A View from the past into our collective future: the oncofertility consortium vision statement

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Abstract

Purpose Today, male and female adult and pediatric cancer patients, individuals transitioning between gender identities, and other individuals facing health extending but fertility limiting treatments can look forward to a fertile future. This is, in part, due to the work of members associated with the Oncofertility Consortium.

Methods The Oncofertility Consortium is an international, interdisciplinary initiative originally designed to explore the urgent unmet need associated with the reproductive future of cancer survivors. As the strategies for fertility management were invented, developed or applied, the individuals for who the program offered hope, similarly expanded. As a community of practice, Consortium participants share information in an open and rapid manner to addresses the complex health care and quality-of-life issues of cancer, transgender and other patients. To ensure that the organization remains contemporary to the needs of the community, the field designed a fully inclusive mechanism for strategic planning and here present the findings of this process.

Results This interprofessional network of medical specialists, scientists, and scholars in the law, medical ethics, religious studies and other disciplines associated with human interventions, explore the relationships between health, disease, survivorship, treatment, gender and reproductive longevity.

Extended author information available on the last page of the article

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Introduction

Since the term “oncofertility” and the relatively small oncofertility consortium of research scientists and allied clinicians were organized in 2006, the group has become a robust and productive community from over 45 countries around the globe [1–12]. Since its inception, there have been a number of scientific advances, including sustained in vitro follicle growth in allogeneic hydrogels (with the achievement of live birth in mice, the first metaphase II (MII) egg in human, and the first non-human primate embryo), development of the first cryoprotectant specifically designed for and tested on non-human primate and human ovarian tissue, and the first ovarian bioprosthetics (with techniques involving decellularization, 3-D printing, and reconstituted tissue papers) and autografting of cryopreserved prepubertal testis tissue to produce sperm and offspring [1, 13–27]. These scientific discoveries have been matched by clinical advances that include expanding options to pediatric and adolescent and young adult populations and patients with differences in sex development, transgender, and gender-diverse populations, as well as the development of optimized ovarian procurement and testicular biopsy sampling and documented methods for tissue transport [12, 28–36]. Prepubertal testicular tissue cryopreservation is now also performed in a number of centers worldwide, although this technique still remains experimental [25, 37]. In addition, there has been a growing emphasis on the full range of patient, parent, and partner considerations including questions of legal ramifications and religious and ethical concerns [28, 38–41]. Based on the extraordinary work from groups around the world, ovarian tissue cryopreservation (OTC) is no longer designated experimental [42]. Moreover, ten US states require insurers to cover fertility preservation costs for cancer patients or any patients receiving gonadotoxic therapy. This change in the US is being mirrored in other countries and the leverage created by having a globally linked organization (Fig. 1) allows for more rapid uptake of necessary procedures [4, 43, 44]. In just over 10 years, the collective progress made by the broad and engaged stakeholders in this field has been outstanding. Now, as we approach the next 10 years of the field, our communal goal is to ensure that similar progress will be made in the future and by this coordinated effort, patients’ needs will continue to be prioritized and met. As such, in early November 2019, the Oncofertility Consortium introduced a multi-month, multi-stakeholder discussion regarding the future of the field of oncofertility. Herein, we present the thoughts and conclusions of our engaged, global leadership.

Beginning in 2007, a broadly attended annual meeting has been held that created context, community, and critical mass for collaboration and increased momentum during a time frame when scientists and clinicians were working largely on their own [45, 46]. The meeting has served as a platform for international collaboration and support in oncofertility program implementation. It has also served as a training ground and mentorship for residents, fellows, early-stage scientists, nurses, and allied health professionals from around the globe, as well as a pipeline for high school students [47–49]. The 2019 meeting had record attendance, illustrating the interest to gather and collaborate as a field. However, convening is only one dimension of our work. The community is thinking strategically about how to facilitate this meeting and how to grow the field even more broadly to advance the science and its clinical application for our patients. As such, all stakeholders were invited to participate in a strategic planning process called Vision 2030: A Roadmap for Oncofertility Research and Practices.

