# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

# Centre for Clinical Practice – Surveillance Programme

## *Recommendation for Guidance Executive*

## Clinical guideline
CG156: Fertility

## Publication date
February 2013

## Surveillance report for GE
April 2015

## Surveillance recommendation
The Evidence Update on CG156: Fertility identified 2 potential impacts on the guideline.

An additional 2 potential impacts were identified from external correspondence with NICE and identification of related new evidence.

Following further discussion of the impacts at a Triage Panel, GE is asked to consider the proposal to:

- Update the following question in CG156 using a Standing Committee for Updates via the Clinical Guidelines Update Team:
  - What is the effectiveness of intrauterine insemination (IUI) in people with unexplained infertility, mild endometriosis or 'mild' male factor infertility?

GE is asked to note that this 'yes to update' proposal will not be consulted on.

## Key findings

| | | | **Potential impact on guidance** | |
|---|---|---|---|---|
| | | | **Yes** | **No** |
| Evidence identified from Evidence Update | | | ✓ | |
| Anti-discrimination and equalities considerations | | | | ✓ |
| Feedback from Triage Panel meeting | | | ✓ | |
| No update | **CGUT update** | **Standard update** | Transfer to static list | Change review cycle |
| | ✓ | | | |

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Centre for Clinical Practice – Surveillance Programme

### Surveillance review of CG156: Fertility

### *Recommendation for Guidance Executive*

## *Background information*

Guideline issue date: 2013
2-year review: 2015

NCC: National Collaborating Centre for Women's and Children's Health

## *2-year Evidence Update*

1. The Evidence Update on CG156: Fertility was used as a source of evidence for this surveillance review and considered new evidence since the guideline was published. The search dates of the Evidence Update were 01 December 2011 to 17 September 2014. A summary of the evidence is provided in the Evidence Update.

2. The Evidence Update identified 2 areas in which there may be an impact on current guideline recommendations:
   - Use of gonadotrophin-releasing hormone (GnRH) agonists in the luteal support protocol.
   - The choice or composition of embryo culture media.

   These areas would be considered for a standard update at the next surveillance review point.

## *Triage Panel*

3. The new evidence that may potentially impact on guideline recommendations was considered by the Triage Panel.

4. ***Clinical question: What is the effectiveness of intrauterine insemination (IUI) in people with unexplained infertility, mild endometriosis or 'mild' male factor infertility?***

5. NICE received a query about the formulation of the recommendations on IUI. Additionally, a further RCT[4] on IUI was highlighted by the Chair of the Evidence Update Advisory Group during sign-off of the completed Evidence Update. This study suggested that IUI is non-inferior to in-vitro fertilisation (IVF). The panel felt that the new study provided new evidence that should be considered in an update and felt that this question should be updated with more urgency than the other questions under consideration.

   **Decision:** NICE to update this clinical question using Standing Committee for Updates via the Clinical Guidelines Update Team.

6. ***Clinical question: What is the effectiveness of luteal phase support as part of an ovarian stimulation strategy for women undergoing IVF or ICSI treatment?***

7. The Evidence Update included a systematic review[9] suggesting that addition of gonadotrophin releasing hormone (GnRH) agonists to the luteal support protocol was associated with a higher probability of live birth compared with standard luteal support. The panel agreed that the new evidence is not ground-breaking and that adding GnRH agonist treatment in the luteal phase is not routine practice currently. However, the panel recommended on the basis of the new evidence that this question is considered as part of a standard update of the guideline. Updating this question was not thought to be urgent and would be carried forward to the next surveillance review for consideration.

   **Decision:** NICE to consider this clinical question to be included in a standard update at the next review point.

8. ***Clinical question: What are the effects of culture media on outcomes of IVF?***

9. The Evidence Update included 2 studies relevant to this question. A Cochrane review[12] found that adding high levels of hyaluronic acid to culture media was associated with increases in live births. An additional quasi-randomised study[13] found significant differences in height and weight of children at 2 years depending on which of 2 branded culture media was used during IVF. The panel discussed whether culture media were covered by the scope of the guideline and whether widening the scope would necessitate looking at other environmental factors not currently covered by guidance. The panel felt strongly that culture media could have an important effect on the outcomes of IVF but the exact composition of culture media is not known to clinicians. Updating this question was not considered to be urgent.

