

## NICE Guideline: Fertility problems: assessment and treatment

### Stakeholder scoping workshop collated notes, 2 February 2022

<b>Welcome and presentations</b>
<b>SCOPE: Overall impression</b>
<p>➤ Overall, have we struck an appropriate balance between the need to keep the scope manageable and the relative importance of areas that could be included?</p>
<p>Stakeholders made the following comments:</p> <ul style="list-style-type: none"><li>• Some feel scope is comprehensive and covers all important areas for day to day fertility care.</li><li>• In scope: 'treatment to allow access to same-sex couple who have fertility problems'. In practice this can be discriminatory, because same sex couples have to somehow demonstrate they have fertility problems. This can lead to equalities issues such as these same-sex couples needing to spend a lot of money completing a threshold number of rounds of IUI; or leading to use of unregulated sperm. Could be restricting access rather than encouraging. Agreement from most that the current definition of fertility problems is outdated and does not cover same-sex couples.</li><li>• Queries around whether psychosocial support/ interventions are going to be covered by 'Information and Support' as no detail is given in the scope document. This needs to be provided in the scope for the sake of clarity. Equality statement covers provision of support but this was written in 2014 and we are now looking at a changing demographic with different specific needs. Should the section be 'Counselling, information and support'? Others echoed this concern, including comment that previous NICE guidelines have poor sections about this area in comparison to other areas of information and support. Advice needs to be sought from someone who has expertise in evidence/ data in this area so we can get the PICO absolutely right to make sure we don't miss studies about psychocial treatment/ support in relation to fertility.</li><li>• Queries around single women and potentially single men? Need to be clear about if they are included in the scope.</li><li>• Comment re: equity, specifically around surrogacy for single people/ same-sex couples. Agreement from others that there is an equalities issues about single people vs couples regarding accessing surrogacy. NICE needs to have a statement in scope about what their stance is on surrogacy in terms of what is out of scope of this guideline. Need to make it clear exactly what it is about surrogacy that we are not covering, because currently the scope reads as though we are not covering any issues with relation to surrogacy regardless of the links to fertility problems. Some are happy with how we are approaching surrogacy.</li><li>• Comment that RQ about experimental treatment may be needed to evaluate where these treatments might be ineffective and make recommendations accordingly (this can help people with fertility issues from spending money on ineffective experimental treatment).</li><li>• Query about guideline being relevant for private practice.</li><li>• Query about recurrent miscarriage being part of the access criteria, it was discussed that recurrent miscarriage was included in CG126 (in terms of progestogens for the treatment of women with recurrent miscarriage).</li><li>• General comment about surrogacy being included, at the very least for women with problems to conceive, but also from an equalities perspective.</li><li>• The wording in the scope needs to be more specific so that is less chance of ambiguity or misinterpretation.</li></ul>

- People with comorbidities should be treated in collaboration with their specialist health care teams.
- Surrogacy: this should be covered up to the point of embryo creation.

### **Scope: Title –Fertility Problem**

- Should this be amended

Stakeholders made the following comments:

- The word 'problems' is ambiguous, it refers to clinical inability only, would the guideline only include people with clinical fertility problems?
- If only people with clinical fertility problems are included, the equality of access for single people and same sex couples will never be addressed.
- The guideline should refer to 'people' or 'individuals' throughout rather than 'couples'.
- Group felt this should be "fertility".

### **Section Scope: Title – Fertility problems**

- Should this be amended?

Stakeholders made the following comments:

- Group felt this should be "fertility".

### **Section 2 – Who the guideline is for**

- Are there any other groups who will need to be aware of this guideline?

Stakeholders made the following comments:

- NICE Guidance is generally focused on NHS services however over 70% of people seek private care and are self-funded so the context here is very important here. The private sector should also be held to a higher clinical standard. Therefore, can some wording be added in this section to reflect this?

People using services, their families and carers and the public:

This should also include surrogacy to the point of embryo creation.

### **Section 3.1 Who is the focus?**

- Do you agree with the groups that will be covered?

Stakeholders made the following comments:

- Where do donors fit into this scope as they are not mentioned?
- Need to define which people who require fertility preservation for non-medical reasons are outside of scope.
- For fertility preservation, are we focusing on people who anticipate potential fertility problems due to medical conditions or due to risk factors? Need to be clear which populations we are looking at. Comment that otherwise this could clash with our preconception health section.
- Single people should be included, they are in the same group as same sex couples.
- It was explained that 'people' covers single people, same sex couples and heterosexual couples.
- Sperm donors not included.
- Surrogacy is an important aspect to cover.
- Healthy but deficient people not covered, such as people with low sperm count
- CE - Fertility issues/concern isn't the correct word; it should be a need. People come to us because they want to have a baby rather than have a known fertility problem. The wording isn't quite correct.
- People with conditions, difficulties or disabilities that require specific consideration in relation to methods of conception:

- Needs clarification of which groups of people are included - it is from a healthcare professional or patient perspective?