The strategic planning process began with an anonymized “appreciative inquiry” survey sent to a group of over 3000 oncofertility stakeholders in December 2019. Appreciative inquiry is a strength-based, positive approach to leadership development and organizational change [50]. Survey recipients included OC leadership, previous conference attendees, advocates, and other individuals who have all interacted with the OC in some way since 2007. The ultimate goal of the short, four-question appreciative inquiry was to identify the OC’s core strengths and to explore how to leverage these strengths to redesign the organization to make it more effective and sustainable. Suggestions were analyzed, and a summary document was provided to the members of the leadership group for their review. Emerging themes included diversity, collaboration, networking, the annual meeting, leadership, team science, sharing, and bringing together stakeholders. (See Fig. 2 for complete appreciative inquiry survey.) Following the appreciative inquiry, on February 7, 2020, a diverse group of leaders from the OC participated in a day-long meeting, to review the appreciative inquiry responses and discuss the resulting next steps for the field. This leadership group included clinicians and basic scientists, nurses, patient navigators, social scientists, and advocates, from the USA and abroad. Disciplines represented included oncology, urology, reproductive endocrinology and infertility, psychology, and specialists in pediatric, adolescent, and adult populations. Many of the participants serve as chairs of their respective
Oncofertility Professional Education Network (OPEN) sub-committees [1] and have exhibited exemplary leadership and engagement in the field. Together this group discussed the current state of the field, the priorities for the next 10 years, and the strategies to be used to ensure that the field is moving forward in a productive and collaborative manner. The group was also tasked with developing the OC’s vision, mission, and value statements (Fig. 3), and to identify four strategic goals for the field which were (1) improve access, (2) advance research, (3) Educate, and (4) Collaborate.

Improve access

Both nationally and internationally, oncofertility professionals face common challenges. These include a lack of awareness among providers and patients, a lack of appropriate clinical research a high-level of shared protocols and experiences. Member leverage work done in affiliated centers to accelerate their formation and services offered [1–7].

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Improve access

Both nationally and internationally, oncofertility professionals face common challenges. These include a lack of awareness among providers and patients, a lack of appropriate
communication between provider and the patient-parent dyad (particularly for pediatric providers), a lack of referral pathways with no standardized models of care, cultural and religious constraints, uncertainties regarding exact risks of cancer-related infertility, insufficient funds to support oncofertility programs, and a lack of insurance coverage, and high out-of-pocket costs for patients [2, 51–53]. As such, we believe in the next 10 years, one major strategic goal of the OC is to improve access to care. This can be facilitated in part by increasing oncofertility awareness through the expansion of OPEN [2]. OPEN is a free, membership-based network comprised of oncofertility professionals from 45 countries. It encourages members to share resources, methodologies, and experiences to collaboratively advance the field and break down barriers to access.

First, we can continue to support new and existing centers with detailed roadmaps and patient navigation expertise to develop, re-organize, and implement oncofertility programs [32, 54]. The OC has worked to provide centers with consent templates, protocols, business plans, and support, to facilitate efficient program implementation. The OC’s network of patient navigators provides professional peer support and unprecedented opportunity for collaboration to serve both patients and programs regardless of their location. Ideally, in the future, a team of patient navigators and oncofertility experts would be equipped with standard operating procedures and guidelines and have the ability to travel to rural, remote, or new clinics and centers to raise awareness; assist with leadership engagement; and subsequently help build robust oncofertility programs. Furthermore, the resources provided by these teams would be in multiple languages, and they would be culturally adapted by local experts, who have a deeper insight into the local culture and knowledge about local resources and processes.

During the February meeting, the OC leadership team also explored the possibility of pursuing a center of excellence designation for qualified member centers. Though time intensive to procure, this designation may help enhance the depth and breadth of oncofertility services offered to patients. We discussed the several advantages to establishing a center of excellence model, including lending further credence to our work and credibility to an institution, clearly identifying high-level institutions for patients seeking to identify a comprehensive oncofertility program at which to pursue care, as well creating a continuum of success for our centers and further incentivizing member institutions to join the OC and OPEN. We also considered, however, certain barriers to pursuing a center of excellence designation. The OC is grounded in altruism, so affixing labels of quality may be exclusionary in some instances; we would not want to disregard any centers, including those centers with limited resources. Moreover, fertility preservation in the cancer setting is extremely time sensitive. In many instances, patients may not have enough time to investigate a center’s designation and respective outcome data. We would never want a center of excellence designation, or lack thereof, to prevent a patient from pursuing family building options. To achieve the full benefits of this model, proper assembly is required [55] and the leadership team will need to further examine the benefits and risks associated with this model. Ideally, as a group, we would need to determine how to create a designation that is customizable and takes into account institutional variation so that it seeks to encourage and highlight positive change and does not penalize or devalue programs that are simply resource poor.

