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Medical egg freezing: the importance of a patient-centered approach to fertility preservation

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Abstract

Purpose This binational qualitative study of medical egg freezing (MEF) examined women's motivations and experiences, including their perceived needs for patient-centered care in the midst of fertility- and life-threatening diagnoses.

Methods Forty-five women who had undertaken MEF were interviewed in the USA (33 women) and in Israel (12 women) between June 2014 and August 2016. Interviews lasted approximately 1 h and were conducted by two senior medical anthropologists, one in each country. Women were recruited from four American IVF clinics (two academic, two private) and two Israeli clinics (both academic) where MEF is being offered to cancer patients and women with other fertility-threatening medical conditions.

Results Women who undertake MEF view their fertility and future motherhood as important components of their identities and recovery and, thus, are grateful for the opportunity to pursue fertility preservation. However, women who undergo MEF have special needs, given that they tend to be a “vulnerable” population of young (age < 30), unmarried, resource-constrained women, who are facing not only fertility loss but also the “double jeopardy” of cancer. Through in-depth, qualitative interviews, these women's MEF stories reveal 10 dimensions of care important to fertility preservation, including five “system factors” (information, coordination and integration, accessibility, physical comfort, cost) and five “human factors” (adolescent issues, male partner involvement, family involvement, egg disposition decisions, emo-

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tional support). Together, these dimensions of care constitute an important framework that can be best described as “patient-centered MEF.”

Conclusions Women pursuing MEF have special medical needs and concerns, which require particular forms of patient-centered care. This study outlines 10 dimensions of patient-centered fertility preservation that are appropriate for MEF patients. This approach may help IVF clinics to be better prepared for delivering top-quality care to mostly young, single women facing the daunting prospect of fertility loss and life-threatening medical diagnoses.

Keywords Medical egg freezing (MEF) · Patient-centered care · Cancer · United States · Israel

Introduction

Fertility preservation via oocyte vitrification is increasingly being recommended to young women whose medical diagnoses put them at risk of future infertility. Cancer patients scheduled to undergo treatment with cytotoxic chemotherapy are candidates for fertility preservation [1–3], as are women with a range of other fertility-threatening medical conditions (e.g., autoimmune disorders, severe endometriosis, genetic profiles including BRCA1 and BRCA2, Turner syndrome, fragile X syndrome) [4]. In such cases, medical egg freezing (MEF) is a recommended option to prevent future infertility and reproduction-related regret [1, 5].

The risk of losing one’s reproductive ability and the chance to conceive genetic offspring may come as a major blow to women—not only to their self-esteem and gender identity but also to the future in which motherhood and children are viewed as definitive. The few qualitative studies that have probed the connection between women’s fertility desires and fertility preservation focus almost exclusively on cancer patients, showing that diagnosis is a pivotal life event foreshadowing a potential future without motherhood [3, 5–7]. Women who have completed cancer treatment but without fertility preservation may feel “robbed” of time and choice, experiencing a “preoccupying sorrow” about the loss of their reproductive potential, amid other sorts of fears and agony [7].

Despite increasing provision of MEF over the past 5 years for both cancer patients and those with other fertility-threatening conditions, a range of studies demonstrates the ongoing challenges women are facing. These include the inadequate presentation of information about fertility and MEF [6, 8, 9], lack of timely and direct referral to IVF clinics [10–12], and patient-provider communication issues [11], particularly physician uncertainty about the success of MEF and their discomfort in raising future fertility among women who are facing the threat of death [5, 9, 13–16]. In a recent

overview of these barriers to fertility preservation among cancer patients, both intrinsic factors (i.e., patients’ attitudes and health literacy, clinicians’ approaches and skills, doctor-patient relationships) and extrinsic factors (i.e., fertility preservation resources, institutional characteristics) were found to influence patients’ and healthcare professionals’ decision-making at the time of cancer diagnosis [17]. A recent meta-analysis also shows that oncofertility services and support are often not delivered to eligible patients according to current guidelines [18].

Studies have shown that women are more likely to undergo MEF if they have received adequate fertility counseling, by either a fertility nurse specialist, a reproductive endocrinologist, or a gynecologist [5]. However, the amount of information given to women from healthcare professionals varies considerably. In one qualitative study of 19 breast cancer patients in the UK, only half had been given the opportunity to pursue MEF, with most women reporting that they had received little information or support [6]. In another study of 34 Dutch women with cancer, a counseling consultation on MEF was considered by women to be very important, with most expressing “general satisfaction” with the timing and content of the information presented [19]. However, Dutch women still reported “unmet needs,” revolving mostly around the complexity of decision-making in very short time frames, and the need to assert themselves in order to receive adequate information. Women in the Dutch study had several recommendations to improve patient care, including standardization of information provision, improvement of communication among clinicians and medical centers (e.g., between oncology services and IVF clinics), and availability of MEF-specific patient information materials [19].