10. **Decision:** NICE to consider this clinical question to be included in a standard update at the next surveillance review point..

11. During discussions with topic experts at the triage panel it was noted that a number of the areas of the guideline not updated in 2013 were now out of date and that a larger standard update would probably be required. However, no key evidence in these areas was picked up by the Evidence Update process on which this surveillance review was based. It was agreed that this would be considered at the next full surveillance review in 2017, which would consider the totality of the guideline and any new evidence, including those areas identified above.

## *Ongoing research*

12. No ongoing research was identifed.

## *Anti-discrimination and equalities considerations*

13. None identified.

## *Implications for other NICE programmes*

14. This guideline relates to a quality standard, QS73: fertility problems.
    a. None of the quality statements are likely to be affected by the proposed area for update by the CGUT team.

## *Conclusion*

15. Through the Evidence Update of CG156, new evidence that may potentially impact guideline recommendations was identified in the following areas of the guideline and discussed at the Triage Panel:
    a. Effectiveness of IUI
        i. This area was considered by the Triage Panel, where it was decided that this update could be achieved by updating the following question in the guideline:
        ii. What is the effectiveness of intrauterine insemination (IUI) in people with unexplained infertility, mild endometriosis or 'mild' male factor infertility?
    b. GnRH agoinsts for luteal suport
        i. This area was considered by the Triage Panel where it was decided that the new evidence should be considered in a standard update of the guideline and would be carried forward to the next surveillance review.
    c. Choice of culture media
        i. This area was considered by the Triage Panel where it was decided that the new evidence should be considered in a standard update of the guideline and would be carried forward to the next surveillance review.

16. For all other areas of the guideline no evidence was identified which would impact on recommendations.

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Centre for Clinical Practice
June 2015

# Appendix 1 Decision matrix

Surveillance and identification of triggers for updating CG156. The table below provides summaries of the evidence that were identified and included in the Evidence Update.

