



# Oncofertility in Canada: an overview of Canadian practice and suggested action plan

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## ABSTRACT

### Background

Cancer can be a devastating diagnosis. In particular, malignancy and its indicated treatments have profoundly negative effects on the fertility of young cancer patients. Oncofertility has emerged as a new interdisciplinary field to address the issue of gonadotoxicity associated with cancer therapies and to facilitate fertility preservation. In Canada, these fertility issues are often inadequately addressed despite the availability of resources. The goal of this four-part series is to facilitate systemic improvements in fertility preservation for adolescent and young adult Canadians with a new diagnosis of cancer.

### Methods

Here, we describe the services currently available in Canada and the challenges associated with their utilization. Finally, we outline strategies to help maximize and facilitate fertility preservation in the young cancer patient.

### Results

Despite an existing infrastructure to the oncofertility system in Canada, the ability of that system's components to function together and to coordinate patient care is a challenge. Areas of weakness include poor access and referral to fertility services, a lack of readily available education for patients and health care providers, and inconsistent interdisciplinary coordination in patient care.

### Conclusions

The implementation of a framework for multidisciplinary resource allocation, education, patient

referral, and established lines of communication may facilitate a functional oncofertility system in Canada.

## KEY WORDS

Oncofertility, fertility preservation, cryopreservation, gonadotoxicity, young adult, adolescent

## 1. INTRODUCTION

This four-document series was created to improve education and communication concerning fertility preservation in adolescent and young adult Canadians with a new diagnosis of cancer. This article describes the services currently available in Canada, points out potential challenges, and outlines strategies to help maximize and facilitate fertility preservation in the new young cancer patient.

## 2. CURRENT CANADIAN PRACTICE—STRENGTHS, LIMITATIONS, AND PRACTICAL SOLUTIONS

Despite the overall increasing trends in fertility preservation since the early 2000s<sup>1</sup>, facilitated by an increasing wealth of information, new understandings, and emerging technologies, fertility preservation strategies are not being well used. Every year in Canada, 4250 reproductive-age women (20–39 years of age) are diagnosed with cancer, and yet only a small fraction are referred for fertility preservation every month<sup>2</sup>.

Responding to a Canadian survey, most fertility clinics said that their monthly referrals ranged from 0 to 2, lending credence to the belief that fertility preservation for young women in Canada with cancer is remarkably low. Similarly, more than 2500 men 20–39 years of age are newly diagnosed with cancer in Canada each year, and their monthly referral volumes have been similarly low<sup>3</sup>. Those data also accord with national studies demonstrating low rates of sperm banking<sup>4,5</sup>. A recent national 2-year

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multicentre study showed that, of newly diagnosed adolescents 15–20 years of age, only 19% (50 of 262) successfully banked sperm<sup>4</sup>.

As will be discussed, the foregoing data are likely a reflection of inefficiency in the current Canadian oncofertility system. Fertility preservation resources are available, but they are often limited to local initiatives, rather than operation at broader provincial or federal levels. The final segment of this document addresses national challenges in fertility preservation. Those challenges include establishing concrete resources that are both accessible and available, and building the bridges required to bring those resources together and to the patient.

## 2.1 Services Currently Available

### 2.1.1 Fertility Centres and Distribution of Services

Accessibility of and transportation to health care services can pose a challenge to many patients receiving cancer care, let alone fertility preservation. These challenges may relate to the financial demands of transportation as well as to the physical and emotional exertions required of an already weakened patient. Easy access to fertility centres is therefore extremely important.

As of March 2011, 76 facilities were identified across Canada, with 29 of them offering onsite *in vitro* fertilization (IVF) services, and 47 lacking such services. The provincial distribution of fertility centres roughly matched the geographic distribution of new incident cancers in women. Ontario ranked the highest in new cancer cases (38.2% of women and 37.1% of men in 2011) and was also the location for more than 52% of Canadian fertility centres (44% of IVF centres). Quebec (second highest incidence of new cancers) fell more in line, having 26.5% and 25.8% of the new incident cancer cases in women and men respectively, and being the locale for 21% of fertility clinics and IVF centres. Fertility centres and IVF centres were also appropriately distributed among the other provinces (all falling within 4% of their estimated share of new cancer cases). One notable point was the absence of any IVF clinic in either Prince Edward Island or Newfoundland and Labrador. Although the absence of such a clinic may reflect the distribution of overall demand for fertility services in those provinces, it might also translate to a lack of accessible facilities for certain Canadians<sup>2</sup>.

Despite some concern about the geographic distribution of fertility centres, more substantial concerns exist in the provision of fertility preservation services. For women, 15 of the 24 responding non-IVF fertility centres (63%) said that they do not provide any fertility preservation services, including consultations. Of the 21 responding IVF fertility centres, 17 (80%) said that they provided both consultations and fertility preservation services for women with cancer, with an additional 10% saying that they provide consultations only<sup>2</sup>. For men, only

24 of 78 fertility-related facilities (31%) provided sperm-banking services. Perhaps with an already strained distribution of fertility centres, the maximal application of fertility preservation within those centres should be encouraged<sup>3</sup>.

