighting that members should advise the HFEA on any significant implications for licensing and regulation arising out of scientific and clinical developments in assisted conception, embryo research and related areas.

1.5. Declarations of interest were made by:

- Stephen Troup (Fertility Consultant)
- Geeta Nargund (Founder and Medical Director of CREATE Fertility and abc IVF)
- Alison Campbell (Chief Scientific Officer of the Care Fertility Group and Clinical Advisor for U-Ploid Biotechnologies)

1.6. No further conflicts of interest were declared.

2. Matters arising

2.1. The Executive updated the Committee on the matters arising:

2.1.1. In the October 2024 meeting, it was recommended that the Committee discuss the growing body of evidence against the use of ICSI for non-male and mild-male factor infertility at the February 2025 meeting.

2.1.2. As the publications relevant to the use of ICSI for non-male and mild-male factory infertility are still under review, the Executive proposed that this discussion take place at a subsequent SCAAC meeting. A 'watching brief' for this topic has been introduced as part of the SCAAC's horizon scanning function.

2.1.3. The Executive has updated the 'Time-lapse imaging and incubation' webpage to add the additional randomised control trials (RCTs) discussed at the October 2024 meeting to the reference list. A footer has been added to make it clear that these studies were not subject to the independent statistician's review conducted during the July 2023 add-ons ratings review.

2.1.4. The 'Immunological tests and treatments for fertility' webpage has also been updated to add an additional RCT and highlight that there is evidence of an increased risk of poor outcomes (including pre-term delivery rate and biochemical pregnancy loss) associated with the use of steroids (glucocorticoids).

3. Chair's business

3.1. The Chair provided updates from the Authority:

3.1.1. In October 2024, four new members were appointed to the Authority Board by the Secretary of State for Health and Social Care. Details of the appointments are available on the HFEA website.

3.1.2. The Authority considered the recommendations of the SCAAC concerning the 14-day rule, in vitro derived gametes (IVGs) and stem cell-based embryo models (SCBEMs) and made a series of recommendations at the November 2024 and January 2025 meetings. Minutes of these meetings can be found here. A member noted that the use of the term 'solo motherhood' in relation to IVGs could cause confusion given that it has also been used as a term for women who are having donor insemination (DI) as single parents. The Chair agreed that the HFEA should provide clarity on the terminology related to 'solo parenting' when referring to IVGs.

3.2. The Chair provided further updates on SCAAC membership highlighting that:

- Alex Kafetz has left the Committee since the last meeting, remaining a member of the Authority. The Chair thanked Alex Kafetz for his contributions to the SCAAC.
- As per the Standing Orders, External Advisers (EA) to the SCAAC may only be appointed for a term of three years, with a maximum of two terms. This allows for a refresh of expertise and views, consistent with good committee governance.
- Richard Anderson and Kevin McEleny are completing their second term as EAs to the SCAAC and will be leaving the committee in June 2025, ahead of the next SCAAC meeting. The Chair thanked both Richard and Kevin for their contributions to the SCAAC.
- To replace their expertise, the Executive and SCAAC Chair will soon begin the formal process of recruiting new EAs. Members will be informed when this process is underway.

3.3. The Chair noted that the Executive have begun planning for the HFEA's Annual Horizon Scanning Meeting, due to be held in Paris during the 41st Annual Meeting of the European Society of Human Reproduction and Embryology (ESHRE). The Committee will be contacted about this as required.

4. Relevant public health developments and research findings

4.1. The Chair informed the Committee that this item provides members with the opportunity to highlight research relevant to the interests and role of the SCAAC, including research developments relevant to the add-ons ratings. This may include research that may change a rating for an existing add-on or could be used to suggest new add-ons that are being offered in UK clinics. It may also be used to suggest topics for the horizon scanning priority list.

4.2. No papers were raised for discussion in advance of the meeting.

4.3. The Chair noted that with support of the Executive, Veronique Berman has agreed to prepare an application to propose platelet rich plasma (PRP) as an HFEA rated treatment add-on.

4.3.1. Veronique Berman flagged that many clinics are now offering PRP with a lack of supporting evidence and expressed appreciation for the opportunity to research this in more depth.

4.3.2. The Chair invited members to circulate any specific high-quality publications which would support the PRP add-ons application to the Executive. A member highlighted that there is also now a randomised controlled trial in this area that would support the application.

