

## Setting Up an Ethical Oncofertility Practice in Developing Countries

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**Abstract:** Fertility preservation for cancer patients is a relatively new field in medicine which requires interdisciplinary approach. Improving therapies and rising survival rates require to consider patient's quality of life after cancer is cured which is relevant personal issue regardless of the individual income and the level of development of the country of origin. Fertility preservation offers possible solution but also raises ethical questions. We provide a summary of ethical principles embodied in professional guidelines together with options and restrictions to access fertility preservation in developing countries. We also make a suggestion that oncofertility counselling could be a pillar to address fertility preservation issues in cancer patients. Our proposed decisional support model is patient centred and focuses on patient values, personal philosophy and view of life emphasizing sensitivity to individual patient's needs and wishes. Some fertility preservation concerns in oncology might be addressed mirroring already available expertise while some others will call for innovative and region specific solutions. Therefore, in addition to our proposal we also provide a list of organisations working in oncofertility field.

**Key words:** fertility preservation, cancer, decisional support, ethical counselling, personal philosophy

**Introduction:** Oncofertility stands for "*an interdisciplinary field that bridges biomedical and social sciences and examines issues regarding an individual's fertility concerns, options, and choices in light of cancer diagnosis, treatment, and survivorship*"<sup>1</sup>. However, scientific literature does not always use this term and 'oncofertility' is referred to as 'fertility preservation for cancer (oncology) patients'. Patrizio and Caplan simply call it: "*Fertility preservation is a newly developed branch of reproductive medicine aimed at preserving the potential for genetic parenthood in adults of reproductive age or children, who are at risk of sterility, before undergoing anticancer treatment*"<sup>2</sup>. Being a sensitive and complex issue, fertility preservation in cancer cannot be self standing but an interdisciplinary approach is necessary.

Cancer patients do not usually suffer infertility as a direct cause of cancer. More often it is cancer treatment such as radiotherapy, chemotherapy or surgery, which results in reduced fertility or even sterility in cancer survivors. Infertility in cancer survivors and general population is commonly agreed to be the inability to conceive after one year of intercourse without contraception<sup>3</sup>. Ability to conceive and have children is an important aspect concerning life and its quality for people worldwide. Western countries have been working towards fertility preservation methods and establishing principles for

ethical practices for a few years, while the situation in developing countries is less clear. Some of already existing expertise could be applied globally acknowledging that there might be new region and culture specific concerns which will require innovation and creative approach in order to reach a solution. This article aims to show that fertility preservation for cancer patients is globally relevant, because cancer incidence is increasing even in developing countries. The quality of life after cancer treatment is a relevant personal issue regardless the individual income and the level of development of the country of origin. Existing fertility preservation options allow cancer patients to have a possibility to enjoy parenthood in the future. However, it also raises a number of ethical concerns. Professional guidelines from around the globe reflect on a number of ethical principles which we present in a light of opportunities and restrictions patients in the developing countries might face. Considering global obstacles to access fertility preservation services, we suggest that a thorough oncofertility counselling for all cancer patients could be the first pillar to address fertility issues in cancer patients. We also provide a decisional support model which focuses on patient values and provide a short overview of resources available online to establish an effective oncofertility counselling service in oncology hospitals.

**Cancer Survival Worldwide:** Cancer survival rates are increasing and life after cancer is a real possibility for many patients worldwide. This is why it is also important to speak about life after cancer and take steps to ensure a good quality of life for cancer survivors even before cancer treatment begins. In Europe about one third of adult cancers have a relative 5-year survival rate greater than 80%<sup>4</sup>, combined 5-year survival rates for all childhood cancers is ranging from 70% to 82%<sup>5</sup>. Similar 5-year survival rates for adult and childhood cancers are available from the United States, Canada and Australia<sup>6,7,8,9</sup>. China, South Korea, Singapore and Turkey have slightly lower relative 5-year cancer survival rates ranging between 44-82%<sup>10</sup> and Brazil below 60%<sup>7</sup>. There is no much data from African countries where survival does not exceed 13-22%. In the Gambia and Uganda with exception of breast cancer survival reaching 43%<sup>10</sup>, reports on childhood cancer survival rates vary widely<sup>11</sup>. However, it is estimated that the number of cancer cases in African countries will increase significantly by 2030<sup>12</sup>.