Interestingly, the Netherlands has gone farther than any other country in promoting the conceptual framework called “patient-centered infertility care” [20]. The idea of patient-centeredness connotes “being respectful of, and responsive to, individual patient preferences, needs and values, and ensuring that patient values guide all clinical decisions” [21, p. 589]. As delineated in an Institute of Medicine report, “Crossing the quality chasm: a new health system for the 21st century,” patient-centeredness is one of six key dimensions of quality healthcare, the others being safety, effectiveness, timeliness, efficiency, and equity of access [22].

In a large-scale, joint Dutch and Belgian study involving 925 IVF patients, 227 IVF physicians, and 14 focus groups with 103 infertility patients, the researchers discovered major discrepancies between physician and patient attitudes toward patient-centeredness [23, 24]. Whereas IVF physicians routinely “underestimated” the importance of patient-centeredness in their delivery of infertility care, IVF patients cared greatly about this dimension—so much so that a lack of perceived patient-centeredness was “the most common reason for patients to change clinics” [24, p. 589]. One quarter of the

925 patients surveyed had already switched IVF clinics during treatment, with most citing non-medical factors such as “disrespectful staff or contradictory information” as their reason for leaving [24, p. 589]. Furthermore, the study showed patients’ willingness to travel “significant distances for better quality of care,” suggesting that patient-centeredness was a key dimension in widespread European cross-border reproductive care [24, p. 589].

Building upon these research findings, Dancet et al. developed a useful conceptual framework for patient-centered infertility care, outlining 10 key dimensions [23]. These included six “system factors” (information, competence of clinic and staff, coordination and integration, accessibility, continuity and transition, physical comfort) and four “human factors” (attitude and relationship with staff, communication, patient involvement and privacy, emotional support).

These insights into the key dimensions of patient-centered infertility care have been advanced in a number of different European studies and publications [25–31]. However, most of this research has focused exclusively on infertile couples seeking care in European IVF clinics. The meaning of patient-centeredness may differ, either slightly or significantly, for (1) patients outside of Western Europe, (2) single women patients facing fertility-threatening conditions without partner support, and (3) cancer patients facing the “double jeopardy” of cancer and fertility loss. Indeed, with the growing rate of cancer survival and the advent of MEF, the need for sensitive patient-centered care in IVF clinics around the world may be considerably heightened [32–34].

To understand the situation of women needing MEF because of fertility-threatening medical diagnoses, it is necessary to study the motivations and experiences of those who have gained access to and then have undertaken at least one MEF cycle. By asking women about their illness experiences, their hopes for motherhood, and their motivations for undergoing fertility preservation—as well as the details of their journeys to and through the MEF process—women themselves may be invaluable guides in articulating “what is at stake” [35] in medically related fertility preservation. They may also articulate what they deem most important in the delivery of patient-centered MEF care.

This article develops an approach to patient-centered MEF care based on the experiences and recommendations of women patients who have completed at least one MEF cycle. We follow the framework forwarded by Dancet et al., which they entitled “Patient-centered infertility care: a qualitative study to listen to the patient’s voice” [23]. Like Dancet et al., we listened carefully to what patients told us about undergoing MEF. Many of the same dimensions of patient-centered care outlined by Dancet et al. emerged in our study. However, women who undergo MEF have special needs, given that they tend to be a “vulnerable” population of young (age < 30), unmarried, resource-constrained women, who are facing not

only fertility loss but also the double jeopardy of cancer. Thus, in this article, we forward 10 dimensions of a patient-centered approach to fertility preservation that focuses specifically on young, unmarried women with cancer and other fertility-threatening conditions.

Methods

This study was part of a binational, medical anthropological, qualitative investigation of oocyte cryopreservation among women who had completed at least one MEF cycle. The study took place from June 2014 to August 2016 and was supported by the US National Science Foundation’s Cultural Anthropology and Science, Technology, and Society programs. The study was conducted in the USA and Israel, two countries where clinical approval of oocyte vitrification, including for medical purposes, occurred relatively early, in 2012 and 2011, respectively. Women who had undertaken MEF were recruited from six IVF clinics offering oocyte cryopreservation, four in the USA (two academic, two private) and two in Israel (both academic).