4.4. A member flagged that the results of a large trial looking at the outcomes of the Zishen Yutai Pill (YTP), a traditional Chinese medicine, on live birth rate are due to be published soon.

4.5. A member highlighted that there are an increasing number of trials on the use of glucagon-like peptide-1 (GLP-1) as a weight loss intervention and its impact on fertility treatment. The Chair agreed that weight loss injections are becoming readily available, and it would be useful for SCAAC to advise on the research therein as it is published.

5. Health outcomes in children conceived by ART (including the impact of culture media)

5.1. Health outcomes in children born from ART (including the impact of culture media) was last discussed by the SCAAC in October 2023, when the Committee highlighted the need for long term follow-up linkage studies establishing cause of potential differences between patient cohorts.

5.2. The literature review identified 49 studies published between September 2023 and December 2024. The literature review noted studies whose results point to a higher risk for adverse maternal and perinatal outcomes in twin pregnancies.

5.3. The Executive noted that the composition, quality and safety of culture media is not within the regulatory remit of the HFEA, falling within the remit of the Medicines and Healthcare products Regulatory Agency (MHRA). However, SCAAC monitor the effect of culture media in the context of its safety for the embryo, and the health of any children born following assisted conception.

5.4. The Committee discussed the recent developments on the topic:

5.4.1. The Committee congratulated the Executive on the paper and noted that it was comprehensive.

5.4.2. The Director of Strategy and Corporate Affairs noted that several researchers have used the HFEA Register to carry out long term linkage studies. There are currently a number of ongoing research projects looking at the long-term effects of ART on both children and patients, however, it was noted that much of this research has used the anonymised dataset. It was confirmed that the HFEA database does not hold information on culture media but since 2008, it does hold the NHS number of any child born as a result of ART as a way of linking back to clinical records.

5.4.3. The Chief Executive noted that previously there was concern that clinics should not be faced with the burden of reporting unnecessary additional information. Once the PRISM integration and data validation is finalised, recommendations on the information collected will be revisited by the SCAAC.

5.4.4. The Chair reminded members of previous discussions in relation to recording culture medium on the HFEA Register and the concerns expressed regarding the ingredients and how often they change. Another limitation is the number of stages and media involved in the embryology process, including for example, the polyvinylpyrrolidone (PVP) media, fertilisation media and buffers. As such, recording all the different types of media used would be labour intensive.

5.4.5. It was also noted that culture media could have epistatic effects, and it would be important to enumerate the variables of the culture media. In support of this, CO_2 tension, and osmolality shifts could have an impact, and therefore automation in terms of incubation and dish preparation may make a positive difference in reducing the impact of other variables.

5.4.6. A member highlighted that there is pressure on companies to become more transparent about the composition of culture media and that, under the European Union Medical Device Regulation (EU MDR), companies are required to undergo the revalidation process for every product at least every two to three years. As part of this process, the documentation is very comprehensive and lists detailed information about the components of the culture media, in addition to an updated literature review on the effects of the culture media.

5.4.7. It is the responsibility of the clinic to ensure that they are using high quality media and being transparent about what they are using, in addition to weighing the risks and benefits of fresh versus frozen embryo transfer.

5.4.8. A member suggested that, due to the trend towards freeze all cycles, the Committee should continue to monitor health outcomes of frozen embryo transfers (FET) in addition to fresh transfers and cumulative linkage. It was noted that the study by Rios et al. (2024) highlighted the risk of childhood leukaemia, in particular lymphoblastic acute childhood leukaemia with FET.

5.4.9. It was flagged that the ability to do qualitative follow-up studies with patients or children born from ART could be difficult as many people who go through treatment may have found this a difficult experience and therefore do not want to focus on this aspect of their lives.

5.4.10. Another member noted that the biggest limitation of long-term linkage studies is that they are not representative of modern clinical practices, for example, the change in practice from day three to blastocyst (day five) transfers.

5.4.11. **Recommendation:** Introduction of a new topic looking at the health outcomes for ART patients (including gestational surrogates, egg donors, and the impact of treatment using donated eggs) as part of the horizon scanning function.

6. Impact of stress on fertility treatment outcomes

6.1. The Committee were reminded that the impact of stress on fertility treatment outcomes was introduced as a horizon scanning topic in June 2022 and is currently considered a medium priority topic.

6.2. The Executive highlighted that the last literature search in June 2022 noted that a clear link between stress and fertility treatment outcomes had not been established.

