



Published in final edited form as:

Cancer Treat Res. 2010 ; 156: 391–401. doi:10.1007/978-1-4419-6518-9_30.

Healthcare Provider Perspectives on Fertility Preservation for Cancer Patients

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Introduction

For many people, cancer is the most feared health diagnosis imaginable and brings about immediate thoughts of death. Even cancer healthcare providers have been shown to exhibit a sense of hopelessness and negative attitudes toward a cancer diagnosis. Yet, overall cancer survival rates have been increasing over the past 30 years, suggesting that a diagnosis of cancer should not necessarily be associated with impending death or giving up hope of survival. Five-year cancer survival rates over the past 30 years have increased from 56 to 64% for adults and 56–75% for pediatric and adolescent cancers. As a result, there are approximately 450,000 cancer survivors in the current population between the ages of 19 and 39, and it has been estimated that by 2010, 1 in every 250 young people in the United States will be cancer survivors. Increased survival rates have caused a shift in thinking toward a more comprehensive model of cancer care. Survival and cancer treatment still take precedence, but recent focus among healthcare providers, researchers, organizations, and policy makers shows increased attention to the long-term psychosocial aspects of cancer survival. The National Institute of Medicine's 2001 compendium, *Crossing the Quality Chasm*, demands the healthcare system no longer focus on survival alone, but instead focus on "quality survival." Interest in the quality of life experienced by cancer survivors and a focusing on improving self-reported rates of quality of life have been on the forefront of the National Cancer Institute's National Cancer Plan, as well as part of the philosophy and policy of many organizations such as the Lance Armstrong Foundation and the Susan G. Komen Foundation.

In addition to ongoing physical and physiological effects from cancer treatment, cancer survivors often face financial, employment, social, emotional, and educational challenges. The physiological effects of chemotherapeutic agents and irradiation have been associated with a range of long-term impairments such as cardiac and lung dysfunction, hearing loss, alopecia, and neurological disorders. These same treatments have also shown to decrease fertility, or in many cases, cause permanent sterility. For the breast cancer patient in her fifties or the prostate cancer patient in his seventies, this loss may not be highly significant. However, to young men and women who survived cancer as a teen and dreamed of being a parent one day, this loss of fertility is often a devastating blow.

The exact risk of sterility from chemotherapy or radiation is not known and depends mostly on the age of the patient, the type of therapy, the site of the cancer, and the stage of the disease. Studies suggest that between 40 and 80% of female cancer patients are at risk of becoming infertile and between one-third and three-quarters of male cancer patients may become sterile following treatment for cancer.

Given the possibility that cancer patients might be faced with impaired fertility or sterility in the future, what options do they have for future childbirth and or parenting? The American Society for Clinical Oncology (ASCO) [13] and the American Society for Reproductive Medicine (ASRM) [12] recommend that physicians should discuss the risks of infertility with all cancer patients of reproductive age. They further suggest that interested patients should be provided with information to answer their questions about possible fertility preservation and should be referred to reproductive specialists and psychosocial providers as needed.

Interested male cancer patients have more straightforward options if they have already reached puberty. Males can bank sperm at a sperm banking facility or even in the privacy of their own home or hospital bed with mail-in kits. Pre-pubertal males may also have the option of experimental procedures such as cryopreservation of testicular tissue. Fertility preservation for females is more involved. To date, cryopreservation of embryos and ovarian transposition are the only non-experimental options available to women. Other experimental options include oocyte cryopreservation and ovarian tissue cryopreservation. One fact that impacts both males and females with cancer is that there is a narrow window of opportunity for pursuing fertility preservation. The most successful results are achieved among patients who preserve DNA prior to cancer treatment. These options are discussed in more detail in Part I.

Although addressing potential fertility loss may be overwhelming for newly diagnosed patients and their families, multiple studies suggest that failure to confront the possibility can cause regret and distress to cancer survivors and significantly impact their quality of life. Multiple studies with survivors, particularly adult survivors of pediatric or young adult cancer, suggest patients do not recall having a discussion about loss of fertility. It is not known if these discussions did in fact occur for the majority of patients but resulted in patients not remembering them or if the conversations did not take place at all. What is known is that the ability to parent a biological child is of great importance to cancer survivors. Several studies suggest that as many as 75% of childless patients who are diagnosed with cancer wish to have a child in the future. Studies conducted among survivors of pediatric cancer indicate a strong fear that they will be rejected by future partners due to their inability to have a child.