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| 156-01 Providing information | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-02 Psychological effects of fertility problems | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-03 Specialist and generalist care | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-04 Chance of conception | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-05 Frequency and timing of sexual intercourse or artificial insemination | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-06 Alcohol | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-07 Smoking | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-08 Caffeinated beverages | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| 156-09 Body weight | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-10 Tight underwear | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-11 Occupation | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-12 Prescribed, over-the-counter and recreational drug use | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-13 Complementary therapy | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-14 Folic acid supplementation | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-15 Defining infertility | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-16 Investigation of suspected male factor infertility | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-17 Investigation of suspected ovulation disorders<br>• How accurate are tests of ovarian reserve in predicting pregnancy and its outcomes for women with infertility undergoing ovulation induction or ovarian stimulation treatment assisted reproduction (including unexplained infertility and IVF) | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| 156-18 Investigation of suspected tubal and uterine abnormalities | | | |
| The Evidence Update included a systematic review[1] and meta-analysis of 30 studies to compare ultrasound hysterosalpingography (HSG) with laparoscopy for diagnosis of tubal occlusion in women with fertility problems.<br>Ultrasound HSG had sensitivity of 92% for diagnosing tubal occlusion and specificity of 95%.<br>In studies comparing both ultrasound HSG and standard HSG with laparoscopy as the reference standard, no significant differences were noted between ultrasound HSG and standard HSG. | Not applicable | Not applicable | Evidence suggests that ultrasound HSG may be as effective as standard HSG for diagnosing fallopian tube occlusion, and both appear to have high sensitivity and specificity compared with laparoscopy. The Evidence Update concluded that no impact on NICE CG156 was expected because ultrasound HSG is already recommended as an alternative to standard HSG for women who are not known to have comorbidities and where appropriate expertise is available. |
| 156-19 Additional investigations for viral infection and cancer<br>• What is the effectiveness and safety of sperm washing to reduce the risk of viral transmission?<br>– What is the risk of transmission by vaginal intercourse when HIV positive male partners are on treatment?<br>– What is the risk of transmission by vaginal intercourse when HIV positive male partners have a low viral load?<br>– What is the risk of transmission by vaginal intercourse when HIV negative women use pre-exposure anti-retroviral prophylaxis? | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-20 Strategies for management of fertility problems | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-21 Medical management of male factor fertility problems | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| 156-22 Surgical management of male factor fertility problems | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-23 Management of ejaculatory failure | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-24 WHO Group I ovulation disorders<br>• What is the effectiveness and safety of ovulation induction strategies in women with WHO Group I Ovulation Disorders? | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-25 WHO Group II ovulation disorders<br>• What is the effectiveness and safety of ovulation induction strategies in women with WHO Group II Ovulation Disorders? | | | |
| The Evidence Update included a Cochrane review[2] of 26 RCTs (n=5560) of aromatase inhibitors in women with anovulatory polycystic ovary syndrome and infertility. Letrozole significantly increased live birth rate compared with clomifene citrate (OR=1.64) with no difference in rates of ovarian hyperstimulation syndrome (OHSS; RR=0.00) and lower rates of multiple pregnancy. | Not applicable | Not applicable | Evidence suggests that in women with polycystic ovary syndrome, letrozole appears to be associated with a higher live birth rate, lower rates of multiple pregnancy and lower incidence of OHSS than clomifene citrate. However, the Evidence Update concluded that because of the low quality of the evidence base, no impact on NICE CG156 is expected. |
| The Evidence Update included a systematic review and meta-analysis[3] of 7 RCTs (n=334) of metformin compared with placebo or no treatment in women with polycystic ovary syndrome treated with gonadotrophins. Metformin plus gonadotrophins was associated with a significantly higher live birth rate compared with gonadotrophins alone | Not applicable | Not applicable | Evidence suggests that in women with polycystic ovary syndrome who are known to be resistant to clomifene citrate, metformin plus gonadotrophins may be associated with higher live birth rates than |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| (OR=1.94). Adding metformin to gonadotrophins also significantly increased the pregnancy rate (OR=2.25). No significant effect of metformin was seen on multiple pregnancies, miscarriages or OHSS. | | | gonadotrophins alone, without affecting rates of multiple pregnancies or OHSS. This evidence was considered unlikely to have impact on NICE CG156, because of the low quality of the included studies. |