6.3. The literature review identified 30 studies published between May 2022 and December 2024.

6.4. The paper highlighted that research continues to be inconclusive on whether increased stress levels during treatment have a negative impact on outcomes. Studies on interventions to manage stress found that while they had a positive impact on stress/emotional well-being, this did not always translate to IVF outcomes, or the association was unclear or weak.

6.5. This latest paper also identified a new area of research, the impact of stress on the decision to discontinue fertility treatment.

6.6. The Committee made the following comments and recommendations:

6.6.1. Members congratulated the Executive on the paper.

6.6.2. A member noted that treatment outcomes cannot be linked to the levels of the stress that patients are experiencing when undergoing treatment. However, it is clear that in practice providing emotional support and talking therapy does make the process more manageable and also allows patients to better deal with the outcome.

6.6.3. It was highlighted that stress is a common reason for patient complaints. Within the private sector, patients commonly request refunds as a result of stress and with NHS funded cycles, patients are likely to request another cycle due to stress.

6.6.4. Furthermore, stress could arise as a result of funding decisions being dependent on patient postcode in the UK or the financial consequences of seeking private treatment.

6.6.5. Several papers were referred to including those that noted withdrawal from treatment due to the physical stress of undergoing it, in addition to stress related to not receiving public funding. Long term impacts of stress during the entire treatment process can have a negative effect on how the patient responds post treatment, for example, their ability to bond with and parent the child, and their decision to withdraw from treatment if going through another cycle.

6.6.6. ~~A~~ member also pointed to the long-term effects of antidepressants, which is important to consider as patient support groups have found that the long-term effects of undergoing fertility treatment can leave patients feeling lonely, having suicidal thoughts and depression.

6.6.7. Although the studies are generally poor quality and stress is subjective, thus difficult to measure, the Chair supported the comments noting the significance of the impact of stress on patient withdrawal from treatment in addition to the importance of clinics providing psychological support.

6.6.8. A member expressed that even though most clinics will offer emotional support, in most cases patients are only provided with one session following which further sessions would involve expenditure on behalf of the patient/couples; many of whom report already spending a significant amount of money on the treatment itself.

6.6.9. A member noted that page 29 and 30 of the paper, in addition to 3.1, 3.2 and 3.5 can be used to summarise the conclusions, acknowledging that: although treatment may be a stressful process for patients, measurements of stress are heterogeneous making the impact between stress and treatment outcomes difficult to determine. Despite this, interventions to reduce stress in whatever form appropriate for the patient, could have a positive impact on stress and emotional wellbeing during the treatment cycle, regardless of the impact on outcomes. Patients should consider cost effective strategies to manage their stress during treatment, beyond that limited to paid interventions.

6.6.10. Members agreed that there is no evidence to say either way that stress has any impact on fertility treatment outcomes however this is one of the biggest patient concerns.

6.7. **Recommendation:** The Executive to publish a statement on the website to highlight that there is no conclusive evidence as to the impact of stress on treatment outcomes.

6.7.1. A member raised that in mice the evidence shows that stress is trans generationally and epigenetically heritable. The member proposed that the Committee should keep an eye on

whether there is any evidence that children who are born to couples experiencing high levels of stress are subject to similar neurological traits or phenotypes. Where evidence is relevant, this may be considered under the health outcomes topic.

7. Mitochondrial donation: polar body transfer

7.1. The Committee were reminded that the topic of mitochondrial donation was last discussed by the SCAAC in October 2024.

7.2. The topic was brought back to the committee to discuss research that has been conducted on polar body transfer (PBT) techniques since the last review in November 2016 by the mitochondrial donation expert panel.

7.3. The paper concluded that although PBT techniques may be able to address concerns with mitochondrial heteroplasmy seen across established methods of mitochondrial donation, the research is still in experimental stages.

7.4. In relation to this topic, the Committee discussed the following:

7.4.1. A member raised that a 2014 paper[1] which was conducted on mice to compare spindle transfer with pronuclear transfer, first polar body (PB1) and second polar body (transfer), illustrated a clear advantage of using PB1 in transfer. PB1 contain very few residual mitochondria, as such the offspring that are born (F0, F1, F2), contain no detectable mitochondria carry over in a heteroplasmic situation. PB1 transfer has been attempted in humans, however, the results of the research did not prove to be advantageous. It was noted that application of the micromanipulation technique in a clinical setting requires an expertise and that this may have impacted the results of the research.