Current guidelines attribute the onus of these multifaceted conversations to oncologists. However, patient-provider interactions are complex and providing an optimal exchange of information along the continuum of care for cancer patients is challenging. The current ASCO guidelines perhaps fail to account for the fact that discussions about fertility preservation need to be ongoing and must be modified to meet the specific needs of each patient. For example, at the point of diagnosis, information on fertility preservation may not take precedence over information about survival. Healthcare providers should insist that patients and families hear and consider fertility preservation information regardless of patients being overwhelmed or distraught. During treatment, patients should be given information on how that particular treatment regime may affect their future fertility. Finally, after patients are cancer-free or have completed treatment, they may have questions about childbearing in regard to their health and the health of their potential offspring. Thus, discussing fertility preservation should not be viewed as a one-time task to be checked off on a care plan, but as an evolution of health information exchanges between healthcare providers, patients, and their families. Providing this information in a comprehensive, honest, and consistent manner may improve the patient's long-term health related to their quality of life.

Oncologists

Given the important role that healthcare providers play in the dyadic exchange of fertility preservation information, it is critical to understand their perspectives, perceived barriers, and potential solutions in discussing fertility preservation with cancer patients. This section summarizes the existing fertility preservation evidence from healthcare providers who treat adult patients.

Physicians face many communication challenges when discussing fertility preservation with patients. These challenges can be related to (1) physician characteristics, (2) patient factors, and/or (3) healthcare system factors. Multiple studies with oncologists indicate that knowledge barriers can inhibit a discussion about fertility preservation with a newly diagnosed cancer patient of childbearing age. Two key knowledge barriers often faced by oncologists are: knowledge of where to refer patients and knowledge of fertility preservation treatment options. Although online directories do exist for sperm banking, physicians often cite that it is difficult to know where to refer a male patient. This is further compounded by lack of knowledge on the most up-to-date fertility preservation technologies, especially for females. As previously noted, several of these technologies are still experimental; however, without a basic understanding of available options, a physician may miss an opportunity to refer a patient with the mistaken belief that there are no options for the patient. In a study by Schover et al. [1, 2], a knowledge quiz was distributed to 162 oncologists who treat male cancer patients. The results showed that on average, most physicians answered only 10 out of 15 questions correctly. More than one-half of the physicians in the sample did not know that males were more likely to become infertile than females, overestimated the number of sperm samples needed, and did not know what the costs of sperm banking were. While about 90% of oncologists in this study indicated that sperm banking should be offered to men, only 10% noted they did so in routine practice. A 2009 study by Quinn et al. [14] conducted among a representative sample of US oncologists showed 25% did not know where or how to refer a patient for fertility preservation options.

There is less information available in the existing literature on patient factors that may serve as communication barriers. Several studies have identified communication barriers among those patients with low health literacy levels or those from cultures or religions that do not support assisted reproduction, as well as for patients who do not speak English. A qualitative study by Quinn with physicians at a single institution noted that the discussion of fertility was “Awkward enough but compounded in difficulty if done through an interpreter.”

Perhaps the most intricate patient issue that serves as a barrier for discussion is the patient who has late stage disease or a poor prognosis. Several studies of physician behavior indicated this key barrier to the discussion. Posthumous parenting or posthumous reproduction is a term used to describe a patient who stores sperm or embryos or other DNA and then allows the use of the stored materials for assisted reproduction with a partner or spouse after his or her death. In addition to some physicians' attitudes that this is not an acceptable practice, others are unaware of this option for some couples or partnerships and thus do not suggest fertility preservation. As noted by one physician in a study on barriers to discussion of fertility with oncology patients, “I am very uncomfortable telling a patient that she has a 20% chance of survival and then adding, by the way, have you ever thought about having children?”