| 156-26 Hyperprolactinaemic amenorrhoea – dopamine agonists | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-27 Monitoring ovulation induction during gonadotrophin therapy | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-28 Tubal microsurgery and laparoscopic tubal surgery | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-29 Tubal catheterisation or cannulation | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-30 Surgery for hydrosalpinges before in vitro fertilisation treatment | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-31 Uterine surgery | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-32 Medical management (ovarian suppression) of endometriosis | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| 156-33 Surgical ablation of endometriosis | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-34 Ovarian stimulation for unexplained infertility<br>• What is the effectiveness and safety of ovarian stimulation agents in women with unexplained infertility? | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-35 Intrauterine insemination<br>• What is the effectiveness of intrauterine insemination (IUI) in people with unexplained infertility, mild endometriosis or 'mild' male factor infertility? | | | |
| No new key evidence was included in the Evidence Update. A further RCT[4] on IUI was highlighted by the Chair of the Evidence Update Advisory Group during sign-off of the completed Evidence Update. The RCT (n=602 couples) compared in-vitro fertilisation (IVF) using single embryo transfer with IVF in a modified natural cycle, and with IUI using controlled ovarian hyperstimulation. Birth of a healthy child occurred in: 52% of couples in the IVF using single embryo transfer group; 43% of those in the IVF in a modified natural cycle group; and 47% of those in the IUI using controlled ovarian hyperstimulation group. Both IVF in modified natural cycle and IUI using controlled ovarian hyperstimulation were non-inferior to IVF using single embryo transfer. Mulltiple pregnancies did not differ significantly between groups. | Not applicable | Not applicable | Evidence suggests that IUI may be comparable to IVF in people with unexplained infertility, mild endometriosis or 'mild' male factor infertility. This may be a potential impact on NICE CG156, which currently has a 'do not do' recommendation around routine use of IUI, although IUI is recommended for certain populations. |
| 156-36 Prediction of IVF success<br>• What are the factors which predict the success of IVF? | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| 156-37 Procedures used during in vitro fertilisation treatment | | | |
| The Evidence Update included a Cochrane review[5] of reviews that summarised 58 published Cochrane reviews on assisted reproduction procedures. Interventions that significantly improved live birth rates were:<br>• Endometrial injury performed in the month before ovulation induction<br>• Embryo culture in low oxygen concentrations.<br>• Hyaluronic acid in embryo culture media.<br>• Use of growth hormone in women who respond poorly to IVF. | Not applicable | Not applicable | The available evidence suggests that several interventions may improve the outcome of assisted reproduction procedures. The Evidence Update included several of the individual Cochrane reviews and considered potential impacts of each individual review. |
| 156-38 Pre-treatment for IVF<br>• What is the effectiveness of pre-treatment as part of an ovarian stimulation strategy for women undergoing IVF or ICSI treatment? | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-39 Down-regulation or other regimens to avoid premature luteinising hormone surges<br>• What is the effectiveness of down-regulation as part of an ovarian stimulation strategy for women undergoing IVF or ICSI treatment? | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-40 Controlled ovarian stimulation in IVF<br>• What is the effectiveness of the following strategies as part of an ovarian stimulation protocol in women undergoing IVF or ICSI treatment:<br>– stimulation with gonadotrophins<br>– 'milder' stimulation<br>– adjuvant growth hormone and di-hydro-epi-androsterone (DHEA) treatment for women with a previous poor response? | | | |
| The Evidence Update included a systematic review[6] and meta-analysis of 10 RCTs (n=900) of metformin in women with polycystic ovary syndrome undergoing IVF or intracytoplasmic sperm injection (ICSI). Gonadotrophins plus | Not applicable | Not applicable | This evidence suggests that in women with polycystic ovary syndrome who are undergoing IVF, adding metformin to |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| metformin was not associated with significantly different live birth rates or pregnancy rates compared with gonadotrophins plus placebo or no treatment. The rate of OHSS was significantly lower with metformin. | | | gonadotrophins may not increase live birth rate compared with gonadotrophins alone, although incidence of OHSS may be reduced. This evidence was considered unlikely to affect NICE CG156 because of limitations of the evidence and the absence of an increase in live birth rate. |
| 156-41 Triggering ovulation in IVF<br>• Which is the most effective ovulation trigger to use as part of an ovarian stimulation strategy for women undergoing IVF or ICSI treatment? | | | |
| The Evidence Update included a Cochrane review[7] of 2 RCTs (n=248) investigating the dopamine agonist cabergoline for preventing moderate or severe OHSS in women undergoing assisted reproduction procedures. Cabergoline was associated with an overall reduction in moderate or severe OHSS. However in subgroup analysis, moderate OHSS was significantly lower in women who received cabergoline, but severe OHSS was not. No significant effect on clinical pregnancy rate or multiple pregnancies was seen. | Not applicable | Not applicable | Evidence suggests that cabergoline may be associated with a reduction in OHSS without affecting rates of pregnancies or multiple pregnancies. This evidence was considered unlikely to have an impact on NICE CG156, because no significant effect was seen on severe OHSS, which is of greater clinical concern than moderate OHSS. |
| 156-42 Oocyte and sperm retrieval in IVF | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| 156-43 Embryo transfer strategies<br>• What is the effectiveness and safety of different embryo/blastocyst transfer strategies in relation to both:<br>– number of embryos (comparing single with double)<br>– timing of transfer (comparing cleavage with blastocyst stage). | | | |
| The Evidence Update included a systematic review and meta-analysis[8] of 8 studies to compare embryo transfer at blastocyst stage with transfer at cleavage stage. Blastocyst-stage transfer was associated with higher risk of very preterm delivery, defined as delivery before 32 weeks (RR=1.22). Preterm delivery, defined as delivery before 37 weeks, was also significantly more likely after blastocyst-stage transfer. However, blastocyst-stage transfer was associated with a lower likelihood of delivery of a baby that was small for gestational age. | Not applicable | Not applicable | This evidence suggests that embryo transfer at the blastocyst stage may be associated with higher rate of preterm and very preterm birth than transfer at the cleavage stage, but may be associated with lower frequency of babies born small for gestational age. However, the Evidence Update concluded that limitations in the evidence base mean no impact on NICE CG156 is expected. |