Some assisted reproduction technology services require highly technical skills and specialized embryologic techniques (for example, *in vitro* maturation and ovarian tissue freezing). The limited number of available centres might therefore seem even more inaccessible without proper patient channels. Of IVF centres providing fertility preservation services to women, 100% provide embryo cryopreservation, 82.4% provide oocyte freezing, 29.4% provide *in vitro* maturation services, and 17.6% provide ovarian tissue preservation<sup>2</sup>. It might be argued that the availability of those services mirrors their frequency—and perhaps the emphasis on their use in the literature. However, the improved success rates and potential for maximizing fertility by combining all of those strategies should support better access and increased implementation across all Canadian centres.

### 2.1.2 Access and Referral

“Accessibility of services” also refers to the ease with which referrals are made and contact with fertility specialists is facilitated. Ideally, a seamless and almost automatic referral system should be in place. Oncofertility literature has prided itself in suggesting treatment strategies for minimizing the time required for fertility preservation, often completely avoiding delays in cancer treatment<sup>6</sup>. However, referral times may still be the limiting factor, and in situations in which cancer treatment cannot be delayed, a long referral process may result in the use of less-established forms of fertility preservation (for example, foregoing ovarian stimulation) and therefore lesser success rates, particularly in women<sup>7</sup>. One prospective study in breast cancer patients emphasized that early referral for fertility preservation not only shortened the delay before treatment was initiated, but also yielded significantly more oocytes and embryos per patient by potentially allowing for more than 1 cycle of ovarian stimulation<sup>8</sup>. Expediting oncology referrals is therefore essential in improving success rates. Still, 37.5% of Canadian fertility facilities have stated that the average time needed to organize medical referrals from a female cancer patient is 1–3 weeks (the remainder see patients within 3 days)<sup>2</sup>. Referral times are faster for men, with almost 80% of the centres that offer male fertility preservation services arranging appointments within 2 days of referral (a maximum of 4 days was noted)<sup>3</sup>. Possible solutions to these delays involve setting up collaborative, well-established relationships between cancer care teams and fertility specialists, which currently depend on local initiatives<sup>3</sup>. Moreover, prompt disclosure to patients of the effects of treatment on future fertility, the possible options to circumvent those effects,

and the Canadian resources available (that is, health professionals, fertility centres, education resources) should be prioritized soon after diagnosis<sup>9</sup>.

Some of the other factors that could facilitate improved access to resources pertain to hours of operation and reducing travel stress<sup>10</sup>. Clinics throughout Canada are variably open during weekends and less during evenings. In the Canadian survey study by Yee *et al.*, one third of the responding centres were prepared to provide sperm cryopreservation kits for off-site use, and just short of half (48%) indicated that satellite clinics could be used for cycle monitoring for women living out of town<sup>3</sup>. Those factors could both be improved upon.

### 2.1.3 Psychosocial Services

Quantitative improvements in cancer prognosis have also accentuated the importance of qualitative survival and of diminishing the psychosocial impact of a new cancer diagnosis<sup>11,12</sup>. Young women and men may feel psychologically distressed and overwhelmed by information and by fast-occurring changes in their health. Moreover, they may experience significant amounts of anxiety, fear, and confusion related to their mortality and to their future ability to bear children. Complex decisions with respect to treatment and lifestyle choices often have to be faced<sup>7</sup>. Adolescents and young adults may also be particularly reliant on their peer groups. Changes in self-image associated with cancer therapy may therefore contribute to feelings of isolation and social removal, making it more difficult for patients to address those issues with others<sup>12</sup>. Young women may be even more affected than young men, given that cryopreservation of oocytes (compared with spermatozoa) requires more invasive techniques<sup>13</sup>. However, significant emotional grief and distress and feelings of loss, depression, and anxiety have been described in patients whose fertility is either threatened or whose cancer treatment resulted in infertility<sup>7,14,15</sup>.

In studies of non-cancer-related infertility distress, psychosocial interventions—including counselling, education programs, and even Web-based treatment<sup>16,17</sup>—have produced overall improvements in psychological parameters. In an analysis of 25 studies, Boivin *et al.* showed decreased infertility-related distress with a psychosocial intervention<sup>18</sup>. In a later meta-analysis of 22 studies<sup>19</sup>, reduced infertility-related anxiety and depression were shown. Only one recent meta-analysis, by Hammerli *et al.*<sup>20</sup>, who looked at 21 controlled studies (and excluded 363 others), noted no significant improvement in depression, anxiety, or mental distress with psychological intervention.

Accordingly, patients should also have psychosocial supportive resources in place. Although patients may informally turn to family, friends, and other patients in similar situations for guidance, some women may require additional support. That additional assistance may come in the form of support

groups, professional counsellors, psychiatrists, family doctors, or other mental health providers<sup>21</sup>. Importantly, patients should feel able to openly discuss psychologically or socially troubling issues that may (or may not) pertain to their future fertility. Those issues may be less comfortable to address with their treating physicians<sup>7</sup>. Counsellors can assist patients in their decision process and can help to complete whole-patient care by providing feedback to the medical team about a patient's psychological status. The emphasis on these additional psychosocial resources has also been endorsed by a number of professional organizations and societies<sup>14,22</sup>. They are an invaluable resource to the oncofertility network.

