Author’s response to reviews

Title: Oncofertility healthcare circuit and networks worldwide: what are the issues?

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Reviewer reports:

(Reviewer 1)

Thank you for the opportunity to review your manuscript. This is a thorough and well-written review on an important topic, with is still not familiar to a proportion of oncology professionals.

> We thank the reviewer for this appreciation. Thank you for identifying the importance of this topic and the issues it raises.

I see that the manuscript is intended as a Debate article type, but I do not really see there is a debate in the way the data is presented and discussed.

> The reviewer is correct. This classification seemed the most appropriate in the debate overview previously published. Indeed, this article is not a Research Article. We have corrected this. We focused on a discussion of structural differences in oncofertility circuits in different countries and issues.
I think that the paper would flow better if it started with a discussion of the term Oncofertility, which is the term that has been chosen by the authors. In my opinion is "Fertility Preservation" the most accurate term to describe and discuss the methods and options to safeguard fertility potential aiming to attempt future fertility treatments and possibilities. Also internationally, it is the term that has been chosen at the American Society of clinical Oncology, ASCO, at ARSM and at ESHRE.

>Thank you for bringing this to our notice. The reviewer is correct. The term “Fertility preservation” is the most accurate term. The discussion of the term oncofertility introduced in the line 48 of the introduction was placed at the beginning of the introduction and enriched. The term “fertility preservation” introduced in the line 43 of the introduction, is the general term for all available techniques to preserve the possibility of having a child after any treatment potentially toxic for the reproductive tract. Fertility preservation concerns other indications than cancer, such as autoimmune diseases, certain hematological diseases (sickle cell anemia, essential thrombocytic anemia) and more globally, all diseases that can be treated with gonadotoxic molecules. Oncofertility is a field of medicine concerned with minimizing the negative effects of cancer treatment on the reproductive system and fertility and with assisting individuals with reproductive impairments resulting from cancer therapy. These two terms are therefore used for different purposes. The term « oncofertility » has been replaced by the term « fertility preservation » wherever it is appropriate.

In February 2017, ESHRE proposed a Special Interest Group Fertility Preservation entitled « Female oncofertility care ». The aim of this group was to assist medical staff and patients, to evaluate the possibility of preserving patients’ fertility potential and if so, the most appropriate strategy to follow for augmenting chances of success.

We are aware that the term “oncofertility” is a new term that gradually takes its place among health professionals.

The title also suggests that it is a systematic review, but it is obvious that this is not.

> The reviewer is correct. We have corrected the title as follow: Oncofertility healthcare circuit and networks worldwide: what are the issues?

This is a review article and although the reference list seems to me relevant and includes several recent papers, it should be considered by the authors that Fertility Preservation is a rapidly moving field, and most recent references in this topic should be included and the reference list updated as well. There is only one reference from 2015 and the remaining are all older that that.
For example, data from all the five Nordic countries has been published in 2016 as regards to female fertility preservation by cryopreservation of ovarian tissue and oocytes (Acta Obstet Gyn Scand, 2016).

If this is a systematic review these data should be presented, as well as the German data from the Fertiprotect consortium.

>Thank you for bringing this to our notice. The reviewer is correct. It is not a systematic review. We have completed the list of references with more recent bibliographic references.

The references are also presented in French! That has to be corrected.

> The reviewer is correct. Indeed, articles written in French are cited in French. We have corrected the references list in the manuscript.

Also references 1 and 2 seem wrongly inserted.

> The reviewer is correct. We have corrected their insertion as follow:

In 2020, more than 7.9 million women worldwide will be diagnosed with cancer: around 3.7 million in Asia; 1.7 million in Europe; 1.5 in America; 604,000 in Africa and 50,000 in the Caribbean (1). Among female cancer survivors, 1 in 250 occurs in reproductive age (2).

I would encourage the authors to review their article according to this comments and present updated global data that would fit the intention of their paper. This is an important subject for the growing population of young women that are in need of procedures of Fertility Preservation. I think an improved manuscript should be published.

> We thank the reviewer for this appreciation.
The authors present a debate article that reviews oncofertility healthcare circuits and networks worldwide. The authors contend that while two international networks are in place, a paucity of referral nationwide networks lead to a structural gap in health care policies. Overall, the concept behind this review is an interesting evaluation of fertility preservation worldwide. I recommend several changes to improve the quality of this manuscript.

> We thank the reviewer for this appreciation.

1. Title should be changed to remove the term "systematic review" since this was not a systematic review

> The reviewer is correct. It is not a systematic review. This article was classified in the section Debate. We have corrected this as follow: Oncofertility healthcare circuit and networks worldwide: what are the issues?

2. A description of the methods of the literature search should be included in the manuscript.

> We have corrected this and was introduced a short method in the Debate manuscript.

3. The section on current strategy for the oncofertility circuit for young women: This appears to be an overview of currently available fertility preservation modalities. Figure 1 is a bit confusing in describing the options available. Would recommend more of an international overview. For instance, while fertility preservation options available in Canada are reviewed, would compare this with other countries as well.

> Thank you for bringing this to our notice. We have made the correction as requested. We do not have enough data to realize an overview for the others countries. Would you wish that we delete figures?

Table 1 should not list AnRH agonist treatment as a fertility preservation treatment as it's benefit is currently still debatable.

> Thank you for bringing this to our notice. This has been corrected and removed from the Table 1.
4. Organizational support of oncofertility worldwide: this is an important section of the article that makes it unique from other review articles on oncofertility. Would add more text to this section. Also, doesn't ESHRE have fertility preservation guidelines as well? Table 5 does not seem to be a complete representation of all studies evaluating patient experiences with fertility preservation. It would be interesting to tabulate all studies evaluating patient experiences and analyze for a difference among countries.

>Thank you for bringing this to our notice. This section has been enriched by following your recommendations.

5. The conclusion that there is a need for structure for oncofertility in low and middle income countries should be supported by identification of oncofertility circuits in low or middle income countries and compare this to high income countries.

> This is a relevant point. However, we did not identify, in the literature, oncofertility networks in low and middle income countries. In the Caribbean, where we work, this circuit is clearly non-existent and the access to this circuit is globally made via metropolises.

6. There are a number of grammatical and spelling errors in this manuscript that need to be addressed.

>Thank you for bringing this to our notice. We corrected some mistakes and we are currently awaiting corrections by a native English-speaking medical writer.