All six IVF clinics in this study, whether academic or private, received the majority of their MEF patients through direct referrals from other physicians, primarily university- or community-based oncologists, gynecologists, and surgeons. Self-referral for MEF also occurred in a few cases where medical referrals had not been made in a timely fashion. All six clinics in this study also offered fertility preservation counseling, either by a full-time counselor or staff or through an IVF clinic referral to a counselor specializing in fertility issues. Depending upon the patient’s medical condition, counseling usually involved discussion of the impact of the medical condition and its treatment on future fertility, options for egg and embryo freezing (with or without a partner), ovarian tissue freezing, and the use of GnRH agonists for suppression.

Given the focus of this study on MEF, 45 women who had undertaken at least one MEF cycle volunteered to participate. In the US portion of the study, 33 women were interviewed, including seven who had undertaken MEF when it was still considered as experimental, and 26 who undertook MEF after its clinical approval in 2012. In Israel, 12 women volunteered for the study, seven of whom undertook MEF in the experimental period and five after clinical approval in 2011. In the USA, recruitment occurred primarily by email flyers sent out by the four participating clinics. Women who were interested in volunteering for the study then contacted the first author, either directly or through the clinic. In the two US academic IVF clinics, some women were given the study flyer directly by their clinicians during appointments and were invited to contact the first author if they were interested in participating in the study. In Israel, recruitment occurred by phone, with IVF clinicians and their assistants inviting women

to participate in the study. Women who volunteered to participate were then contacted by phone by the second author, who set a time and place for the interview at the women's convenience.

Women who volunteered for the study signed written informed consent forms, agreeing to a confidential, audio-recorded interview in a private setting. All the interviews were conducted by the first and second authors, who are medical anthropologists with years of experience in interviewing assisted reproduction patients. The interviews were semi-structured, usually lasting about 1 h, but ranging in length from 0.5 to 2 h. The American anthropologist interviewed all the American participants in the study (in English), while the Israeli anthropologist interviewed all the Israeli participants (in Hebrew). Because the American women lived in a variety of US cities on both the East and West coasts (e.g., New Haven; New York; Baltimore; Washington, DC; San Francisco; San Jose) as well as in a number of other metropolitan areas, only one quarter of the interviews could be conducted in person, with the rest carried out by Skype or phone. In Israel, on the other hand, all but one of the interviews were conducted in person, generally in the two major cities of Tel Aviv and Haifa.

In both the USA and Israel, the same IRB-approved, semi-structured interview schedule was used to conduct interviews, although the schedule was translated into Hebrew for the Israeli participants. All the women in the study were asked a brief series of sociodemographic questions (i.e., age, place of birth, current residence, education completed, current employment, marital status, ethnicity, religion), as well as relevant details of reproductive history (i.e., age at menarche, contraceptive use, any known reproductive problems). Following these close-ended sociodemographic and reproductive history questions, a series of open-ended, semi-structured questions was posed, focusing on 10 major themes: (1) the medical diagnosis and treatment plan faced by each patient, (2) egg freezing as a fertility preservation option (who introduced the possibility, what counseling was offered), (3) patient decision-making (motivations to undertake MEF, desires for future motherhood, fears and concerns), (4) support systems (family, friends, partners, and coworkers), (5) MEF financing (with or without health insurance, by whom), (6) physical responses to the MEF procedure (including hormonal stimulation, anesthesia, egg retrieval), (7) perceptions of the MEF process and outcomes (perceptions of clinical care, number of eggs retrieved and in storage), (8) egg disposition (options presented and decisions made, including for posthumous disposition), (9) retrospective reflections upon MEF completion, and (10) future hopes and plans. Because these interviews were semi-structured and open-ended, women often "led" the interviews, telling their egg freezing stories to the anthropologists, who then asked follow-up questions when necessary.

Completed interviews were transcribed verbatim by research assistants at Yale University and the University of Haifa. At the University of Haifa, interview transcripts were then translated from Hebrew into English by a professional bilingual translator. All interview transcripts were uploaded into a qualitative data analysis software program (Dedoose), and detailed case synopses were written to summarize each interview. Descriptive statistical information was transferred into Excel files. As is usual for qualitative, interview-based research, the main data analytic strategy was to systematically search for and examine themes and patterns emerging from the interview materials and to compare the similarities and differences between the US and Israeli data, based on careful review and comparison of all interview transcripts by the two medical anthropologists, who shared their research materials, including interview transcripts and case summaries. The research protocol was approved by the academic institutional review boards and by the ethics committees of all the collaborating IVF clinic sites.