7.4.2. Members highlighted that even though only two offspring were produced, the study on the single macaque demonstrates that PB1 could potentially be a beneficial technique, that does appear to reduce contamination by the affected mitochondria.

7.4.3. In addition, the two papers published in 2017 by Wu et al. illustrate the feasibility of PB1 and PB2 in humans. Nonetheless, these studies used very small sample sizes, conducted very limited investigations of the embryo as they only developed to the blastocyst stage, and performed limited analysis of mitochondrial DNA carry over in more differentiated cells.

7.4.4. It was noted that the study by Ji et al. (2025) reports on the first use of PBT in oocytes with pathogenic mitochondrial DNA mutations; however, information was limited to that provided in the abstract. Further research of this type would be appropriate, ahead of any action.

7.4.5. Although there has been some progress, members felt that the benefit of PBT in lowering risk of carryover is yet to be confirmed and that the focus of research remain on establishing whether PBT is a reliable technique.

7.4.6. Members agreed that progress on PBT has been slow and there is not yet enough additional research, to make a strong case to for legislative change. As there are currently two legalised

[1] Wang T, Sha H, Ji D, Zhang HL, Chen D, Cao Y, Zhu J. Polar body genome transfer for preventing the transmission of inherited mitochondrial diseases. Cell. 2014 Jun 19;157(7):1591-604. doi: 10.1016/j.cell.2014.04.042. PMID: 24949971.

techniques and an established research and clinical programme, continued monitoring of research is appropriate.

7.5. **Recommendation:** The Executive to continue to monitor polar body transfer under the horizon scanning topic of mitochondrial donation. A review of evidence by the panel could be considered once further data has been published.

8. Prioritisation of horizon scanning topics and committee workplan 2025/26

8.1. The horizon scanning process is an annual cycle that highlights relevant issues in fertility treatment and embryo research identified from journal articles, conference attendance, and expert recommendations. This review considers the period from January 2024 to December 2024.

8.2. The frequency at which topics are discussed by the Committee is determined by their priority, date of last discussion, and relevance to the ongoing work of the HFEA.

8.3. The Executive highlighted that two new topics have been proposed for inclusion as medium priority topics including:

- Health outcomes for ART patients (including gestational surrogates, egg donors, and the impact of treatment using donated eggs)
- Reproductive organoids

8.4. As put forward in the horizon scanning paper, the Executive introduced a list of 'watching brief' topics to help the SCAAC monitor issues that present concerns or opportunities which may warrant continued oversight by the Committee. These include:

- Artificial wombs for early or whole gestation (ectogenesis)
- Impact of environmental toxins on fertility treatment outcomes
- Understanding the genetic basis of infertility
- Use of ICSI for non-male and mild-male factor infertility
- Impact of stress on fertility treatment outcomes

8.5. Unlike the prioritised horizon scanning topics, topics categorised under the watching brief will not be scheduled for specific discussion at the SCAAC meetings, but relevant quality publications can be raised under the standing item 'Relevant public health developments and research findings'. A full literature search will then be conducted every two to three years and presented with the horizon scanning paper.

8.6. The Committee made the following comments and recommendations on the prioritisation of horizon scanning topics:

8.6.1. A member noted that scientific discussions related to 'Alternative methods to derive embryonic-like stem cells', may be less relevant to the SCAAC committee given that most of the work focuses on induced pluripotent stem cells. The Chief Executive clarified that the HFEA are interested in the potential consequences of the research in relation to generating embryo-like material.

8.6.2. Members commented that due to the ongoing work to further progress the HFEA's proposals on law reform, '14-day rule', 'SCBEM' and 'IVGs' should remain as high priority.

8.6.3. Members advised that 'Testicular tissue transplantation to restore fertility in males' is already being carried out in Europe and is covered by HFEA-HTA joint statement, therefore this should be medium priority.

8.6.4. Since 'Germline/heritable genome editing' is not currently legal under any jurisdictions and there have not been any recent developments, it was recommended that this topic be moved down to medium priority.

8.6.5. The Executive noted that the topics of 'Health outcomes in children born from ART (including the impact of culture media)' and 'Health outcomes for ART patients (including gestational surrogates, egg donors and the impact of treatment using donated eggs)' are not considered within the scope of the HFEA remit because 'health outcomes' are monitored outside of the fertility clinic and therefore does not fall under HFEA regulation; However, these topics can be prioritised accordingly if advised by SCAAC. A member noted that from a legal point of view, the HFEA does not have regulatory responsibility for this.