## 2.2 Provider and Patient Knowledge of Fertility Preservation

Knowledge resources and fertility counselling are integral to informed patient decisions and have a strong impact on quality of life for the patient—regardless of whether the decision is made to proceed with fertility preservation<sup>23</sup>. A number of studies have suggested that patients are still not routinely informed about the potential risk to their fertility posed by cancer and its treatments, nor are they informed of options to circumvent those risks<sup>24</sup>.

### 2.2.1 Patient Knowledge

The state of patient knowledge in Canada, as it pertains to the effects of cancer and its treatment on fertility and to fertility preservation options, is disconcerting<sup>2</sup>. Referred women, for example, seem limited to an awareness of embryo cryopreservation; they rarely know about other available options<sup>2</sup>. That situation may be related, first, to a lack of accessible education resources and to a deficiency in the modalities of patient education. A recent survey found that 96.6% of physicians relied on verbal communication alone when discussing fertility preservation options<sup>24</sup>. A single verbal communication in the already overwhelming context of a cancer diagnosis may not be the easiest way for patients to understand, digest, and retain information. Indeed, in a Canadian study of male fertility patients undergoing sperm-banking (79 respondents, 50% response rate), 81% said that they were unaware of any education resources on fertility preservation beyond the information verbally provided by their physicians<sup>25</sup>. Even within the context of fertility centres, 25% of responding women and 29% of responding men said that the centres in Canada do not provide any educational materials on fertility preservation<sup>2</sup>. Moreover, the Web sites for 74% of fertility centres lacked information on sperm-banking<sup>3</sup>.

The lack of information transmission from medical team to patient has been an additional problem<sup>7</sup>. Professional organizations have commented that patients often feel that oncologists are not attentive to



their fertility needs and do not inform them of available options—or do so in a way that is not conducive to information and resource transmission<sup>11</sup>. Canadian fertility specialists have perceived both inadequate education and inadequate awareness of infertility risk, together with a lack of support from oncology providers, as the top reasons for poor referral volumes<sup>3</sup>. Among 1093 postpubertal patients, male and female, the rates of physician-led fertility preservation discussions varied from as low as 34% to 86%<sup>26–29</sup>. Furthermore, patients rely on endorsement from their oncology health care providers in deciding whether to pursue fertility preservation<sup>25,27,30</sup>, even with multiple knowledge resources in place<sup>31</sup>.

Improving the availability of information and diversifying education resources is therefore an important challenge to be met. Tangible education resources (for example, pamphlets and brochures) are used only variably by fertility centres<sup>2,3</sup>, and these items may easily fall out of date. The Internet has proved to be an adaptable and interactive platform that could facilitate centralized and up-to-date access to education resources<sup>32</sup>; however, among the fertility facilities across Canada with online resources (44 of 76, 58%), only 16% had any information pertaining to fertility preservation<sup>3</sup>. Other innovative suggestions include information sessions presented by fertility experts using computerized and interactive media<sup>21,33</sup>. Print and broadcast media may also be an important venue for disseminating information to the general population<sup>3</sup>. Finally, trained nonphysician care providers (for example, social workers, oncology nurses)<sup>3,33</sup> or oncofertility-devoted patient navigators<sup>34</sup> may further facilitate the education and referral process.

The importance of patient knowledge and involvement in reproductive choice, regardless of whether active treatment is pursued, has also been emphasized in the literature<sup>35</sup>. Patient participation leads to reductions in both anxiety and depression<sup>35,36</sup>. Anecdotal accounts have outlined the positive psychological effects that can come with an understanding of cancer-related ovarian damage, its pathophysiology, and fertility prognosis<sup>37</sup>. A recent study involving 122 female cancer survivors demonstrated significantly higher depression and distress in the women who felt that they had inadequate knowledge about their reproductive options<sup>38</sup>.

### 2.2.2 Provider Knowledge

Plausible contributors to the lack of patient education and information dissemination by members of the health care team may include their own inadequate knowledge in these areas. An understanding of cancer-related infertility and of fertility preservation options and resources are lacking in the general medical community<sup>3</sup>.

The problem begins with knowledge awareness. In a U.S. survey study of 249 oncologists, the risks of

amenorrhea associated with particular chemotherapy regimens were correctly quantified just 36%–62% of the time<sup>39</sup>. A Canadian survey study of 152 oncologists examined knowledge of cancer-related infertility and fertility preservation. In the 6-item assessment, 5 questions were answered correctly by only 19%–43% of respondents. Significant differences in the knowledge of fertility preservation were also noted between oncologic subspecialties. Gynecologic oncologists scored the highest, followed by medical oncologists and urologists. Radiation oncologists scored the lowest<sup>24</sup>. The study also suggested a significant discrepancy between physicians who practice in teaching hospitals (scoring highest) and those practicing in non-teaching hospital settings (scoring lowest)<sup>24</sup>.