We can also improve access by optimizing internet-based resources and by utilizing telehealth technologies to reach patients in remote locations or low-resource settings [56]. As the working world continues to evolve and patients face geographical and physical barriers to care, the utilization of telehealth would improve awareness and access to oncofertility care [57]. The transformation of clinical care through the use of telehealth due to the COVID-19 pandemic has demonstrated that timely fertility consultations can be provided remotely when patients otherwise may not have had the opportunity to be counseled on fertility risk and preservation options before beginning cancer therapy. Telehealth platforms that are Health Insurance Portability and Accountability Act (HIPAA)-compliant are being utilized to access vital healthcare services. Although many oncofertility procedures require in-person care, the initial consultations prior to treatment could be performed remotely and the patient would then be directed to the nearest clinic for treatment [58, 59]. Telehealth services provide a centralized service for initial consultation not just during trying times, but as a model for getting expertise to vulnerable or remote communities, enabling more efficient initial steps. In the USA, the recent change in Medicare reimbursement rules to cover telemedicine consults has dramatically accelerated the financial feasibility of utilizing telemedicine for fertility preservation. Advocating for these changes to become permanent is a critical policy component for improving and maintaining access to fertility preservation expertise. Assembling a team of skilled patient navigators to conduct these remote consultations could be a priority in the field so we are able to nimblly adapt to current and future challenges.

It is important to note that we must also be mindful of the economic and geographic hindrances of oncofertility services while we explore approaches to improve access. While patients have struggled with previously reported barriers to care, specifically high out-of-pocket costs, the COVID-19 pandemic has shed light on geographic barriers to care. Although a patient can still receive timely intervention and consultation through the use of telehealth technologies, they may not be able to travel to designated centers for in-person care and procedures due to travel restrictions. The OC will continue to support translation of innovation and cutting-edge clinical
or research advances into tangible solutions at the grassroots level. For example, in low-resource settings, member institutions can provide training to the local youth to access telemedicine technology and help set it up for patients. Similarly, member institutions can channel philanthropic resources to provide transportation for patients requiring travel to sites specializing in oncofertility procedures. The diversity of the OC membership provides us the platform to understand needs of our community and effect change at local, regional, national, and international level.

One of the steepest barriers to care remains the high cost of fertility preservation services. This is both because of the relatively high costs associated with the procedures themselves and due to the lack of insurance coverage. The OC works with other groups and professional societies, namely the Alliance for Fertility Preservation (the AFP), to advocate for improved insurance coverage. This has now been achieved in ten states, but much work remains. The OC can leverage its members’ geographic diversity to form AFP “working groups” locally, to work both with their institutions and within their states toward the attainment of greater coverage. Existing template bills, sample private insurance policies, toolkits, and other materials can be shared to expedite legislative and regulatory initiatives in several states.

Advance research

Our second strategic goal is to advance basic science research since this is the backbone of all that we do. In 2007, when the OC was founded, we brought together numerous research projects with the idea that this research would eventually translate to extraordinary clinical care for cancer patients who face fertility loss. Additionally, we would have been unable to advance the field of oncofertility without establishing the current baselines of clinical need and patient outcomes. As such, it is crucial to continue the support of basic science, clinical, and translational research projects throughout the OC.

We have defined a field within science and medicine and created corridors of communication that have led to options for fertility preservation and hormone restoration in pediatric, adolescent and young adult, and adult cancer patients. We have disseminated our clinical research findings and taught our bench technologies to enable additional resources and perspectives to expand and expedite our impact. We are leading the field through team science and connected common goals and interests to enable a network of engaged professionals and trainees, both in the USA and abroad, who share a passion for oncofertility and reproductive health [60]. These teams have created a series of key intellectual and didactic products. Collectively, members of the OC have been involved with many of the groundbreaking discoveries that have defined our field. We reported the first restoration of reproductive function—endocrine hormone production and live birth—using engineered ovarian transplants in mice [17]. The OC has leveraged discoveries from advances in genomic medicine to improve oncofertility care by collaboration with geneticists and genetic counselors. Researchers at the frontier of bioengineering and 3-dimensional printing have enabled deployment of this exciting technology for development of the bioprosthetic ovary [61]. Moreover, we reported the first human MII eggs developed after in vitro growth of early secondary human follicles [8, 21].