Because the design of our study included two countries and two types of patients (oncofertility and others with MEF indications), we were able to undertake a comparative analysis of patients' MEF experiences and to explore the particular dimensions of patient-centered MEF among women desiring fertility preservation in the two countries. Following the patient-centered care framework developed by Dancet et al. [23], we explore how these dimensions relate to MEF patients in particular and how MEF patients' special needs necessitate particular forms of patient-centered care. We also examine how oncofertility patients compare to those without life-threatening diagnoses and how differences in payment for MEF in the USA versus Israel affect patients' experiences of care. Subtle and not-so-subtle differences in MEF experiences and care emerged between the two countries and between medical conditions, as will be described in the "Results" section.

Results

Cancer diagnoses were the primary reason for MEF cycles in 35 of 45 (78%) of the women in our study, including 23 Americans and 12 Israelis. Of these, breast cancer was the most common indication (15 cases or 43%), followed by blood cancers (leukemia and lymphoma) (11 cases or 31%) and a variety of other cancers (9 cases or 26%). As shown in Table 1, the remaining 10 women, all American, had undergone MEF for other medical reasons, including severe endometriosis or dermoid tumors requiring full or partial oophorectomies (four women), BRCA-positive genetic profiles requiring prophylactic future oophorectomies (two women), a benign pituitary tumor (one woman), and autoimmune disorders (three women).

Table 1 Medical egg freezing: characteristics of the study population

Characteristics	Number of women	Percent
Nationality		
American	33	73
Israeli	12	27
Medical diagnosis		
Breast cancer	15	33
Blood cancer	11	24
Other cancer	9	20
Other condition	10	22
Educational level		
High school	11	24
University	16	36
Graduate school	18	40
Age at MEF		
<20	5	11
20–29	16	36
30–39	22	49
≥40	2	4
Year of MEF		
2000–2010	11	24
2011–2016	34	76
No. of eggs frozen		
<5	7	16
5–10	15	33
11–15	6	13
16–20	8	18
21–25	2	5
>26	6	13
Unsure	1	2

Given the high proportion of cancer diagnoses, the majority of women in our study (40 of 45 or 89%) needed urgent referrals to IVF clinics, where most were able to complete only one MEF cycle, generally prior to chemotherapy. More than half of the cancer patients in this study had advanced or aggressive forms of cancer. Five women had cancer that had metastasized to the lymph nodes, bones, lungs, and/or brain. Four had recurrent blood, tongue, thyroid, and breast cancers, and four had been newly diagnosed with “highly aggressive” breast cancer. In other words, a significant number of women in this study were seriously ill and needed to make fertility preservation decisions as swiftly as possible.

As shown in Table 1, these MEF patients were relatively young (average age 29; ranging from 16 to 41), unmarried (except for one woman in Israel), and facing serious medical diagnoses and had the potential loss of their fertility. In both the USA and Israel, most of these women came from working- or middle-class backgrounds and were thus facing financial and employment difficulties brought on by their diagnoses. In

general, they comprised a particularly vulnerable patient population, where the need for patient-centered fertility preservation seemed vitally important. All of these women had chosen to undertake MEF in the hope of retaining their reproductive abilities. The threat of fertility loss was often framed as being “devastating” or “horrifying,” leading to feelings of extreme “anxiety,” “worry,” and “fear.” Women explained that losing their fertility would be radically life altering, a barrier to their future happiness, and the destruction of their vision of themselves as women and as mothers. Such fertility loss was almost always cast within larger discourses of the importance of motherhood and love for children. Women often made comments such as, “Bearing children is the thing I want most in life, to have children of my own.” Women’s motherhood desires depended somewhat upon age (e.g., whether a woman was a teen or in her late 30s), as well as her relationship status (e.g., whether she was single or partnered). Nonetheless, the importance of becoming pregnant and becoming a mother, either now or in the future, was an abiding theme. Although a few women in this study were slightly less sanguine about biogenetic motherhood and its importance in their future lives, even these women decided to pursue MEF in order to preserve a future motherhood option.

Having undertaken at least 1 cycle of MEF, most women experienced a mixture of gratitude and relief. Women deemed themselves lucky to have been able to access a cutting-edge technology, one that had given them hope, security, and peace of mind. In both the USA and Israel, but especially in the USA, women often described MEF in exalted terms, such as a “gift,” “blessing,” “miracle,” and form of “empowerment.” Even though a few women in the study were disappointed by the results of their ovarian stimulation cycles (less than five eggs retrieved), most women had banked a significant number of eggs, 14 on average. Women often described their frozen eggs as a type of “insurance policy,” even while acknowledging that frozen eggs were “no guarantee” of a future pregnancy.