### **Section 3.2 Settings**

- Do you agree with the settings listed?

Stakeholders made the following comments

- Include private clinics, as discussed earlier.

### **Section 3.3 Review Topics**

- Do the topics listed in the scope (Section 3.3) cover the most important priorities for developing guidance on fertility problems?

Stakeholders made the following comments:

#### Preconception health

- Who is the population? Is it opportunistic (GP having, e.g. gynae consultation and provides that info, or is it always initiated by the person enquiring about fertility)? The areas in preconception care re: fertility tend to be targeted at general population where opportunities are taken to give information about fertility/ risk factors more generally that also affect fertility. However, this scope seems to be focusing on timely help seeking, i.e. people who are enquiring about potential fertility problems.
- Sexual health checks – do we mean fertility or STI checks?
- Note for Systematic Reviewers that we need to consider the different populations and who will be included in PICOs because ‘preconception health’ can be very murky/ ambiguous.
- Risk factors listed in scope are illustrative and not exhaustive (there are others such as FGM).
- Comment that the ‘what’ is comprehensive, but ‘who’ may not be. Populations may be opportunistic or targeted.
- Needs to be clear this includes both male & females.
- Q. From a users’ perspective there is a lot of info for preconception, how well is this all going to link up? A. There are links to relevant information.
- Q. It is important to consider adding in education about menstrual cycles. A. this can be covered in the information and support topic area.
- 1.1 Advice: is too broad, this needs to be more specific.
- 1.3 Risk factors for reduced fertility: steroids should be specified as there is strong evidence for this.

#### Information and support needs

- See comments under ‘overall impression’ re: issues surrounding whether psychosocial support/ interventions will be covered.
- Comment that there should be a Review Question that covers Mental Health issues and psychosocial interventions (maybe quant instead of qual?).
- What happens to people who have unsuccessful treatment and then need information and support? Need to look at long term consequences of fertility problems, including for those who are no longer on a pathway and not just experiences during care/ while receiving treatments.

#### Male investigations:

- WHO recently published a manual, which specifies semen analysis should be done and other tests are add-on. DNA fragmentation is not currently available on NHS right now – this guideline needs to assess evidence around DNA fragmentation. Understanding that the evidence base is limited on this topic
- General feeling that people are pleased male infertility investigations are covered.
- 3.1- Medical History is helpful. Add testicular biopsy.

### Female investigations:

- Need to investigate the following: is there a hierarchy of tests, is one better to look at first than the other, what happens if tests are discordant (which test do we trust/ does the result from one test take precedence over another?).
- Re: urine and blood tests: Should covid vaccine be included in clinical investigations done when considering potential effect on fertility? Emerging evidence on effects of covid on pregnant women. This was echoed for MMR vaccine.
- Controversy re: immunology testing, natural killer cell testing – we need to search for evidence regarding these investigations to potentially prevent people spending money on this unnecessarily.
- 4.1 “chlamydia test” not correct wording; there are antibody tests ect so wording needs to be updated.
- Ultrasound scan/fallopian tube patency testing – should be 2 bullet points.

General comment: women with comorbidities (eg cardiac disease) can have poorer outcomes. Working in collaboration with their specialists early on is important.

### Access criteria:

- Predictive factor for successful interventions should also include safety.
- Some predictive factors may inadvertently bias against certain subgroups (e.g. sperm parameters as access criteria may affect people with certain environmental exposures). How will people who have certain profiles for other reasons be taken into account when looking at predictive factors?
- Comment highlighting the existence of predictive models that control success which have been derived from historical data and therefore may not be up-to-date. Need to use recent and contemporary predictive models because this will be an equalities issue otherwise.
- Plea for committee to keep criteria as simple as possible as we have seen clinical commissioning groups ‘reinterpret’ implementation of the guideline and lead to other equalities issues. Need to be unambiguous.
- Need to consider what clinical effectiveness looks like across the board.
- Are we talking about access criteria for IVF only or other fertility treatments as well? Need to clarify access criteria for other treatments as well.
- Comment wanting clarity that access criteria are related to success of treatment.
- Need to have sensible cut-off point for number of years spent trying for pregnancy before fertility treatment can be accessed, and this needs to be sensitive to certain criteria such as age.
- Query: do we have access criteria in England for PGTA and SSR?