Resource awareness is equally lacking. In the survey study by Yee and colleagues, 24.8% of respondents said they did not know where to refer patients for sperm-banking, and 45%, for female fertility preservation. Those results were also found to have a high dependence on the actual frequency of referrals (rare with respect to male patients in almost 50% of respondent physicians and with respect to female patients in 70%:  $\chi^2 = 20.354, p < 0.001$ ;  $\chi^2 = 21.194, p < 0.001$ )<sup>24</sup>. Similar discrepancies were also noted in resource awareness between subspecialties. Urologists were almost 16 times more likely and medical oncologists, 4.5 times more likely than radiation oncologists to know where to refer patients for sperm freezing<sup>24</sup>. Moreover, physicians working in a teaching hospital or a cancer centre were 15 to 28 times more likely than community practitioners to know where to refer male patients and 6.5 to more than 7 times more likely to know where to refer female patients<sup>24</sup>. Accordingly, surveyed fertility centres for men have also noted large differences between the subspecialties from which referrals are sent. Medical oncologists and urologists refer patients frequently; pediatric oncologists, radiation oncologists, surgical oncologists, and family doctors refer very seldom. Those trends likewise correspond to differences noted between the specialties with respect to fertility preservation education and awareness<sup>3</sup>.

Finally, fertility referral may not be offered by the oncologist because of time restrictions before treatment onset, lack of awareness of the increased success rates with fertility preservation techniques, or a feeling that the cost to the patient might present a barrier to access<sup>13</sup>. The result can be discrepancies in the importance that oncology care providers, compared with patients, place on fertility concerns. Those discrepancies could, in turn, influence proper dissemination of fertility preservation information. The provider-instilled urgency that may accompany a new cancer diagnosis might lead to a disregard of discussion or discouragement of fertility preservation<sup>32</sup>.

### 2.3 Building the Bridges of Communication

In an ideal system, fertility preservation services would be placed where required, and the referral of patients would be natural and effortless. The reality of the Canadian oncofertility system is quite different. The fundamental services necessary for fertility preservation are present, but finite. They are also ill-connected through poor lines of communication and an inadequate referral system. In reality, the true functionality and adequacy of Canadian fertility resources is yet to be determined and will depend on building well-defined and sustainable bridges of communication and improving integration in levels of care (community, primary, and tertiary)<sup>40</sup>.

The time-sensitive and multifactorial decision process for both cancer treatment and fertility preservation should therefore first emphasize the importance of a national multidisciplinary partnership. Reproductive specialists, oncologists, and others on the health care team should have a unified and collaborative approach to management decisions and care of the cancer patient. This cooperative approach should be predetermined, should begin automatically from the point of diagnosis, and should not require any complex referral processes. Moreover, the seamless integration of other multidisciplinary team members such as social workers, psychologists, and other patient advocates are of equal importance. Modern technologies—video conferencing, for example—could also easily facilitate the process of interdisciplinary discussions about patient care. This cooperative strategy has been intensely advocated by a number of professional and international fertility organizations<sup>11,22</sup>.

Possible facilitators to good cooperation might involve assigning predetermined inter- and multidisciplinary teams to a catchment area. The U.S. National Physicians Cooperative provides one successful example of this approach. The group has 50 sites dispersed across the United States, each associated with a different team of interdisciplinary specialists and physicians, and yet each taking a common approach to clinical practice, oncofertility education, patient resources, and patient advocacy<sup>13</sup>. Importantly, the National Physicians Cooperative has integrated a nationwide system of rapid referral, taking into account geographic proximity of the patient to fertility centres, the cancer diagnosis, planned treatment, fertility preservation options, and patient preference<sup>13</sup>.

Collaborative teams are important for facilitating bridge-building and interdisciplinary work, but their complexity might also hinder the process if they are not well organized. A second important element is therefore to facilitate the bridge-building process. To maintain the lines of communication, a universally applicable and predefined referral system could be implemented. (A suggested model for Canada is discussed in the next subsection). Various health

care providers and components of the oncofertility process would be specifically integrated into the referral system, maintaining a multidisciplinary–integrative trajectory. Not only would such a system help to lessen the burden on oncologists in initiating the process, but it would also ensure that a patient's understanding of fertility preservation comes from multiple different angles, that his or her knowledge is reinforced and complete, and that a decision to pursue or decline fertility preservation is well thought-out, with multiple opportunities to alter decisions<sup>41</sup>. Several studies have already supported the positive effects of a “well-defined” system<sup>31,42,43</sup>. A 12-month pilot project by Quinn *et al.*<sup>31</sup>, involving an established patient education and referral system, increased the number of consultations with fertility specialists by a factor of 9 (122 vs. 13 in the preceding year). Similarly, an 8-year study of more than 4800 men 18–55 years of age examined differences in fertility preservation after implementation of a formalized oncofertility program incorporating patient and provider education and referral. Consultation and sperm freezing improved by factors of 2.4 and 2.7 respectively (both  $p < 0.01$ ), and factors of 1.9 and 1.8 for the 18–40 age group (both  $p < 0.05$ )<sup>42</sup>.