Given women’s strong desires for motherhood and especially their high hopes for positive MEF outcomes when fertility (and often life) was at stake, women in this study had special needs for patient-centered MEF care. In this regard, the patient-centered care framework forwarded by Dancet et al. [23] is quite useful, and we have utilized it in Table 2. Utilizing five of the same categories determined by Dancet et al. (information, coordination and integration, accessibility, physical comfort, emotional support), we show how these factors take on special significance for patients being referred for MEF care. In addition, we highlight five other dimensions, mostly human factors, that emerged in our interviews and are either unique to, or especially important among, the MEF patient population. These include cost, adolescent issues, male partner involvement, family involvement, and egg disposition decisions. All of these emerged as major dimensions of

Table 2 Dimensions of patient-centered fertility preservation: the special needs of women patients undergoing medical egg freezing

Dimensions	Special needs of MEF patients
System factors	
Information	<ul style="list-style-type: none"> • Providing detailed information on both fertility risks and MEF, provided face to face and in a timely fashion • Setting realistic expectations for MEF outcomes based on single cycles
Coordination and integration	<ul style="list-style-type: none"> • Timely referrals from oncology to MEF services • Support for integrated oncofertility services, with team-based approach to cancer treatment and fertility preservation • Coordination with pharmacies offering online discounts and/or free donations of hormonal medications • Provision of information on cancer charities, including those that provide services and financial help to patients undergoing MEF • Coordination of medication donation and sharing within IVF clinics
Accessibility	<ul style="list-style-type: none"> • Accessibility to IVF clinics from community and pediatric hospitals • Emergency accessibility to IVF clinics for cancer patients on strict treatment timelines
Physical comfort	<ul style="list-style-type: none"> • Assistance with hormone injections • Private areas within IVF clinics devoted exclusively to young (and often single) MEF patients, apart from couple-oriented infertility patient waiting areas
Cost	<ul style="list-style-type: none"> • Compassionate care discounts for patients with cancer and other fertility-threatening conditions • Income-based discounts for low-income cancer patients • Access to MEF financing, including loans and monthly payment plans • Acceptance of credit card payments for MEF services • Discounts or waivers of annual storage fees for MEF patients (who are often young and out of work)
Human factors	
Adolescent issues	<ul style="list-style-type: none"> • Addressing fear of needles and injections and providing injection assistance • Explaining MEF physical discomforts, including transvaginal procedures • Providing extra emotional and medical support for adolescent patients
Male partner involvement	<ul style="list-style-type: none"> • Asking whether patient has a male partner and whether she would like to include the partner in fertility discussions • Discussing both MEF and embryo freezing, including pros and cons • Providing extra emotional support for patients whose partners have left them in the midst of a medical crisis
Family involvement	<ul style="list-style-type: none"> • Asking whether patient has family members, especially parents, and whether she would like to include them in MEF discussions and decisions • Incorporating parental involvement in MEF discussions and decisions with young patients • Recognizing MEF as parents' hope for future grandchildren and attempting to alleviate pressures this might place on patients
Egg disposition decisions	<ul style="list-style-type: none"> • Explaining egg disposition options to sick patients, especially those with advanced cancer • Counseling patients on disposition of frozen eggs to parents, sisters, or other family members, including the pros and cons • Clearly defining guidelines on posthumous egg disposition
Emotional support	<ul style="list-style-type: none"> • Incorporating psychologists and social workers within IVF clinic settings who specialize in oncofertility and MEF • Providing information on oncofertility support groups, especially in IVF clinics serving many cancer patients

patient-centered care in our study. Thus, unlike the infertile IVF clinic patients in Dancet et al.'s study, who were mostly coupled and tended to be in their late 30s and early 40s, MEF patients in our study were mostly younger women (teens to mid-30s), who were relying heavily on the support of family and sometimes male partners during their MEF cycles. Their needs for patient-centered MEF care thus diverged in some ways from the original patient-centered infertility care framework. In the following sections, we describe each of the 10 dimensions of patient-centered care emerging in our study, emphasizing why they are important to this particular population of young, unmarried MEF patients.

System factors

Information

Women undergoing MEF, unlike infertile IVF clinic patients, often lack any previous acquaintance with the subjects of fertility and infertility. Therefore, when they arrive at IVF clinics, they are often grateful for expert fertility counseling, which can provide hope in the midst of a medical setback. This is especially true for cancer patients, who often feel "overwhelmed" by their diagnoses, are "in complete shock," and describe the early days as a "blur." The urgent nature of

treatment—which some women describe as being on a “fast track,” in a “complete whirlwind,” all “under pressure”—means that information on MEF must be conveyed in a timely fashion, to help women make the best possible decisions on how to proceed. Furthermore, cancer patients need to be given realistic expectations for what can be achieved in a single cycle of MEF.