| 156-44 Luteal phase support after IVF<br>• What is the effectiveness of luteal phase support as part of an ovarian stimulation strategy for women undergoing IVF or ICSI treatment? | | | |
| The Evidence Update included a systematic review and meta-analysis[9] of 6 RCTs (n=2012), which investigated the effects of adding GnRH agonist treatment in the luteal phase on live birth rates after IVF or ICSI. Overall, addition of GnRH agonists to the luteal support protocol was associated with a higher probability of live birth compared with standard luteal support (risk difference=0.16). Results were similar when analysed separately depending on whether ovarian stimulation was performed with GnRH agonists or antagonists. | Not applicable | Not applicable | This evidence suggests that addition of GnRH agonists to the luteal support protocol may be associated with increases in live birth rate after IVF. This evidence was considered to have a potential impact on NICE CG156. |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| 156-45 Gamete intrafallopian transfer and zygote intrafallopian transfer | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-46 Indications for intracytoplasmic sperm injection | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-47 Genetic issues and counselling | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-48 Intracytoplasmic sperm injection versus IVF | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-49 Cost effectiveness of intracytoplasmic sperm injection | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-50 Clinical indications for donor insemination | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-51 Information and counselling | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-52 Screening of sperm donors | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-53 Assessment of the woman | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-54 Intrauterine insemination versus intracervical insemination | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| 156-55 Unstimulated versus stimulated donor insemination | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-56 Indications for oocyte donation | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-57 Screening of oocyte donors | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-58 Oocyte donation and 'egg sharing' | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-59 Cryopreservation of semen, oocytes, embryos and ovarian tissue<br>• What is the effectiveness of cryopreservation (including vitrification) in fertility preservation strategies? | | | |
| No new key evidence was found for this section | Not applicable | Not applicable | Not applicable |
| 156-60 Long-term safety of ovulation induction and ovarian stimulation<br>• What is the long-term safety of ovulation induction and ovarian stimulation strategies in women with infertility and their children? | | | |
| The Evidence Update included a cross-sectional study[10] investigating the risk of venous thromboembolism and pulmonary embolism in pregnant women who conceived after IVF (n=23,498) compared with matched women with natural pregnancies (n=116,960). The proportion of women with IVF pregnancies who were diagnosed with venous thromboembolism was 4.2 in 1000 compared with 2.5 in 1000 for women with natural pregnancies. Pulmonary embolism occurred in 8.1 per 10,000 women in the IVF group compared with 6.0 per 10,000 women who had natural pregnancies. The heightened risk was mainly in the first | Not applicable | Not applicable | This evidence suggests that women with pregnancies conceived with IVF appear to be at greater risk of venous thromboembolism and pulmonary embolism, particularly in the first 3 months, than women with pregnancies conceived naturally. The Evidence Update concluded that this evidence is not expected to impact NICE CG156, which |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| trimester after IVF, and may be due to the proximity in time to the IVF procedure. | | | does not include recommendations about risks associated with IVF treatment. |
| 156-61 Long-term safety of IVF<br>• What is the long-term safety of IVF in women with infertility and their children? | | | |
| The Evidence Update included a population-based study[11] in Australia to determine hospital use in the first 5 years of life for children born after assisted reproduction procedures. Frequency, duration and costs of hospital admissions were compared for singleton children born after assisted reproduction procedures (n=2199) and singleton children born after natural conception (n=224,425).<br>Children conceived by assisted reproduction procedures were more likely to be delivered by emergency caesarean section and to be born prematurely. Children born after assisted reproduction procedures were significantly more likely to be admitted to hospital in the first 5 years of life. | Not applicable | Not applicable | This evidence suggests that children born after use of assisted reproduction procedures, to mothers who are wealthier and healthier but older, appear to have a greater likelihood of admission to hospital in the first 5 years of life than children born after natural conception. This evidence was considered unlikely to affect NICE CG156 because the absolute increase in admissions to hospital was small. |
| 156-62 New question – what are the effects of culture media on outcomes of IVF? | | | |
| The Evidence Update included a Cochrane review[12] of 17 RCTs (n=3898) to determine the effects of using embryo transfer media containing adherence compounds on live birth and pregnancy rates in assisted reproduction. Overall, high-dose hyaluronic acid was associated with an increase in live births compared with low-dose or no hyaluronic acid. In another study of culture media,[13] 2 types of culture medium were compared to assess postnatal growth in the first 2 years of life. At 2 years of age, children born after Vitrolife | Not applicable | Not applicable | These studies suggest that the choice or composition of culture media may affect live birth rates and the growth of children up to 2 years after birth. The Evidence Update concluded that this evidence may have a potential impact on NICE CG156, which does not contain recommendations |