### 2.4 Meeting the Costs

#### 2.4.1 Systemic Costs of Organization

Fertility preservation services are already in place, and the financial conventions for individual patient treatment have long been established. A relatively small, but not insignificant, cost burden would need to be absorbed to facilitate an organizational structure and communication within the Canadian oncofertility system. Those costs would include the cost of education resources for physicians and patients (multimedia, advertisements, Internet resources, pamphlets), the cost of facilitating easy communication between health care workers, and the cost of upkeep for a proactive oncofertility oversight organization aimed at maintaining maximum efficiency in fertility preservation. Given the systemic nature of the proposal, yet subdivided into catchment areas, provincial governments could potentially assume those health care costs.

#### 2.4.2 Individual Costs of Treatment—Patient Financing and Feasibility

The substantial costs associated with fertility preservation services themselves may be an additional challenge to overcome. The upfront costs for gamete preservation in women tend to be much higher; they are less commonly prohibitive for men<sup>25,44</sup>. Socio-economic class and, particularly for younger patients, financial dependence on family may play a strong role in managing fertility preservation expenses<sup>4</sup>. Young adults may still be in the midst of their education, often with loans and without a financial cushion that would allow for large expenditures. Many patients are

also unaware of exact fee information or the financial resources available, and they often overestimate their required contribution<sup>45</sup>.

The actual costs for fertility preservation procedures vary between sites as well as between techniques and procedures. A national inquiry into costs obtained fee information posted online by 21 clinics. Oocyte retrieval followed by intracytoplasmic sperm injection ranged from \$6000 to \$8150, embryo cryopreservation ranged from \$500 to \$1200, and oocyte retrieval followed by cryopreservation ranged from \$2900 to \$5400. Those costs do not take into account medications, which can range as high as, or higher than, the procedure cost. Initial costs associated with sperm cryopreservation vary from \$200 to \$500. All cryopreservation procedures require an annual maintenance fee, which can range from \$200 to \$800. Most centres also impose initial administration fees of \$150–\$500 (data drawn from an informal survey of fees posted on Canadian IVF clinic Web sites at February 2012).

Fortunately, a number of resources in Canada offer help to patients so that they can afford fertility-preservation services. Many Canadian clinics have waived administration and other non-treatment-related fees for referred oncology patients. Reduced cryopreservation storage fees often apply. Most centres also have compassionate funds set aside for fertility-related medications, procedures, and facility costs. Alternatively, patients may turn to other independent financial subsidies and charitable organizations throughout the country that can help to cover the expense. Quebec is currently the only province that covers these services entirely (for men and women).

### 3. IMPROVING FERTILITY PRESERVATION FOR CANADIAN CANCER PATIENTS—PRACTICAL SOLUTIONS

The government agency Assisted Human Reproduction Canada initiated the impetus toward “bridge building”—a necessary step for an oncofertility alliance across Canada that could truly benefit young adults diagnosed with malignant disease. Through an established steering committee, the agency recognized the necessity for a document that would review the status of the oncofertility field in Canada and suggest an action plan. The present four-part series was created for that purpose. This review and action plan lays the foundation for a feasible framework that would be coordinated on the federal level.

To implement the plan, a coordinating body is also required. Assisted Human Reproduction Canada could presumably assume that role through their established oncofertility steering committee. In the present document, this suggested coordinating body has been called “the oncofertility agency.”

As discussed earlier, the present document was created to facilitate bridge-building to improve education and referral systems for fertility preservation

within the unique Canadian context. To promote fertility preservation in adolescent and young adult cancer patients and to enable the process, the recommendations that follow have been suggested as a framework for improvement within the Canadian oncofertility system.

- In consideration of knowledge, education, and dissemination of relevant information:
  - Comprehensive, up-to-date, and well-promoted educational resources should be made widely available to patients and care providers alike. The Internet may be an ideal channel to disseminate this information. The Cancer Knowledge Network sites, with their affiliated journal *Current Oncology*, have provided one model of an education resource and collaborative effort to help bridge the gap between cancer patients and caregivers in Canada (<http://multimed.current-oncology.com>). The Cancer Knowledge Network and other Web sites (such as that of the Canadian Cancer Society) could become partners in our mission to provide up-to-date information to potential referral sources (for example, oncology medical teams) and to patients.
  - Updated information about fertility concerns and preservation options for their patient populations should be made readily available to care providers. This information should be readily and proactively disseminated to patients shortly after diagnosis.
  - Efforts should be made to ensure that patients are aware of fertility effects and the potential for fertility preservation regardless of health team presumptions concerning a patient's social, family, or financial situation. Patient autonomy is of the utmost importance.
  - The costs of fertility preservation and the available financial subsidies and resources should be made openly and readily available.
- In consideration of fertility preservation access and availability:

Regional division of Canadian health care and fertility resources into catchment areas should be established. Each catchment area would be arranged as follows (Figure 1):

- **Outer Resource Circle**  
Comprises the members of the patient's general health care team—that is, oncologists, hematologists, family practitioners, nurse practitioners, and so on.