Coordination and integration

Women with cancer were particularly grateful for well-coordinated and integrated oncofertility services, with continuity of care between clinics. They appreciated timely referrals by their oncologists to local IVF clinics, as well as what they described as a “team-based” approach to treatment. In Israel, such coordinated oncofertility services are now well developed in several major hospitals. But, in the USA, because of its sheer size and healthcare structure, coordinated services are not necessarily guaranteed. Thus, women who arrive at IVF clinics are appreciative of the ways in which clinics themselves provide integrated services, for example, by helping link them to outside agencies, including cancer charities and pharmacies providing either free or discounted MEF medications.

Accessibility

Most women in this study received direct referrals to IVF clinics from either their oncologists, gynecologists, surgeons, or family practitioners (especially in Israel). Among the cancer patients, many expressed gratitude for being seen in IVF clinics on an emergent basis. For example, some women reported receiving a cancer diagnosis 1 day and attending their first IVF clinic appointment on the next. Such easy and seamless access was of great comfort to the women in this study. However, in a few cases in both countries, IVF referrals and access were not forthcoming. Fertility was either not mentioned in the cancer workup, or women were expected to do all the work of finding an MEF-providing IVF clinic on their own. Furthermore, some teens reported that their friends in pediatric oncology settings were not routinely referred for MEF. Thus, referral and access sometimes involved having to advocate for oneself, which added significant strain.

Physical comfort

Many of the women needing MEF are young and single and encountering their first major medical setback. Furthermore, most have never borne children and may have had few contacts with gynecologists. For these women, IVF clinics themselves may be daunting settings, where needles, vaginal exams, anesthesia, and surgery are part and parcel of the MEF experience. Learning how to inject oneself, or being

injected on a daily basis, was often traumatic at first. Furthermore, some women in this study described MEF as “painful and invasive,” even if it also gave them hope. Any efforts by IVF clinic staff to reduce physical discomforts and to relieve overall anxiety were greatly appreciated by MEF patients.

Cost

Although cost is not outlined as a system factor in the framework for patient-centered infertility care, we found that it was an important factor for MEF patients, particularly in the US setting. All cancer patients in Israel receive MEF cycles free of charge through Israel's National Health Insurance, even though such insurance coverage is not provided for other medical indications. In the USA, on the other hand, almost all patients—whether suffering from cancer or other fertility-threatening medical conditions—must pay for MEF on their own, because MEF is rarely covered by health insurance. Even in IVF-“mandated” states, such as Maryland or Massachusetts, MEF is not mandated for insurance coverage. Thus, MEF costs are difficult to cover for many young patients. In this study, for example, the average cost of MEF was US\$6966, even after substantial clinic discounts.

As outlined in Table 2, US IVF clinics in this study had instituted various ways of reducing MEF costs and financial burdens, for which patients were extremely grateful. These included “compassionate care” discounts for both cancer and low-income patients, loans and monthly payment plans, acceptance of credit card payments to ease upfront costs, and discounts or waivers on annual storage fees. Helping with MEF costs was particularly important to the youngest patients, many of whom were still in school, dependent upon their families, or unemployed because of the disruptions of cancer treatment.

Israeli patients in this study, all of whom had cancer diagnoses, faced no cost-related financial pressures. This was the major difference in MEF care between the two countries, one that proved to be a major detriment for American women and their families. But, it is also important to acknowledge that Israeli patients with non-cancer-related medical indications must pay for MEF on their own. Thus, the absence of these kinds of Israeli patients in our study may reflect these women's inability to pay for MEF. In the USA, the only patients who were able to undertake more than one MEF cycle were patients with conditions other than cancer. However, because these women were young and sometimes very sick (e.g., with serious autoimmune disorders), they, too, had to rely on their parents to help fund their MEF cycles. In short, in our study, issues of cost and the lack of insurance coverage for MEF were paramount concerns for women in the USA, although not in Israel. This system dimension of patient-

centered MEF care was the major difference between the two countries in our study.

Human factors

Adolescent issues

As determined in this study, the youngest patients may need the most support, which is why adolescent issues are at the top of our list of human factors in patient-centered MEF care. Adolescents may be particularly frightened by needles and transvaginal procedures, and they may need special assistance from nurses and other clinic personnel. In general, adolescents diverge the most from other IVF clinic patients, and their emotional needs may be quite different from the perspective of patient-centered care. For example, being in the couple-oriented world of older IVF patients may be experienced as unsettling, or simply “weird,” as one 17-year-old MEF patient put it. Thus, any attempt to provide private areas within IVF clinics for young MEF patients was greatly appreciated, even if separating MEF from IVF patients is logistically difficult. Adolescent patients may also want to be accompanied by their parents, especially their mothers, throughout the MEF process, and they may need extra attention from fertility clinic counseling staff.