Another patient centered issue that serves as a barrier to discussion of fertility preservation centers on treatment delay. While males can typically pursue sperm cryopreservation within a day or two of diagnosis if an appropriate facility is available, females who are interested in cryopreservation often require a 2–6-week period of time for ovarian stimulation. In some cases where tumor resection is the first course of treatment for the patient, ovarian

stimulation can occur during the healing period after surgery and before adjuvant or neo-adjuvant therapy begins. However, in other medical scenarios, most oncologists reported they would not recommend a female patient delaying chemotherapy to pursue fertility preservation. The oncologists' recommendation that a patient should not delay treatment to use fertility preservation was often cited as a barrier to discussing fertility preservation options. A physician in the Quinn 2007 qualitative study noted, "It seems unfair to tell a patient there are options available to have a child in the future, but not for you, your cancer is too aggressive and if you want a better chance at survival you have to start treatment ASAP. I'd just rather not bring it up, especially if the patient has not brought it up." Concerns about treatment delay are often intermingled with the concept of posthumous reproduction. While little research has been conducted on this concept from the patient perspective, some female patients have suggested that having a biological child in the future is as equally important to them as surviving. A female patient posted the following on a website for young cancer survivors, "My husband and I have discussed this at length, I'd rather have the chance to be pregnant and bring a child into the world than live without that experience. I've wanted to be a mother my whole life; it's all I've ever wanted. My husband knows he may raise our child alone. This is our choice. I appreciate the medical advice and the cautions but this is what we want."

Finally, there are healthcare system barriers for physicians attempting to communicate about sterility and fertility preservation with newly diagnosed patients. Physicians may have a high patient caseload and competing demands on the time that they have available to spend with each new patient. Quinn et al.'s [3] qualitative study of 16 physicians noted that time was scarce during office visits and therefore, fertility preservation was not necessarily a top priority for discussion. As one physician said, "You always do your best to cover all the bases but with an acute disease there is too much going on to think about."

Despite the existence of national guidelines by ASCO and ASRM, individual hospital-level policies or practice guidelines about fertility and preservation may not exist and as such, physicians may be either unaware of the need or be required to deal with each patient on a case-by-case basis. Educational materials do exist and are available from the Fertile Hope organization, the Lance Armstrong Foundation, and the Oncofertility Consortium. However, knowledge and distribution of these materials to patients by physicians is quite low. Quinn et al.'s [4] study of US oncologists showed less than 25% were aware of or distributed educational materials to their patients.

In addition to communicating the potential loss of fertility to patients and stating that fertility preservation options may be available, oncologists are also responsible for referring interested patients to reproductive endocrinology specialists. To date, Quinn et al. [4] has conducted the only national study of physicians who treat oncology patients in an attempt to understand their practice patterns and factors associated with referral to a specialist for fertility preservation. In total, 613 physicians across the United States were surveyed (response rate of 33%) and the unadjusted results suggest that less than one-half of physicians "always" or "often" refer oncology patients to a reproductive specialist when they have questions about fertility preservation. After controlling for several individual- and practice-level characteristics, the study also found that female physicians, physicians with a positive attitude toward fertility preservation, and physicians whose patients inquired about the effects of cancer treatment on fertility preservation were more likely to be referred to specialists as compared to their referent groups.

Overall, there have been few studies about adult oncology providers' views, practice patterns, perceptions, and barriers to discussing fertility preservation. Yet, the results are fairly consistent. Healthcare providers lack knowledge to address fertility preservation, and

even though ASCO and ASRM have recommended that all oncology patients who ask for information receive it, and if appropriate, also receive a referral to a reproductive specialist, less than 50% of providers offer follow those recommendations. Healthcare providers have also indicated that fertility preservation materials should be improved and be created at appropriate language, culture, and literacy levels.