8.6.6. A member proposed that 'Impact of long-term cryopreservation of gametes and embryos' should be made high priority. However, the Executive highlighted that in February 2024, the SCAAC agreed that this that 'Impact of long-term cryopreservation of gametes and embryos' should remain medium priority as there was not sufficient research given that the extension in the storage period of embryos and gametes was introduced in July 2022.

8.6.7. A member advised that research in 'Artificial wombs for early or whole gestation (ectogenesis)' is advancing, however the Chair raised that most of the research focuses on looking at premature foetuses rather than early embryos. The Executive confirmed that advances in embryo culture systems and early ectogenesis will be monitored through the topics of 'Reproductive organoids' and 'Scientific developments relevant to the 14-day rule'.

8.6.8. A member suggested that 'Impact of the microbiome on fertility and fertility treatment outcomes' should be a low priority topic given that it is not within the HFEA remit and predominantly limited to observational studies of poor quality. The Chair challenged this, noting that there is growing public interest in the microbiome and increasing commercialisation of testing available within the private fertility sector.

8.6.9. Members agreed and added that microbiome testing is impacting treatment choices due to an increase in the number of patients deferring treatment, even if patients have a low ovarian reserve or a history of unsuccessful implantations. Members were concerned that there is a lack of evidence as to the effect of microbiome testing or treatment on treatment outcomes.

8.7. Recommendation: The Executive to update the topic prioritisation list as follows:

- 'Testicular tissue transplantation to restore fertility in males' to move to medium priority.
- 'Germline/heritable genome editing' to move to medium priority.
- 'Health outcomes in children born from ART (including the impact of culture media)' to move to high priority.
- 'Health outcomes for ART patients (including gestational surrogates, egg donors and the impact of treatment using donated eggs)' to move to high priority.

8.8. The Committee made the following comments and recommendations on the Committee workplan 2025/26:

8.8.1. The Executive clarified that two to three topics can be discussed at each meeting and frequency of topic discussions are based on their priority or relevance at the time. The topics currently proposed on the workplan have not been discussed for either a long period of time or at all.

8.8.2. The Chair proposed and received agreement from the Committee that 'Germline/heritable genome' should be moved down as it was last discussed in February 2024. The Committee also agreed that given the increase of the use of AI in clinics, 'Artificial intelligence, robotics and automation in fertility treatment' should be moved up the work plan.

8.8.3. Members agreed with the remainder of the workplan.

8.8.4. The Chair invited members to suggest and email any speakers specialising on any of the topics in the 2025/26 work plan.

8.8.5. A member raised that 'AI' may be considered quite a generic term and suggested that in order to find a speaker, the Committee should consider what aspect of AI is relevant and how AI translates into practice.

8.8.6. A member highlighted that there is relevant research being conducted on various horizon scanning topics in China. The Executive clarified that their literature searches are restricted to English language journals only and therefore these may not be included in the research presented to the Committee.

8.8.7. A member suggested that it may be useful to contact Reproductive BioMedicine Online (RMB) to provide an update on topics that are coming through the journal.

8.9. **Recommendation:** The Executive to update the Committee's workplan for 2025/26 as follows:

- 'Germline/heritable genome' to be moved to the June 2026 meeting.
- 'Artificial intelligence, robotics and automation in fertility treatment' to be moved to the October 2025 meeting.

9. Androgen supplementation as a treatment add-on

9.1. The Chair welcomed expert Statistician, Andy Vail, from the University of Manchester.

9.2. The Committee were reminded that at the June 2024 meeting an application to rate androgen supplementation as a treatment add-on was reconsidered against the updated decision tree. Following discussions with the add-ons review panel, it was agreed that both testosterone and dehydroepiandrosterone (DHEA) should be assessed for an add-on rating, identifying live birth rate (LBR), ongoing pregnancy rate (OGPR) and oocyte retrieval as relevant outcomes.

DHEA Supplementation

9.3. Members discussed the rating for DHEA supplementation The following comments and recommendations were made:

9.3.1. The Chair clarified that DHEA supplementation is usually taken for up to eight to 12 weeks prior to and during the treatment cycle, generally stopping at egg collection or at least before the embryo transfer.

9.3.2. The expert confirmed that the outcome of 'oocyte retrieval' is defined as the average number of eggs collected per woman.