Male partner involvement

Although MEF patients are often young and single, this is not necessarily the case for all patients. Of the 33 American women interviewed for this study, 13 had serious male partners (i.e., boyfriends), who supported them throughout the MEF process. For example, two boyfriends of women with breast cancer offered to marry them in a hurry—one for an emotional “pick me up” for his girlfriend and the other to obtain paid family medical leave when his girlfriend’s breast cancer metastasized to her brain. Such male partners were often described as “amazing” support systems. Thus, some women were keen to factor their partners—including as future spouses—into their MEF decision-making. This involved the difficult decision about whether to freeze eggs or embryos with partners’ sperm. Often, this decision had to be made well in advance of any future plans for marriage. Thus, in these cases, women often found it important for their partners to be present at clinic appointments and to be part of the fertility “conversations.”

On the other hand, in six American cases and two Israeli ones, women were literally “dumped” by their boyfriends in the midst of cancer crises. One boyfriend broke up via text message as his girlfriend came out of her mastectomy surgery. Another woman’s partner told her that he “couldn’t handle it” when she was diagnosed with breast cancer. Thus, she lost the man she planned to marry—a breakup that she “wouldn’t

wish on [her] worst enemy.” Still, the anger she experienced gave her the “strength to fight,” and she described MEF as “one of the best decisions” that she could have made. Women in these difficult “lost partner” situations may require extra care and support in IVF clinic settings, as they go through the MEF process bereaved and alone.

Family involvement

With only one exception, family members were significantly involved in the MEF cycles of every woman in this study. Family members were usually the ones to accompany patients to clinic appointments and their egg retrieval surgeries. They sometimes assisted women with hormone injections, and in the USA, they were most often the ones to subsidize the MEF costs when their daughters and sisters needed financial support. Given the critical role of family, especially parents, in MEF, their role needs to be acknowledged in IVF clinic settings. Patients should be asked if they would like to include family members in MEF discussions and decisions, and this is especially true for younger patients. However, striking a balance in terms of family involvement is also important. In some cases, subtle pressure may be exerted by parents on their daughters to produce “future grandchildren” through MEF.

Egg disposition decisions

In this study, we also found that family members mattered in women’s egg disposition decisions. Several women in this study hoped to donate or “will” their frozen eggs to their sisters. For example, in one case, a woman wanted her younger sister with Turner syndrome to be able to use her frozen eggs if she herself could not use them. Counseling women about their egg disposition options is particularly important, especially in cases of advanced cancer, where posthumous egg disposition must be considered.

Given the ethical and legal dilemmas surrounding the donation or destruction of frozen gametes and the lack of established laws on posthumous disposition, it is important that clinics offer sound guidance to patients and their families. In this regard, all of the clinics in this study provided counseling on egg disposition and required patients to sign informed consent forms choosing one of three available options: disposal, donation to research, or designated donation. However, within the designated donation category, there were substantial differences between countries and clinics. In Israel, the Ministry of Health regulations permit a woman to donate her eggs to another woman, but only anonymously. Although oncofertility patients may attempt to designate or “will” their eggs to survivors (as has been done for young Israeli men with cancer), to date, posthumous disposition and future use of eggs have not been tried in Israel. In most cases, if a woman dies, her eggs will be discarded. In the USA, on the other

hand, most clinics, including all of the clinics in this study, allow for some form of designated donation according to the ASRM guidelines. However, between clinics, there are differences in practice—for example, a surviving spouse may gain “custody” of his deceased wife’s eggs, but not a woman’s parents, if she is unmarried. In other clinics, custody may be granted to whomever inherits the deceased woman’s estate, or by court order. In the USA, the lack of legal regulation makes posthumous disposition decisions unclear and potentially fraught.

Emotional support

Such difficult issues—including speaking to a young woman about egg disposition after her death—make clear how important emotional support is within IVF clinic settings. MEF patients invariably benefit from access to clinical staff, including psychologists and social workers, who can help them through their MEF journeys and refer them to services, including young adult cancer support groups. However, IVF physicians themselves can offer emotional support in a manner that should not be underestimated. Many patients in this study in both countries exclaimed, unprompted, that they “loved” their IVF physicians, who they complimented for providing emotional reassurance, generous MEF discounts, and continuity of care, even after the MEF procedure was completed. In general, MEF patients greatly appreciated the friendliness and kind gestures of IVF clinic staff. Clearly, emotional aspects of patient-centered MEF care were of vital importance.