### Fertility preservation

- General feeling that people are very happy that fertility preservation for cancer patients is being considered
- Need to also consider fertility preservation for people likely to experience impaired fertility as a result of the treatment/ medication for a condition, because the treatment/ medication may affect fertility even when the condition doesn’t.
- Are psychological conditions covered?
- Do we need to talk about social freezing of eggs and what that is and whether NICE would recommend it? (response that this is not in scope)
- Query around ‘non-oncology conditions’ for fertility preservation and whether this covers single people and trans people, because these are not ‘conditions’. Need to get wording right.
- Change the word “condition”, trans people wouldn’t see this as a condition.

### Medical and surgical treatment and assisted reproduction techniques:

- 7.1 “retrieval of retrograde sperm” is not correct terminology, there is an NHS document on this.
- 7.1 Drug & hormone treatments: Add supplements and distinguish which supplements i.e. preconception for a healthy baby vs those calming to boost fertility. There are Cochrane reviews for over-the-counter supplements that claim to boost fertility, however some of these combinations are unhelpful or maybe even harmful to fertility.
- 7.3 Specify the add on treatments (e.g. PGDA, lipid induction) will be reviewed. The important issue here is prioritising what you will be looking at here. CE suggested using HFEA classification of add ons, but it is not without controversy.

### Interventions

- Supplements – is this an add-on or something that goes in preconception? Comment that in practice, tests will be done and it follows that supplements will be prescribed despite limited evidence base and high cost. Need to look at evidence re supplements and other add-ons as treatment, to potentially prevent people spending money on them when there might be no evidence of effectiveness.
- General feeling is very positive towards the inclusion of add-ons. Hope that this will cover a wide range of them, to have an up-to-date body of evidence as per their efficacy. Belief that this will prevent people being encouraged to spend money on ineffective treatments. Comment that this is particularly important for complementary and alternative medicines, e.g. psychosocial add-ons.
- Need to be clear about which add-ons will be assessed – comment that NICE will not be able to catch up with continuous evolution/ development of add-ons so need to have a good list of more expensive/ invasive/ harmful/ most commonly used ones, and prioritise these for inclusion.

### Interventions for unexplained infertility

- Also here ‘expectant management’. Comment that patients do not like expectant management when already they have tried for a long time without success.

### Interventions for Female fertility:

- Add drug and hormone therapy.
- Add in Single embryo transfer.

### Interventions for unexplained fertility:

- Add drug and hormone therapy.
- Add in ART.

### Other interventions

- Need to have time-limited interventions.
- Query: do we have access criteria in England for PGTA and SSR?
- 1 of the areas of concern is the adequacy of donor screening because there is emerging evidence of donors failing to disclose significant genetic/ criminal information. Considering use of gamete/ embryo donation, is it possible to make recs about adequacy of proper screening which can be verified?
- 7.8 Gamete is very specific, so should be a separate point.
- Clarification: are men included in ART?

### Safety

- Comment reiterating importance of donor screening.
- Access criteria should be presented very clearly, clearly distinguish between what is based on evidence and what is a judgement made by the committee.

<ul style="list-style-type: none"> <li>• Some commissioners use access criteria as a checklist, and it would be very helpful to clearly explain the evidence behind it. If there's evidence, then it should be a 'rule', if not it should be presented as 'advice'.</li> <li>• When assessing predictive factors, also report the success rate based on the entire picture, for example, age should not be considered in isolation.</li> </ul>
<p>➤ Are there any important omissions, or any topics on the list that should be deleted?</p>
<p>Stakeholders made the following comments:</p> <ul style="list-style-type: none"> <li>• Unexplained infertility should also cover IVF and IUI.</li> <li>• Clearly distinguish between predictive factors and access factors.</li> </ul>
<p>➤ As mentioned, we are exploring different ways to develop the guideline, and may publish some sections at different times, e.g. Preconception health. Are there any other areas of the guideline where this approach could work? Preservation of fertility?</p>
<p>Stakeholders made the following comments:</p> <ul style="list-style-type: none"> <li>• This would make commissioners work more difficult, very time consuming the review the same guideline multiple times.</li> <li>• Most attendants considered that publishing preconception health before the other work would work, as long as it does not interfere with other sections of the guideline, such as predictive factors or access criteria.</li> <li>• Making preconception health available earlier would also make people to start following it before the updated evidence on treatments is available, which could be very valuable.</li> </ul>
<p>➤ Does each issue to be covered in the guideline have an important review question identified?</p>
<p>N/A</p>
<p>➤ Do the proposed review questions represent the priorities for developing the guideline, or would some refocussing within the topic areas to be included be appropriate?</p>
<p>N/A</p>
<p><b>Section 3.4 Main Outcomes</b></p>
<p>➤ What are the most important outcomes?</p>
<p>Stakeholders made the following comments:</p> <ul style="list-style-type: none"> <li>• If using gestation of delivery as outcome, why not weight of delivery as outcome? Need to be wary of composite outcome (e.g. 'healthy baby') vs splitting up into components.</li> <li>• General feeling that people are glad to see MH outcomes because e.g. anxiety and depression are important outcomes. Comment that we also need trauma as an outcome as there is increasing evidence that people are experiencing trauma related to fertility problems/ care – would 'trauma' cover PTSD? If so maybe we should look at any and all MH outcomes.</li> <li>• Comment that long term psychological outcomes should be considered for people who are unsuccessful, not just people who are successful.</li> <li>• Positive feeling towards health related QOL as an outcome. Comment that there should also be fertility related QOL.</li> <li>• Treatment discontinuation as an outcome?</li> <li>• What do we see as outcomes for 'preconception care'? What outcomes should we cover there?</li> <li>• Comment that a good outcome would be 'cumulative live birth from one stimulation cycle' when it comes from IVF.</li> </ul>