9.3.3. The expert noted that the review by the Executive is limited to more recent papers in comparison to a previous meta-analyses by Cochrane which includes earlier studies.

9.3.4. A member questioned whether the inclusion of earlier studies would have impacted the number of RCTs included. The expert noted that this would have not been the case as two of the earlier studies did not include randomised comparisons.

9.3.5. The expert confirmed that pregnancy rate is reported per cycle started. However, it is important to note that women are randomised preceding the cycle and therefore some participants actually may never start the treatment.

9.3.6. A member flagged that from an ovarian stimulation point of view it's important to define whether frozen cycles were also included, and whether pregnancy rates were reported per cycle cumulative. The expert confirmed that most studies have only investigated one cycle of treatment up until the first fresh transfer.

9.3.7. The expert explained that the studies only investigated the use of DHEA supplementation prior to the stimulation cycle rather than before the transfer.

9.3.8. Members further clarified that the studies conducted a first fresh transfer analysis. They do not investigate the use of DHEA supplementation before a FET, nor do they report cumulative pregnancy rates.

9.3.9. The expert commented that out of the seven trials investigating the use of DHEA supplementation in women with poor/diminished ovarian reserve, only three of the trials were at a low risk of bias, however these studies did not actually illustrate an increase in oocyte retrieval rate for the active treatment arm.

9.3.10. The expert explained that a black rating was assigned for 'oocyte retrieval in women with poor/diminished ovarian reserve' as although there are three studies with no safety concerns and are moderate to high quality, they do not demonstrate an improved oocyte retrieval rate. Nonetheless, a yellow rating was also assigned given that these studies include small sample sizes and therefore a reasonable effect estimate could be missed.

9.3.11. It was clarified that the expert was basing decisions on the ratings of the three studies that were at low risk of bias, even though they did not demonstrate increased oocyte retrieval rates in the active treatment arm. This is because if a confidence interval was put around the estimate, a sizeable difference would not be ruled out given that there were under a total of 1000 women between the three studies combined. The expert explained that in order for the studies to be powered appropriately with a substantial effect, at least a total of 3000 participants would be required.

9.3.12. A member suggested that if we can add a caveat to state that the power of the three studies does not exclude a small benefit, then a black rating would be appropriate. The Chair supported this.

9.3.13. Further support for a black rating was noted given that there is inconsistency between the studies with regard to reporting on metaphase II versus oocyte retrieval.

9.3.14. From a clinical perspective, members flagged that it would be useful to provide patients with a conclusive answer and therefore a black rating would be appropriate.

9.3.15. A member proposed a red rating due to evidence on the role of androgens in breast cancer progressions posing a risk to patients. It was highlighted that this is a debated area and that this concern would be considered as a more long-term outcome, independent of those currently under review. This could be noted under the information on associated risks of this add-on.

9.4. **Recommendation:** The committee agreed the following rating for DHEA supplementation:

- GREY for live birth rate for most fertility patients.
- GREY for oocyte retrieval for most fertility patients.
- GREY for ongoing pregnancy rate for most fertility patients.
- GREY for live birth rate for older women.
- BLACK for oocyte retrieval in women with poor/diminished ovarian reserve.
- BLACK for live birth rate in women with poor/diminished ovarian reserve.

Testosterone Supplementation

9.5. Members discussed the rating for testosterone supplementation:

9.5.1. The expert noted that for testosterone supplementation there were no studies either in the general population or in aged women, indicating a grey rating.

9.5.2. Despite there being 11 studies for poor/diminished ovarian reserve, the GRADE rating would be low or very low because of the high risk of bias and imprecision. In total there were fewer than 1000 participants randomised to this treatment.

9.5.3. When compared with the Cochrane review, which concluded that “pre-treatment with testosterone likely improves live birth and clinical pregnancy rates in women undergoing IVF who have been identified as poor responders”, the Expert Statistician noted that the Cochrane included earlier studies (Massin, 2006; Fábregues, 2009; Kim, 2011) which provided nearly half the evidence in favour of testosterone. By excluding studies older than ten years, the conclusions drawn have differed.

9.5.4. The Expert Statistician also highlighted that initial studies tend to always estimate large effects with more recent studies typically illustrating no or small differences in effect.

9.5.5. A member referred to the T-TRANSPORT trial which is anticipated to illustrate no benefits of testosterone on treatment outcomes. This study has not yet been published, although an abstract with some data was available.