Lower survival rates in developing countries are most likely due to late diagnosis and limited availability of standard treatments<sup>13</sup>, the same problem is reported in Eastern European countries<sup>4,7</sup>. Cancer is predominantly associated with older age, even though it also affects children, adolescents and young adults. Survival rates are known to be the highest for patients aged between 15 and 44 years old<sup>4</sup>. Childhood cancers represent 1% of all recorded malignancies<sup>14</sup>. Moreover, epidemiological data from the USA and Europe also suggests that there has been an increase in childhood cancer incidence by 1% each year<sup>15,16</sup> and the most frequent single diagnoses in children are acute lymphoblastic leukaemia, astrocytoma, neuroblastoma, non-Hodgkin lymphoma, and nephroblastoma<sup>17</sup>.

**Fertility Preservation Solutions and Practices in Western Countries:** Well established fertility preservation methods for women are embryo and oocytes cryopreservation and sperm

cryopreservation for men. These methods are widely described in the literature<sup>18,19,20</sup> and recognised by professional guidelines such as American Society of Clinical Oncology (ASCO)<sup>21</sup>, American Society of Reproductive Medicine (ASRM)<sup>22</sup> and European Society of Medical Oncology (ESMO)<sup>23</sup>. Other fertility preservation methods are less well established and still considered experimental. Ovarian and testicular tissue cryopreservation is the sole fertility preservation method available for prepubertal children<sup>21</sup>. It is still highly experimental and there is no proven benefit that patients who had their fertility preserved using these methods will be able to benefit from them in the future. Ovarian tissue cryopreservation has been used as fertility preservation methods in adult women and nearly 30 live births have been reported using this method<sup>24</sup>. However, there is still no certainty if it can successfully be used when ovarian tissue was obtained from prepubertal ovaries.

Following the guidelines, all cancer patients and /or their parents or guardians should be informed about cancer treatment effects on future fertility and physicians should discuss available options to preserve fertility. Usually there are time constraints to consider all available options because in many cases cancer treatment has to be initiated as soon as possible to achieve good health outcomes. However, despite available guidelines and established methods, recent review of oncologists' attitudes and practices revealed that not all physicians are prepared to discuss fertility related issues with their patients indicating that concerns about patient's prognosis, lack of knowledge and sometimes personal biases prevent them from addressing fertility preservation needs adequately<sup>25</sup>. Meanwhile, patients are interested to receive fertility preservation consultation and appreciate such information as part of shared decision making even if they choose not to preserve their fertility before cancer treatment commences<sup>26</sup>. A number of recent studies suggest that nearly half of cancer patients do not receive appropriate fertility preservation counselling<sup>25,27</sup>. Moreover, in many instances female patients are informed and proceed with fertility preservation less often than men<sup>28,29</sup>. However, despite of fertility importance for female patients it has been reported that globally only less than 10 % would accept lower chances to survival in order to preserve fertility<sup>30</sup>.

**Ethical Implications of Currently Followed Practices:** As it has been shown above, current fertility preservation practices for cancer patients are still far from perfection. Oncofertility field is still new and being multi-disciplinary requires innovative solutions and close cooperation among different healthcare providers. It brings up some new ethical issues but a good number of ethical concerns relating to fertility preservation in oncology are not new, they just have to be addressed in a different light<sup>31</sup>. The following questions are still lacking comprehensive answers in the literature but they could help to initiate a self reflection on developing a personal stand on fertility preservation issue in general.

**Medicine:** How do we set treatment priorities? Is it appropriate to delay cancer treatment to preserve the chance to have biological child if patient survives? Could doctor's suggestion to preserve fertility give false hopes about survival?

**Emotional wellbeing:** What feelings, expectations, and wishes are held by patients and physicians? How do frustration, anxiety and fear affect quality of care?

**Sociology:** What roles does fertility preservation play for patients' identity during and after cancer treatment? Is there societal pressure to be a parent? Is infertility stigmatised?

**Law:** How should storage of cryopreserved biomaterial be regulated? Can cryopreserved gametes be used posthumously? Who decides and under what circumstances? Who decides for the best interest of the child? Can law interfere with parental choices of children fertility preservation?

**Research ethics:** What is the actual status of fertility preservation technologies? Is there a difference between experimental and innovative treatment? Should they be developed further? How should they be introduced for patients?

**Communication:** Why some physicians feel uncomfortable about discussing fertility preservation?

**Decision making:** When is child mature enough to make his/her own decision? When is patient too ill for fertility preservation? Can fertility preservation be denied on the grounds of low prospects to survive? Are there age limits for candidates to preserve fertility? Should there be such limits?