Although the existing literature for healthcare provider practice behavior is insightful, and a first step in improving fertility preservation outcomes for adult oncology patients, there are several gaps in the research that should be addressed. First, most of the existing evidence on providers is focused on oncologists and not on specific cancer specialists. In some cancers, such as breast cancer, a patient may meet with and be treated by a surgeon. This surgeon may serve also as the medical oncologist or may transfer the patient to the care of a medical oncologist after the surgery. In these cases, discussion of fertility preservation may fall through the cracks, with the surgeon assuming that the responsibility for the discussion of sterility falls in the domain of the oncologist prescribing the chemotherapy or the radiologist administering radiation. In every healthcare system, there may or may not be a policy or guidelines to address responsibility for the discussion. Furthermore, although almost every institution requires patients to sign a form understanding the risks and potential associated side effects of chemotherapy, one of which may be sterility, the signing of such a form does not constitute a discussion. It is not known if healthcare organizations have formal policies about fertility preservation and a process for referrals or care plans. Best practices in this field should be documented and shared by international, national, statewide, and local organizations. These are just a few examples of the type of information that is missing from the literature on healthcare provider's experiences with fertility preservation. This information could potentially be used to inform researchers, clinicians, healthcare organizations, and policy makers to better understand where resources can be allocated to most effectively and efficiently improve outcomes.

Adolescent and Pediatric Providers

Perhaps even more daunting is the task that healthcare providers face when addressing fertility preservation with adolescent or pediatric oncology patients. Physician challenges range from being uncomfortable with having discussions with adolescents about sexuality and reproduction to discussing options with parents who are legally required to provide the consent for treatment decisions for adolescents. Compared to studies of healthcare providers who primarily treat adults, more fertility-related studies have been conducted with pediatric oncologists and pediatric oncology nurses who treat oncology patients. However, this may not be surprising given that survival rates are higher for pediatric and adolescent cancer and it follows that more of these patients will have to consider their future fertility as compared with adult oncology patients.

Physician Studies

One of the first studies about adolescent fertility preservation was conducted by Achille et al. [5] and primarily focused on barriers and enabling factors for young men to bank sperm. In-depth interviews conducted with 18 healthcare professionals highlighted that healthcare providers consider the age of the patient when deciding to present information on fertility preservation. Results suggest that a supportive parent or partner was an enabling factor to bank sperm and patients typically did not view sperm banking as a complex procedure, although there were logistical problems in finding an available facility. Other barriers cited by the healthcare workers were cost, cultural beliefs, and sexual orientation. To date, no studies have been conducted that focus solely on female adolescent oncology patients.

A second study by Goodwin et al. [6] surveyed 30 healthcare providers in a hematology/oncology department (response rate 94%) about their attitudes and practices regarding fertility preservation. Although providers had high levels of knowledge about fertility preservation, about one-half were unaware that the risk of infertility is higher for males than females and that pregnancy outcomes of pediatric cancer survivors did not result in higher rates of birth defects. About 35% of healthcare providers routinely consult with a reproductive specialist and about 64% noted that it was difficult to find specialists and facilities for fertility preservation. Specific to adolescents, 86% of healthcare providers indicated that parents often ask about future infertility and the same percentage felt that adolescents should be included in fertility preservation discussions.

In a 2008, qualitative study of 24 pediatric oncologists in the state of Florida, Vadaparampil et al. [7, 8] identified physician, parent, and institutional factors that potentially interfered with fertility preservation discussion with adolescent and pediatric patients. Consistent with findings from the adult literature, about one-half of pediatric oncologists felt that they would like to learn more about fertility preservation, especially the options for females. Although none of the physicians in the study had received any training on the subject of fertility preservation, most were comfortable with discussing fertility with patients and families. Those who were not comfortable wanted educational materials that were more age-appropriate than the current available materials. All of the physicians indicated that they would not recommend delaying treatment for females and a few were unsure if they would recommend delaying treatment for males to sperm bank. Physicians cited that parents' emotional state and culture could be barriers to discussing fertility preservation. For example, many parents are overwhelmed upon learning their child has cancer and even when the child has a good prognosis they are unable to focus on issues of survivorship. As several oncologists from this study noted, "In cultures where assisted reproductive technology is not acceptable it can be difficult to discuss issues like sperm banking. This means talking about masturbation which can be uncomfortable for the parents and having this conversation through a translator can make it worse." Institutional barriers experienced by providers who care for adults such as cost, availability of educational materials, and lack of institutional guidelines were also cited as barriers for adolescents.