Facilitating translational and clinical research is also a priority of the OC. Because the field is relatively young, and impact of therapy on fertility is a late outcome, it is difficult to study and, as such, comprehensive longitudinal data about oncofertility patients does not exist, but is critically needed. A number of international centers have already established registries and collaborative work with other international registries could help to identify challenges in building such large registries [62, 63]. As such, a goal of the OC would be to work with a range of investigators to collaborate on an international scale and establish a comprehensive oncofertility registry to investigate long-term outcomes in patients, such as future fertility, pregnancy outcomes, and age at menopause. This registry could track baseline data and longitudinal outcomes that can be used to guide oncofertility interventions. Though aspirational, a central data coordinating center with the capability to automatically import data from participating institutions is the ideal. Such a platform will allow participating institutions to export their data to the centralized database without the need for additional human resources, minimizing cost, and improving access for smaller institutions. Equal access to the collective, big data provided by participating institutions will allow multiple research questions to be addressed simultaneously, thus catapulting the field in key areas such as approaches to fertility preservation in vulnerable populations, long-term fertility outcomes, gynecologic and urologic late effects of cancer therapies, and barriers to referral. This international database is long overdue and critical to advancing the field.

We have been successful thus far because OC research teams have collaborated across institutions. Strengthening local, regional, and international ties and maximizing interaction among centers creates synergistic opportunities for the field. We will continue to provide the forum and platform to enable these connections through online forums and in-person conferences and training programs that expedite research discovery and we will provide support to investigators in search of research funding.

Additionally, the OC can help pursue opportunities to advocate for funding at the NIH and offer guidance for particular requests for applications (RFAs). Whether this means providing a letter of support for an NIH grant proposal or helping to identify and disseminate relevant grant and funding...
opportunities, the OC is committed to the advancement of scientific research. Furthermore, we will utilize our network to identify potential collaborators to enhance the scientific merit of proposals and grant applications. We will disseminate these research findings in journals and via social media and other outlets to broaden reach and keep the field connected through sustained engagement and an interdisciplinary approach.

Educate

The third strategic goal of the OC is to educate the next generation of oncofertility leaders. To date, OC leaders have trained numerous students, residents, and clinical and research fellows. Despite these continuing efforts, creating new generations of oncofertility specialists remains an unmet need. Treatment options in oncofertility are rapidly expanding, including the recent change to include ovarian tissue cryopreservation as a part of the armamentarium of established care options [42]. We expect that as increasing numbers of medical centers and healthcare providers around the world will start to offer oncofertility services, there will be a corresponding increase in the need for more oncofertility education and training across disciplines. This is especially salient for healthcare providers to ensure that fertility preservation technologies are offered safely and appropriately. Consideration should be given to formal incorporation of oncofertility into the learning objectives and content for medical school, residency, and fellowship curricula. In addition, nurses and advanced practice providers are an increasingly important and engaged cohort among the community of medical providers. Prior research among all of these groups has revealed not only oncofertility educational deficits but also a strong willingness among these cohorts to engage in oncofertility educational initiatives.

We have a rich history in education, and together, with our collaborators, we created numerous educational tools in various formats and multiple languages that have catalyzed the growth of oncofertility [1, 49, 64–66]. These items include online patient and provider resources, the first comprehensive oncofertility textbook, and educational training videos for a variety of different audiences. We also created a free online certificate course as part of the American Society for Reproductive Medicine’s Air Learning platform, and an annual one-day course for trainees in a diverse array of medical specialties including reproductive endocrinology and infertility, medical and pediatric oncology, pediatric and adolescent gynecology, urology, breast oncology, rheumatology, and radiation oncology [47]. The leaders in the field have provided mentorship and hands-on training to clinicians and scientists who are interested in creating or expanding oncofertility programs. Formal pathways to connect mentees and mentors will drive expansion of this field.

One of the great traditions of the OC is our work with high school students in local lab-based programs complimented by the educational opportunity to participate in the annual meeting. We have combined this educational opportunity with digital materials from early childhood to adults education in order to ensure that reproductive health terms are as accessible as possible to the general public [65]. Educating the next generation of students is a core value of the OC and finding ways to connect students to emerging health issues while informing them about their own health are dual wins for society.

Our goal has been to have educational resources that are not only enduring but also easily updated. Educational materials and seminars have been created by a team of experts to provide common patient education materials, oncofertility program guidance, provider education materials, and core educational guidelines for specialized training in oncofertility [67–70]. Moving forward, we envision a strong continuation and broad dissemination of existing resources and the development of new repositories, didactic programs, and partnerships to provide authoritative, comprehensive educational resources to researchers, patients, and providers across pediatric and adult specialties.