| Main findings and conclusion of the 2-year Evidence Update (March 2015) | Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion? | Clinical feedback from the GDG | Impact of findings of this 2-year Evidence Update on guideline recommendations |
|---|---|---|---|
| culture were 188 g heavier and 4.9 mm taller than those born after Cook culture. | | | about choice of culture media. |
| 156-63 New question – what are the effects of oxygen concentration during embryo culture | | | |
| The Evidence Update included a Cochrane review[14] of 7 RCTs (n=2422) comparing embryo culture at low oxygen concentrations (about 5%) with atmospheric oxygen concentrations (about 20%). Low oxygen concentrations during embryo culture were associated with a significantly higher live birth rate than atmospheric oxygen concentrations (OR=1.39). | Not applicable | Not applicable | This evidence suggests that culturing embryos in low oxygen concentration (about 5%) may result in higher live birth rates than culturing at atmospheric oxygen concentration. However, the Evidence Update concluded that no impact on NICE CG156 is expected because the guideline does not specify laboratory conditions for culturing embryos. |
| 156-64 New question – what is the efficacy and safety of endometrial injury to improve outcomes of assisted reproduction procedures? | | | |
| The Evidence Update included a Cochrane review[15] of 5 RCTs (n=591) of endometrial injury performed up to 6 months before treatment with assisted reproduction procedures. Endometrial injury in the month before starting ovulation induction was associated with a significant increase in live birth rate compared with control. Another systematic review and meta-analysis[16] assessed the effects of local endometrial injury reported in 8 studies. Across all studies the clinical pregnancy rate in the endometrial injury group ranged from 27% to 69% and in the control groups ranged from 9% to 44%. In randomised studies the clinical pregnancy rate in the endometrial injury group was more than twice that in the control groups. | Not applicable | Not applicable | These studies suggest that intentional endometrial injury in the month before embryo implantation may be associated with higher rates of live birth than control. However, the Evidence Update concluded that limitations of the evidence base, particularly the need to fully evaluate adverse events after a procedure that causes intentional injury, mean that no impact on NICE CG156 is expected. |

# References


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