Nurse Studies

Another unique factor about the available adolescent fertility preservation literature is the emphasis on nurses' perspectives. This is particularly important as some have argued that nurses have more direct interaction with oncology patients and their families, and perhaps might be better positioned to discuss fertility preservation. Under that framework, several studies have solely assessed pediatric oncology nurses' knowledge, attitudes, and barriers to fertility preservation.

Reebels et al. [9] surveyed 27 nurses about male adolescent fertility preservation (response rate 45%). As with physicians, nurses incorrectly indicated that females were at higher risk for infertility, they were not aware of costs of sperm banking, and only one-fifth knew that young men might have low sperm count and motility at diagnosis. Nurses noted that they would be less likely to discuss fertility preservation if the young man was HIV positive, had aggressive cancer, or was openly homosexual.

In 2007, Vadaparampil et al. [10] published two studies on pediatric oncology nurses' attitudes, practice patterns, and institutional barriers toward fertility preservation using data from a survey completed by 126 pediatric oncology nurses (response rate 65%). In the first study, the findings corroborate the low levels of physician adherence to the 2006 ASCO guidelines in that 73% of pediatric oncology nurses report discussing fertility preservation less than 10% of the time. In the second study, which focused on institutional barriers, the

results showed that only 14% of the nurses indicated that their institution had fertility preservation guidelines on the offering of sperm banking, 8% had guidelines of the offering of ova cryopreservation for females, and three-quarters of the sample indicated that there was a strong need for these guidelines at the institutional level.

Finally, a study by Clayton et al. [11] compared pediatric oncology nurses' attitudes and knowledge about fertility preservation from 2005 to 2006. The importance of this study is that the ASCO guidelines on fertility preservation were released to the public in 2006, making this one of the few studies that can comment on changes in behaviors following the guidelines. Results from the surveys, however, showed little change between pediatric oncology nurses' attitudes about fertility preservation from 2005 to 2006 and 96% indicated that they were unaware of the ASCO guidelines. These results emphasize that creation of guidelines is only part of the answer to establishing best practices toward fertility preservation and that dissemination is equally, if not more, important.

The cost of assisted reproductive technology may be another barrier to discussing fertility preservation with oncology patients, particularly pediatric and adolescent patients. Although cost was rarely cited in physician studies as a primary barrier, other healthcare personnel such as nurses and social workers noted concerns in this area. Two studies examining knowledge and attitudes of nurses [10] and social workers [15] showed the costs associated with fertility preservation were a factor in dampening enthusiasm for discussing or referring a patient. The costs for sperm banking range from \$250 to \$500 for preserving and from \$100 to \$500 per year for storing the sample. Although nurses and social workers found these costs to be associated with their reluctance to discuss, the majority of young men who chose not to sperm bank cited not wanting children in the future or not having received timely information as their number one reason.

The costs associated with female fertility preservation are higher and more medically complicated. The average cost for embryo cryopreservation ranges from \$5,000 to \$12,000 and the costs of in vitro fertilization of stored embryos may also range from \$10,000 to \$25,000 a cycle and may require more than one cycle for a successful pregnancy. Nurses and social workers cited these costs as a barrier to discussing fertility preservation with females. One social worker reported, "We have patients who have no transportation for their treatment and who are living on public assistance. It doesn't seem right to discuss this very expensive option with them when they can't even afford their electricity bill." While physicians are less likely to cite costs as a barrier, it is certainly on their mind. A physician who practices in a very low socio-economic neighborhood commented, "I've had to find shoes for my patients to go home in when they came to clinic barefoot. I'm not comfortable discussing let alone referring them to a specialist for a procedure that I know they can not afford." The concern over referring patients to a reproductive endocrinologist or other infertility specialist was also cited as a deterrent among nurses and social workers. "It's one thing to talk about a service the hospital can provide even if the patient can't afford it, but it's another thing to send them to a specialist knowing they can't even afford the office visit never mind the procedure."