Collaborate

The fourth strategic goal is to continue to collaborate and connect members of the field. Even in the earliest days of the OC, it was evident that the field would benefit greatly by including multiple disciplines and expertise. We brought together a variety of medical disciplines, all with a vested interest in the field. This included reproductive endocrinologists, oncologists, urologists, OB/GYNs, allied health professionals, psychologists, nurses, embryologists, and adult and pediatric specialists. We knew ethicists and religious leaders would inevitably need to be included in the conversation. Most importantly, patients and their partners and their families were included from the beginning to ensure that all of our actions revolved around their care and ultimate well-being. Therefore, from the onset of the OC, we proactively included them as members of the field. These cross-cutting collaborations have set the stage for ongoing partnerships, the advancement of oncofertility care, and have become a hallmark of the field.

We will continue to convene annually at the Oncofertility Conference. The OC will serve as the great facilitator of communications and collaboration among OPEN members and beyond. We will collaborate with other professional societies and regional oncofertility organizations, including, but not limited to, the International Society for Fertility Preservation (ISFP), FertiProtekt, the Japanese Society for Fertility Preservation (JSFP), the Korea Society for Fertility Preservation (KSFP), the Australasian Oncofertility Consortium, and many others [6]. We will connect with
advocacy groups to provide support to all patients and make the critical connections to ensure their needs are being met and guarantee that the patient’s perspective remains a central, guiding force of the OC. There is great value in enhancing international collaborations as we aim to gain important experiences from each other, and the OC conference will continue to serve as the venue to do so.

In addition, we must develop new ways to bring all OC communities together, especially across the oncology services and their multidisciplinary teams, with the intention of providing updated information in the field, jointly elaborating strategies for accessing options by patients and their families and, finally, reducing the resistance to the fact that fertility is an aspect of the quality of survival. Although oncofertility has gained space and prestige since its inception, as stated above, there remain concerns about the effectiveness of communication between reproductive medicine professionals and oncologists, which is evidenced by the absence of programs that offer both approaches in many clinics and hospitals. In this sense, it is also important that there is an approximation of the OC with the clinical and surgical oncology societies, which allows a joint action in the elaboration of comprehensive and broadly applicable assistance protocols.

Leadership is of paramount importance to sustain the OC for the next decade and beyond. Thus, one of the early goals of the next phase will be to conceptualize a plan for leadership and structure. Together we will develop a leadership steering committee model that involves members elected or selected from the global OC community. In addition, the leadership plan should include methods of creating and maintaining engagement, since this will positively affect every goal that the OC plans on achieving in the future.

Progress made outside of the OC

We would be remiss if we did not discuss all of the progress made in the field outside the confines of the Oncofertility Consortium. Our colleagues in Europe specifically, many of whom are not formally part of the OC, have made groundbreaking discoveries and many of the most notable advances in oncofertility and fertility preservation. This includes live births following fertility preservation using in vitro maturation of ovarian tissue oocytes and live births reported using cryopreserved and transplanted ovarian tissue [71–75]. The progress made by these centers has been outstanding and we continue to applaud their work. We believe that if we further coalesce as a field and come together to better enable collaboration and team science, we will rapidly improve the pace of research thereby accelerating clinical breakthroughs that ultimately improve the lives of our patients.

Future directions and final thoughts

The Oncofertility Consortium was created out of the urgent unmet need of young female cancer patients with limited options for fertility management prior to receiving gonadotoxic therapies. We now have an evidence-based field of medicine that offers hope as well as real options that could only be imagined in 2006. Oncofertility has expanded from a field focused on the unmet need of young reproductive age women undergoing cancer therapy into a discipline that provides fertility preservation options for people of all ages and genders. The scope of our efforts has expanded beyond cancer to also provide options for individuals at risk of infertility due to bone marrow transplantation (BMT) for benign diseases, disorders of sexual development (DSD), autoimmune diseases, gender-affirming treatments for transgender/gender-diverse populations, and other non-oncologic conditions, including rheumatology. It has expanded beyond restoration of reproductive function to also include restoration of hormonal function alone or in combination with reproduction. The key to the success of the field is to maintain the level of cooperation and low barriers to communication between leaders and centers worldwide. The multiple publications from the global team provide evidence that the world is ready for communal work and elaborating on this opportunity is part of a successful future for the field and for the OC [1–7, 76]. This paper outlines the strategic goals and collective priorities of our leadership; however, the implementation and tactics for achievement are up to the field. With this new strategic vision and the broad global participation in the shaping of the Oncofertility Consortium’s goals, we believe the time is right for the next chapter of this organization to be written.

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