The goals of the outer circle would be fourfold:

- To provide patients with educational resources and information.



- To provide referral to the “inner circle” when required.
  - To provide additional support and resource referral to patients as needed.
  - To receive reciprocal feedback information about patients previously referred to the inner circle.
- **Inner Resource Circle**  
Comprises male fertility preservation consultants, female fertility preservation consultants, and psychosocial services specific to fertility preservation.

The goals of the inner circle would be sevenfold:

- To accept patient referrals from their outer circle in a timely fashion and to provide consultation regarding all appropriate options for fertility preservation—those available at their centre and those available at other centres.

- To perform fertility preservation or fertility-sparing procedures for referral patients when able.
- To refer patients to other inner circles when required—that is, when resource availability or expertise is lacking.
- To accept patients referred from other inner circles.
- To provide psychosocial support services.
- To provide feedback to the outer circle health care team about referred patients.
- To meet periodically and keep in regular touch with the oncofertility agency regarding system-wide changes or resource availability.

Further systemic characteristics would involve:

- **Inter-circle referral forms**  
The inter-circle referral forms would allow for quick communication between the outer and inner circles, as well as between inner circles at various centres. They would take the form of online or other electronic documents. Importantly, these forms would be uniform, well recognized, and prioritized.
- **Inter-circle communication**  
The outer and inner circles of each catchment area will meet periodically for professional updates and to facilitate mutual communication.
- **The Oncofertility Agency**  
This oversight committee of individuals would have these nationwide goals:
  - Assigning fertility centres, practitioners, and other health care team members to the outer and inner resource circles based on catchment area
  - Providing education resources and workshops for outer resource circles
  - Providing educational materials for patients to be passed on by outer resource circle members
  - Organizing regular oncofertility meetings and maintaining networking connections
  - Initiating support and overseeing the regional meetings of the inner and outer circles for the catchment area
  - Establishing and maintaining a comprehensive oncofertility patient database

Entry point for all cases would be the first outer-circle interaction or receipt of a completed referral form. The database would also serve to document follow-up of pregnancy outcomes and births resulting from fertility preservation treatments, with long-term follow-up of the children and the cancer survivors.

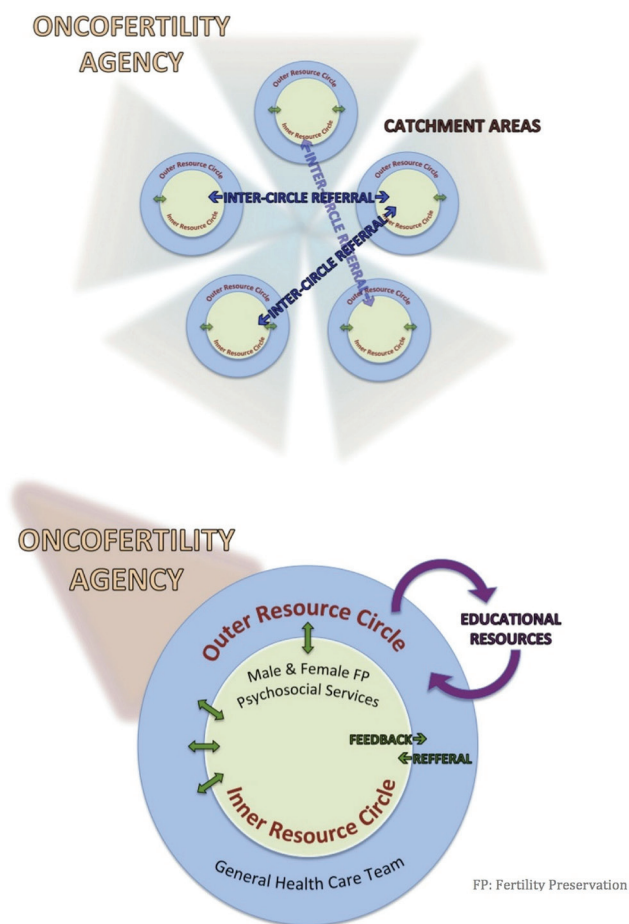


FIGURE 1 Visual depiction of proposed Canadian oncofertility framework.

The overall goals of this organizational structure include

- seamless integration of the multidisciplinary team members;
  - a predefined fertility preservation system, known to all members of the multidisciplinary team;
  - easy access to fertility specialists and preservation services within the context of an automatic referral system;
  - emphasis on the importance of psychosocial services and their ready availability at diagnosis and thereafter; and
  - constant evaluation of the services provided and the need for improvement and expansion.
- In consideration of patient assessment and fertility preservation treatment decisions
    - An assessment of the patient's baseline fertility including age, gonadal function (semen analysis for males, serum and ultrasound markers for females), and other possible predisposing factors for infertility should be completed before cancer treatment begins.
    - Disease should be well defined with respect to malignancy type, stage, and expected physiologic burden.
    - Awareness of cancer treatment on the part of both patient and provider should be comprehensive, including (i) gonadotoxic effects, (ii) possible therapeutic alternatives, (iii) urgency of treatment initiation, and (iv) whether timing of treatment could accommodate the time required for fertility preservation.
    - An attempt to exercise a "combined approach"—with multiple modalities of fertility preservation—should be made in an effort to maximize the possibility of future parenthood.
    - The highest success rates associated with sperm freezing for men and embryo freezing for women should not disregard the use of other fertility preservation techniques, either alone or in combination.