**Economics:** Should preserving fertility for cancer patients be paid by society? Who should bear the costs: healthcare system, private insurance, individual, charity funds?

**Commercialisation of reproductive technologies:** Could the interests of fertility clinics overweight patients' best interest? Are fertility clinics selling fertility preservation services and future hope which is sometimes false hope?

**Human rights:** Does having cancer create a right for fertility preservation? Does European Convention on Human Rights (Art.12) 'right to found a family' have exceptions in case of cancer?

**Interests of potential future children:** Does cancer patient's/survivor's right to have a child comes at the expense of the rights of a child to be born?

Answers to the questions above could be different and could be influenced by one's culture, religion, personal values and beliefs. Medical professionals are still lacking knowledge and skills on how to approach personal biases in order to be able to address cancer patients' needs. Strengthening communication skills and developing counselling services are the possible solutions<sup>3,25,27,32</sup>.

**Guiding Principles in Fertility Preservation for Cancer Patients:** A number of guidelines appeared in the last couple of years proposing that informing cancer patients about cancer treatment effects on fertility should be a standard<sup>21,22,23,33</sup>. In Europe, the European Society of Human Reproduction and Embryology (ESHRE) has been publishing ethical considerations on human reproduction related issues since 2001. Their task force on Ethics and Law does not seem to look at oncofertility related issues and takes a broader view when releasing considerations on posthumous reproduction, cryopreservation, pre-implantation genetic diagnosis. Overall consensus of currently available guidelines is that clinicians should:

Inform patients about fertility preservation options and future reproduction before treatment starts<sup>21,22,23,33,34</sup>;

Parents may act to preserve fertility for minors<sup>22</sup>;

Pre-implantation genetic diagnosis (PGD) to avoid offspring inheriting high risk of cancer is acceptable<sup>22</sup>;

Concerns about welfare of resulting offspring are not sufficient reasons to deny assistance in reproduction<sup>22</sup>;

Patients should be referred to mental health, genetic and financial counsellors if needed<sup>21,22,34</sup>;

Fertility preservation discussion should allow time for reflection and involve partner, if present<sup>33</sup>.

In bioethics literature fertility treatment is not always seen as a positive right where every individual is enabled to procreate<sup>35</sup>. However, right to reproduce is often defended as ability to bear autonomy, personal identity, self-determination and possession of dignity where infertility can be addressed as disability<sup>36</sup>. Concerns can be raised that the hype of fertility preservation options give patients the false hope of survival and future fertility even if the goal of cancer treatment is to cure with the least amount of damage and side effects. Moreover, when physician feels that risks of doing so outweighs the benefits, fertility preservation procedures could be denied or patient referred to another physician<sup>37</sup>.

The currently established clinical pathway is based on informing the patients about cancer treatment effects on fertility, illustrating how fertility can be preserved and referring patients to fertility specialists and support services as soon as possible. Support services include decision coaching<sup>32</sup>, psychosocial support<sup>21</sup> or ethical counselling<sup>25</sup>.

### **Options and Restrictions for Fertility Preservation in Developing Countries:**

Technologies and skills can travel easily around the globe but sometimes restrictions including cultural and religious acceptability, financial constraints and lack of local expertise or regulation are met. Unfortunately, there is very little data on available services and how often cancer patients in developing countries use them. As resources in developing countries are usually scarce, it could be argued that fertility preservation is not a primary health concern, because it is not a medically necessary procedure. However, people without children, especially women, can often be seen as having lower social status and experience ostracism by other members of their society<sup>38</sup>. This implies that fertility preservation is an important and relevant issue globally and should not be ignored. Nonetheless, the following obstacles are found in the developing world.

**Cultural and religious obstacles:** Difficulties with particular aspects of fertility preservation and its acceptance can be detected in most religious traditions. Oncofertility field is new and views on procreation in different religions may vary. Embryo's right to life, duty to procreate, attitudes towards

adoption, meaning of sexual intercourse and acceptable ways on how a new human life can be conceived may assume different values in different cultural context<sup>39</sup>.

**Financial obstacles:** Fertility preservation procedures are expensive and financial constraints might be the major cause why some patients do not pursue them. While in Western countries there are a variety of funding sources available, in developing countries these procedures might be available only for wealthy individuals. However, it is argued that expensive drugs could be replaced with cheaper ones. Low Cost IVF Foundation is currently running clinics in Tanzania, South Africa and Sudan and this is a good example on how IVF costs can be reduced below €200 euro per cycle<sup>38</sup>.