9.5.6. A member flagged that the T-TRANSPORT trial is anticipated to demonstrate harm due to androgenic side effects such as, hirsutism and acne. As such, a red rating could be considered for testosterone supplementation once the study has been published.

9.5.7. The Chair thanked Andy Vail for his contribution.

9.6. **Recommendation:** The Committee agreed the following rating for testosterone supplementation:

- GREY for live birth rate for most fertility patients.
- GREY for oocyte retrieval for most fertility patients.
- GREY for live birth rate in women with poor/diminished ovarian reserve. SCAAC to revisit the rating for this population/outcome when the T-TRANSPORT trial is published.
- GREY for oocyte retrieval in women with poor/diminished ovarian reserve. SCAAC to revisit the rating for this population/outcome when the T-TRANSPORT trial is published.
- GREY for live birth rate in older women.
- GREY for oocyte retrieval in older women.

10. Committee effectiveness review

10.1. The Annual Review of Committee Effectiveness was led by the Chair. A summary of feedback was recorded by the Executive for presentation at the March 2025 Authority meeting.

11. Any other business

11.1. No items were raised.

12. Meeting summary and close

12.1. The Chair thanked Richard Anderson and Kevin McEleny for their contributions to the SCAAC.

12.2. The next SCAAC meeting will be held Monday 9th June 2024 via Microsoft Teams.

12.3. The Chair closed the meeting by thanking the Executive for all the work that goes into the putting the papers together.

13. Chair's signature

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

Chair: Tim Child

Date: Wednesday 5th March 2025

14. Annex A: Revised Committee Workplan 2025/26

14.1. The below table presents the agreed workplan of the SCAAC for 2025/26.

Priority topic	Item	Possible speaker(s)	Last discussed	Meeting
Impact of the microbiome on fertility treatment outcomes	Literature review	Internal	October 2023	June 2025
Application for treatment add-on: Platelet-Rich Plasma (PRP)	Add-ons application review	Internal	N/A	June 2025
Rating review for treatment add-on: Androgen supplementation – Testosterone	Add-ons rating review	Statistician	February 2025	June 2025
Health outcomes for ART patients (including gestational surrogates, egg donors, and the impact of treatment using donated eggs)	Literature review	Internal	N/A – new topic	June 2025
Artificial intelligence, robotics and automation in fertility treatment	Literature review	Internal	February 2024	October 2025
Reproductive organoids	Literature review	Academic	N/A – new topic	October 2025
Testicular transplantation to restore fertility in males	Literature review	Academic	N/A – new topic	October 2025
Horizon scanning and agreeing workplan for 2026/27	Workplan review	Internal	February 2025	February 2026
Impact of long-term cryopreservation	Literature review	Internal	February 2024	February 2026
Emerging technologies in embryo and gamete testing	Literature review	Internal	June 2024	February 2026
Germline/heritable genome editing	Literature review	Academic	February 2024	June 2026
Alternative methods to derive embryonic and embryonic-like stem cells	Literature review	Internal	June 2024	June 2026

14.2. Discussions on further horizon scanning topics, including ‘Scientific developments relevant to the 14-day rule’, ‘Stem-cell based embryo models’, ‘In vitro derived gametes’ and ‘Mitochondrial donation’ will be incorporated into the 2026/27 SCAAC workplan.

14.3. Should the priorities of the Authority change, alterations to the workplan may be agreed independently with the SCAAC Chair.

15. Annex B: Revised Horizon Scanning Topic Prioritisation

15.1. The below table presents the agreed horizon scanning topic prioritisation list.

High	Medium	Low	Watching brief
Alternative methods to derive embryonic and embryonic-like stem cells	Germline/heritable genome editing	None	Artificial wombs for early or whole gestation (ectogenesis)
AI, robotics and automation in fertility treatment	Impact of long-term cryopreservation of gametes and embryo		Impact of environmental toxins on fertility treatment outcomes
Emerging technologies in gamete and embryo testing	Impact of the microbiome on fertility and fertility treatment outcomes		Impact of stress on fertility treatment outcomes
IVGs	Testicular tissue transplantation to restore fertility in males		Understanding the genetic basis of infertility
Mitochondrial donation			Use of ICSI for non-male and mild-male factor infertility
Scientific considerations relevant to the 14-day rule			
SCBEM			
Health outcomes in children born from ART (including the impact of culture media)			
Health outcomes for ART patients (including gestational surrogates, egg donors, and the impact of treatment using donated eggs)			