#### 4. SUMMARY

Cancer is a devastating diagnosis. Despite improvements in treatment and long-term survival, it can significantly impair a young adult's quality of life. This is the concluding segment in a four-part series, drafted to review the ill effects of cancer treatment with respect to fertility, to summarize the available fertility preservation and fertility-sparing options, and to suggest how those options can exist and function within a Canadian health care context. Despite existing infrastructure, the ability of the components of the oncofertility system to function together and

to coordinate patient care is challenging at present. We have suggested a multidisciplinary framework for resource allocation, patient referral, and established lines of communication. Moreover, we have suggested a federal government body that we call the Oncofertility Agency to help oversee this process. It is our hope that through the efficient integration of these suggested elements, a functional oncofertility system can be facilitated in Canada.

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#### 6. CONFLICT OF INTEREST DISCLOSURES

RR is a scientific advisory board member of the Cancer Knowledge Network (CKN) and originally drafted this project under a financial grant from Assisted Human Reproduction Canada. HEGH is a section editor for *Current Oncology* and for CKN (oncofertility), a scientific advisory board member of the CKN, and a member of the scientific advisory board of the Israel Cancer Research Fund.

#### 7. REFERENCES

1. Lee S, Heytens E, Moy F, Ozkavukcu S, Oktay K. Determinants of access to fertility preservation in women with breast cancer. *Fertil Steril* 2011;95:1932–6.
2. Yee S, Buckett W, Campbell S, Yanofsky R, Barr RD. A national study of the provision of oncofertility services to female patients in Canada. *J Obstet Gynaecol Can* 2012;34:849–58.
3. Yee S, Buckett W, Campbell S, Yanofsky RA, Barr RD. A national study of the provision of oncology sperm banking services among Canadian fertility clinics. *Eur J Cancer Care (Engl)* 2013;:[Epub ahead of print].
4. Chong AL, Gupta A, Punnett A, Nathan PC. A cross Canada survey of sperm banking practices in pediatric oncology centers. *Pediatr Blood Cancer* 2010;55:1356–61.
5. Neal MS, Nagel K, Duckworth J, et al. Effectiveness of sperm banking in adolescents and young adults with cancer. *Cancer* 2007;110:1125–9.
6. Baynosa J, Westphal LM, Madrigano A, Wapnir I. Timing of breast cancer treatments with oocyte retrieval and embryo cryopreservation. *J Am Coll Surg* 2009;209:603–7.