**Geographic obstacles and lack of trained specialists:** Medical centres providing fertility preservation services have scarce geographical distribution in developed countries and there are even fewer of them in developing countries. Long travelling distance, and the related expenses, could be one of main restrictions for patients in developing countries to use fertility preservation services. It might also be difficult to find fertility specialist and even be referred to one. Very few studies from non Western countries report that more than half oncologists do not have enough knowledge about fertility preservation to feel comfortable in discussing it with their patients<sup>40,41,42</sup>.

**Lack of regulation or legal restrictions on fertility preservation methods:** Not all countries have legal base which allows fertility preservation methods to be used by everyone. For instance some countries in Latin America only allow artificial reproduction technologies to be used by married couples or only homologous insemination to be used for IVF<sup>38</sup>. Such practices deny reproductive autonomy for individuals who do not qualify for procreation assistance under restrictive laws.

**Patient Centred Counselling:** Providing high quality decisional support services for patients require trained counsellors who master a number of skills. These include helping patient to understand his or her medical condition and reflecting on personal philosophy and view of life which usually shape patient's goals, wishes and expectations<sup>25</sup>. Involving patient's partner is sometimes also encouraged<sup>33</sup> as well as some cultures might see acceptable to have other family members participating in fertility counselling, especially where patients are children. Training of counsellors will take time and require resources but this should be in the agenda of every oncology hospital.

Counsellors should primarily inform patients both on medical conditions and their implications on future life, and also provide information about fertility preservation options. Moreover, they should be able to identify patient's wishes and expectations. Counsellors should also be knowledgeable of local legislation, be prepared to handle patient's emotions, have sensitivity to patients spiritual or religious needs, and be ready to evaluate which fertility preservation options can be affordable, when resources are limited.

**Resources for Ethical Practice:** These are offered by a number of organisations worldwide. The Oncofertility Consortium based at Northwestern University in Chicago (USA) pioneered fertility preservation in Oncology and provides online tools for oncofertility communication. They developed Oncofertility Consortium Web site (<http://oncofertility.northwestern.edu>) for communication among

professional including Biomedical Humanities and the Web site for general public MyOncofertility (<http://myoncofertility.org>).

The American Society for Bioethics and Humanities (<http://www.asbh.org>) have numerous publications on core competences and skills required to qualify as health care ethics consultant and also code of ethics and professional responsibilities for ethics consultants.

The European School of Oncology (ESO) and the European School of Molecular Medicine (SEMM) at European Institute of Oncology (IEO) in Milan, Italy are also developing conceptual tools and providing training for oncologists in ethical counselling (<http://www.semm.it/master.php>).

**Conclusions:** Cancer survival rates are improving and treatment outcomes are promising that there could also be life after cancer. This brings up a new challenge for healthcare professionals who have to address patient's quality of life issues after cancer is cured. Assuring the best quality of life to cancer survivors some issues like fertility preservation have to be addressed before starting the treatment.

Professional guidelines from the USA and Europe suggest that all cancer patients should be informed about treatment effect on their future fertility and available fertility preservation options should also be discussed. However, there are still communication problems induced by lack of time and expertise followed by personal biases held by physicians when initiating discussion on fertility preservation with a patient.

Next to the information provided to all cancer patients about treatment effect on fertility and fertility preservation options other core principles allow parents to act in order to preserve fertility for their children, accept the use of PDG to avoid serious inherited conditions in the offspring, do not justify the denial of reproductive services based on the concerns about the welfare of the future child. Moreover, patients should be referred to other relevant specialists and support services when needed and given time to reflect on fertility preservation discussion and possible choices before making decisions.

There is very little data on fertility preservation services and how often cancer patients use them in developing countries. Cultural and religious constraints, financial restraints, long distance to the facilities and lack of trained specialists as well as lack of regulation and legal restrictions on fertility preservation methods are often met in developed countries and can be relevant globally.

Our proposal is that despite of limited resources fertility preservation issues in cancer patients should be addressed regardless the individual income and the level of development of the country of origin. A set up of ethical oncofertility practice can be started through oncofertility counselling where providing quality decision support services for all cancer patients. Such service would help patient to understand his or her medical condition and possible solutions while reflecting on personal philosophy and view of life which usually shape patient's goals, wishes and expectations. Counsellors will play an important role and in addition to medical knowledge and communication skills will need to be knowledgeable of local legislation, have sensitivity to patient's religious and spiritual needs, be ready

to handle patient's emotions and also help patient to evaluate which fertility preservation options could be affordable when resources are limited.

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