- Long term mental health should be considered, both for people who had a successful and unsuccessful treatment.
- People with low chances of having a successful treatment may choose alternative ways to have children, such as adoption, but attendees were mindful that there are some cultural sensitivities around this, although there should be a reference in the guideline.
- 1 Can we include “single live birth”? It would reduce workload.
- 2 Q. What does patient satisfaction mean in this context? A. The outcomes are broad in the scope but will be more specific when it comes to the review protocol.

## **Equalities**

### ➤ How do inequalities impact on those with fertility problems?

Stakeholders made the following comments:

- Young people tend to be denied access to fertility investigations or treatment due to their age, based on the assumption that young people don't experience fertility problems (illustrated by, e.g. evidence of diagnostic delay in endo diagnosis for young people).
- Single people and same sex people, but if heterosexual couples are still asked to try to conceive for 2 years before being eligible for treatment and same sex couples and single individuals have direct access to treatment, then that could also be an inequality issue.
- The scope includes the references to the protected characteristics.

## **Guideline Committee Composition**

### ➤ Are all the suggestions for guideline committee members appropriate and important? Are there any professional roles or other types of members that are missing?

Stakeholders made the following comments:

- There is currently no one to represent counselling/ psychosocial/ MH issues despite importance of this kind of support for people experiencing fertility problems. Comment that we need someone who is familiar with psychosocial issues surrounding fertility but it does not need to be more prescriptive than that (i.e. don't need to define this member as a counsellor).
- Academic member should be open to people with both medical and scientific backgrounds as the important exercise with this member will be interpretation of evidence and research/ academic experience.
- Medical ethicist and lawyer may be needed.
- Commissioners/ CCG/ representatives - need to include CCGs or at least seek their opinion and input as they will be funding interventions.
- Comment that we need high risk obstetrician - need someone to cover medical conditions that can affect fertility (to cover situations such as when it might not be safe for certain people to access IVF).
- Suggestion we approach academics who have published in the area around trans health and fertility.
- Donor conception committee are an important stakeholder group to consider
- Commissioner.
- Statistician, to help interpret the evidence and to help the committee address the gaps in the evidence base.
- Lay members: people who have had a successful treatment, but also those who have had an unsuccessful treatment.
- The emphasis has always been on women and men are often neglected (or not included). Suggest to include a clinical andrologist (ideally male) who is actively involved on treating male fertility.

- Include a counsellor as they are integral to patient communications
- Suggested to include a specialist regulator.

➤ Are there any other co-opted members that should be added? (at the moment the only co-opted member listed is for the preconception health section of the guideline)

Stakeholders made the following comments:

- Andrologist clinical scientist with expertise in sperm DNA damage.

➤ We are looking for 2 or 3 people with lived experience of fertility problems. As we are looking at male and female factors, is it a sensible approach to specify that we want a male and female lay member?

Stakeholders made the following comments:

- Suggestion to look at engaging someone with lived experience from the trans community as a lay person.
- Is there an option to co-opt certain lay members so they can feed into discussions when we are going to look at an issue/ recs that will directly affect a certain group? May get around issue of limited number of lay members being unable to cover exhaustive list of different subgroups.
- Group 2 - This question was not answered, but attendees suggested that there should also be a transgender person, and if we wanted to make sure that all voices were being represented, then there could be a representative for the LGBTQ+ group.