In this collection of adolescent studies, several themes emerge. First, it is clear that decision making and ethics are a challenge to provider-adolescent communication and referrals to reproductive specialists. Physicians and nurses are faced with acknowledging the adolescent's desires while legally looking to the parent for the ultimate decision on fertility preservation. Some states do have exemptions which allow minors to make medical decisions, but these are mainly focused on pregnant minors and minors who already have children. The law is silent on a minor's rights to make decisions about their future children. Second, even when adolescents are included in the decision-making process it is not clear

how healthcare providers should explain fertility preservation to them. Along the developmental trajectory, adolescents' understanding of fertility preservation should evolve. Younger adolescents may understand that, "they may not be able to have a baby," whereby older adolescents may understand that, "reproductive technologies could help them have a baby in the future if they are infertile." Understanding appropriate terminology and messages is critical for developing fertility preservation educational materials specifically for adolescents and their parents. Studies that create and evaluate the effectiveness of these materials are needed. Third, adding to this complexity is the fact that understanding fertility preservation technology could be related not only to development, but also to parental provision of information on sexuality and reproduction. Fourth, although it is known that parents are the legal decision makers, there have been no dyadic, or even triadic, studies to understand where the views on fertility preservation may diverge or converge for adolescents, parents, and physicians. Finally, costs of procedures have been shown to be a factor in the discussion of fertility preservation with both parents and physicians citing this as an influence.

Conclusion

Regardless if the oncology patient is an adolescent or adult, the need for additional provider education about fertility preservation is cited in the conclusion of almost every existing study. However, stating that education is necessary is marginally useful to medical educators and administrators when time, funding, and expertise are scarce. There is a critical need for studies to determine the most effective educational method to deliver fertility preservation education so that knowledge is increased and sustained in an effective manner. Studies on the educational methods of continuing medical education credits and residency education have shown that didactic training, while the most common method used, is the least effective. Randomized, multi-center studies should be conducted to compare educational methods such as standardized patients, teachable moments, seminars, and computerized training modules, noting that the "optional" model may differ by specialty type or level of overall experience. Without this important information, researchers and advocates will continue to point to lack of provider education as a primary barrier to fertility preservation without being able to make concrete suggestions on how to overcome that barrier.

Studies need to be conducted that begin to understand why certain patients were and were not referred to reproductive specialists. Although surveys are able to capture attitudes toward hypothetical referrals, in reality referrals from oncologists to reproductive specialists may differ by their willingness and ability. Retrospective chart reviews and follow-up interviews with oncologists might help to understand additional patient, family, and systematic barriers to referral. Perhaps these studies would illuminate the need for facility-based policies such as standardized forms or chart notes.

Longitudinal patient studies are needed to ascertain if, and how, fertility preservation information is being provided not just at the time of diagnosis, but during treatment, and later when survivors want to have children. Having a single brochure, pamphlet, or video may not be useful to providers, as different stages across the illness trajectory might require information to be delivered in a variety of ways. For example, do cancer survivors seek information on family planning from their primary care physicians, oncologists, or staff at a late effects clinic? Materials provided may need to be tailored to these specific practice settings.

There is limited evidence in the literature about the knowledge, attitudes, and perceptions about fertility preservation from other healthcare workers such as social workers, care coordinators, or case managers. In a managed care environment, the perceptions of these

healthcare workers may be important, as they have increased interactions with oncology patients. Likewise, appropriate educational methods may differ for these professions.

Finally, more information is needed on how institutional practices, insurance coverage state laws, and other healthcare policies affect healthcare provider interactions about fertility preservation with oncology patients.

Research in the field of fertility preservation for oncology patients has been quickly changing. Social science studies, including the perceptions and impact of healthcare providers, are more important than ever. Although physicians and nurses are often in the first line of defense to counteracting decreased future quality of life for cancer patients, they must have the best tools available for that battle. Instead of focusing on what providers are not doing in regard to fertility preservation, research in this area must continue to evolve and begin to focus on how these improvements can be made. Ultimately, the goal is to improve the lives of cancer survivors; researchers and clinicians should work together to reach accomplish this mission goal.

Acknowledgments

This research was supported by the Oncofertility Consortium NIH 8UL1DE019587, 5RL1HD058296.

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