7. Rosen A, Rodriguez-Wallberg KA, Rosenzweig L. Psychosocial distress in young cancer survivors. *Semin Oncol Nurs* 2009;2:268–77.
8. Lee S, Ozkavukcu S, Heytens E, Moy F, Oktay K. Value of early referral to fertility preservation in young women with breast cancer. *J Clin Oncol* 2010;28:4683–6.
9. Hickey M, Peate M, Saunders CM, Friedlander M. Breast cancer in young women and its impact on reproductive function. *Hum Reprod Update* 2009;15:323–39.
10. Payne S, Jarrett N, Jeffs D. The impact of travel on cancer patients' experiences of treatment: a literature review. *Eur J Cancer Care (Engl)* 2000;9:197–203.
11. Ethics Committee of the American Society for Reproductive Medicine. Fertility preservation and reproduction in cancer patients. *Fertil Steril* 2005;83:1622–8.
12. Bleyer A. Young adult oncology: the patients and their survival challenges. *CA Cancer J Clin* 2007;57:242–55.
13. Woodruff TK. The Oncofertility Consortium—addressing fertility in young people with cancer. *Nat Rev Clin Oncol* 2010;7:466–75.
14. Lee SJ, Schover LR, Partridge AH, *et al.* on behalf of the American Society of Clinical Oncology. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. *J Clin Oncol* 2006;24:2917–31.
15. Duffy C, Allen S. Medical and psychosocial aspects of fertility after cancer. *Cancer J* 2009;15:27–33.
16. Cousineau TM, Green TC, Corsini E, *et al.* Online psychoeducational support for infertile women: a randomized controlled trial. *Hum Reprod* 2008;23:554–66.
17. Sexton MB, Byrd MR, O'Donohue WT, Jacobs NN. Web-based treatment for infertility-related psychological distress. *Arch Womens Ment Health* 2010;13:347–58.
18. Boivin J. A review of psychosocial interventions in infertility. *Soc Sci Med* 2003;57:2325–41.
19. de Liz TM, Strauss B. Differential efficacy of group and individual/couple psychotherapy with infertile patients. *Hum Reprod* 2005;20:1324–32.
20. Hämmerli K, Znoj H, Barth J. The efficacy of psychological interventions for infertile patients: a meta-analysis examining mental health and pregnancy rate. *Hum Reprod Update* 2009;15:279–95.
21. Thewes B, Meiser B, Rickard J, Friedlander M. The fertility- and menopause-related information needs of younger women with a diagnosis of breast cancer: a qualitative study. *Psychooncology* 2003;12:500–11.
22. Multidisciplinary Working Group convened by the British Fertility Society. A strategy for fertility services for survivors of childhood cancer. *Hum Fertil (Camb)* 2003;6:A1–39.
23. Letourneau JM, Ebbel EE, Katz PP, *et al.* Pretreatment fertility counseling and fertility preservation improve quality of life in reproductive age women with cancer. *Cancer* 2012;118:1710–17.
24. Yee S, Fuller-Thomson E, Lau A, Greenblatt EM. Fertility preservation practices among Ontario oncologists. *J Cancer Educ* 2012;27:362–8.
25. Yee S, Fuller-Thomson E, Dwyer C, Greenblatt E, Shapiro H. “Just what the doctor ordered”: factors associated with oncology patients' decision to bank sperm. *Can Urol Assoc J* 2012;6:E174–8.
26. Duffy CM, Allen SM, Clark MA. Discussions regarding reproductive health for young women with breast cancer undergoing chemotherapy. *J Clin Oncol* 2005;23:766–73.
27. Schover LR, Brey K, Lichtin A, Lipshultz LI, Jeha S. Knowledge and experience regarding cancer, infertility, and sperm banking in younger male survivors. *J Clin Oncol* 2002;20:1880–9.
28. Partridge AH, Gelber S, Peppercorn J, *et al.* Web-based survey of fertility issues in young women with breast cancer. *J Clin Oncol* 2004;22:4174–83.
29. Anderson RA, Weddell A, Spoudeas HA, *et al.* Do doctors discuss fertility issues before they treat young patients with cancer. *Hum Reprod* 2008;23:2246–51.
30. Quinn GP, Vadaparampil ST, Lee JH, *et al.* Physician referral for fertility preservation in oncology patients: a national study of practice behaviors. *J Clin Oncol* 2009;27:5952–7.
31. Quinn GP, Vadaparampil ST, Gwede CK, Reinecke JD, Mason TM, Silva C. Developing a referral system for fertility preservation among patients with newly diagnosed cancer. *J Natl Compr Canc Netw* 2011;9:1219–25.
32. Jona K, Gerber A. MyOncofertility.org: a Web-based patient education resource supporting decision making under severe emotional and cognitive overload. *Cancer Treat Res* 2010;156:345–61.
33. Canada AL, Schover LR. Research promoting better patient education on reproductive health after cancer. *J Natl Cancer Inst Monogr* 2005;(34):98–100.
34. Scott-Trainer J. The role of a patient navigator in fertility preservation. *Cancer Treat Res* 2010;156:469–70.
35. Crawshaw MA, Sloper P. “Swimming against the tide”—the influence of fertility matters on the transition to adulthood or survivorship following adolescent cancer. *Eur J Cancer Care (Engl)* 2010;19:610–20.
36. Fallowfield LJ, Hall A, Maguire P, Baum M, A'Hern RP. Psychological effects of being offered choice of surgery for breast cancer. *BMJ* 1994;309:448.
37. Letourneau JM, Melisko ME, Cedars MI, Rosen MP. A changing perspective: improving access to fertility preservation. *Nat Rev Clin Oncol* 2011;8:56–60.
38. Carter J, Raviv L, Applegarth L, *et al.* A cross-sectional study of the psychosexual impact of cancer-related infertility in women: third-party reproductive assistance. *J Cancer Surviv* 2010;4:236–46.
39. Forman EJ, Anders CK, Behera MA. A nationwide survey of oncologists regarding treatment-related infertility and fertility preservation in female cancer patients. *Fertil Steril* 2010;94:1652–6.
40. Sutcliffe SB. A review of Canadian health care and cancer care systems. *Cancer* 2011;117(suppl):2241–4.
41. Gardino SL, Jeruss JS, Woodruff TK. Using decision trees to enhance interdisciplinary team work: the case of oncofertility. *J Assist Reprod Genet* 2010;27:227–31.
42. Sheth KR, Sharma V, Helfand BT, *et al.* Improved fertility preservation care for male patients with cancer after establishment of formalized oncofertility program. *J Urol* 2012;187:979–86.
43. Ogle SK, Hobbie WL, Carlson CA, Meadows AT, Reilly MM, Ginsberg JP. Sperm banking for adolescents with cancer. *J Pediatr Oncol Nurs* 2008;25:97–101.

44. Quinn GP, Vadaparampil ST on behalf of the Fertility Preservation Research Group. Fertility preservation and adolescent/young adult cancer patients: physician communication challenges. *J Adolesc Health* 2009;44:394–400.
45. Köhler TS, Kondapalli LA, Shah A, Chan S, Woodruff TK, Brannigan RE. Results from the survey for preservation of adolescent reproduction (SPARE) study: gender disparity in delivery of fertility preservation message to adolescents with cancer. *J Assist Reprod Genet* 2011;28:269–77.

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