Discussion

To date, this is the first qualitative study exploring the experiences of women who have undertaken MEF because of cancer diagnoses and other fertility-threatening medical conditions. During in-depth interviews, women shared their journeys to and through MEF, including their experiences and expectations of the fertility preservation process. Most were grateful for access to this fertility preservation technology and had high hopes for future motherhood.

Paying close attention to the many insights offered by these women during their interviews has allowed us to produce a specific set of patient directives that we define as “patient-centered MEF,” in line with the original patient-centered infertility care framework outlined by Dancet et al. [23]. Although many of the dimensions of patient-centered MEF care were similar to those found in the original framework, we discovered the special needs of MEF patients, who tend to be young (< 30), unmarried, and resource-constrained, thus highly vulnerable. Furthermore, most of these women are facing the frightening double jeopardy of cancer and fertility loss.

In both countries, we found that MEF patients had specific needs and concerns. Women were upset when they were not given adequate information about MEF, were forced to search for IVF and fertility preservation specialists on their own, needed to “run from one office to another” in order to coordinate their own treatment, or were asked to wait for an IVF clinic appointment, especially when cancer treatment was urgent. Israeli patients are often used to these “systemic” problems, because most Israelis rely, first and foremost, upon a public healthcare system. However, when cancer struck, Israeli women, like American women, wanted prompt and seamless referral, “teamwork” between their various physician specialists, and a “smooth passage” through the MEF procedure. When such integrated, coordinated, informative, patient-centered care was received, both American and Israeli patients were extremely grateful, often complimenting their physicians and their clinics and sometimes adding that the MEF was “the best part” of their difficult treatment journeys.

A major difference emerged between the USA and Israel regarding cost. Given the lack of insurance coverage in the USA and the steep prices of MEF, American women and their families were very grateful for the ways in which IVF clinics had attempted to ease their financial burden, by offering a variety of MEF discounts, payment plans, and referrals to charities. In Israel, on the other hand, the public funding of MEF for cancer is now taken for granted and is viewed as an integral part of cancer treatment and recovery. Israeli women in this study, all of whom were cancer survivors, felt fortunate that MEF had been offered to them free of charge. Thus, unlike American patients, their MEF experiences were almost uniformly positive.

In both countries, it was clear that cancer created multiple pressures and anxieties for women. Women routinely described their “shock” over learning of a cancer diagnosis, the feeling that their lives were now on hold and in danger, the impending threat of fertility loss, and the urgent time frame for both cancer treatment and MEF. The double jeopardy of potentially losing one’s life and one’s fertility was a dominating anguish. Thus, for cancer patients, MEF was only part of an extensive encounter with serious illness and the medical system. MEF was deeply entangled with these women’s overall cancer treatment and their ardent hopes for full recovery and long-term survival.

These sobering realities were much less apparent among the 10 women in this study who had medical conditions that were non-life-threatening, or at least not immediately so. In their interviews, they described a longer path to MEF, which was undertaken in consultation with their physicians, their family members, and in some cases, their male partners and friends. Furthermore, unlike most cancer patients, these women were not limited to one MEF cycle. Thus, among the 10 women in our study who pursued MEF for non-cancer-related

medical reasons, four had undertaken 2 cycles of MEF, often yielding higher “egg counts” in the process.

Regardless of the “type” of MEF, the importance of “human” factors in the delivery of patient-centered cannot be overestimated. Women expressed their needs for emotional support throughout the MEF process, not only from clinic staff but also from family members and sometimes male partners who accompanied women to their IVF clinic visits. The incorporation of these “significant others” into the MEF clinic routine seemed necessary, especially for the youngest adolescent patients, who often wanted their mothers by their side. Family members are also crucial to women’s egg disposition decisions. In this study, for example, some women wanted to donate or “will” their eggs to their sisters and clearly indicated this on medical consent forms. Thus, clinics need to provide careful guidelines about egg disposition, including following a patient’s death.

We must acknowledge that, as the first qualitative investigation of women’s experiences of MEF, there are some limitations. The overall number of participants recruited was relatively small (45), with more than three times as many cancer patients (35) as those with other medical indications (10). Furthermore, women in both countries were recruited from a relatively small number of cities and states, limiting the generalizability of the findings. In addition, because this was a binational study, coordinated between researchers and clinics in the USA and Israel, the women who participated were recruited somewhat differently between the two countries, and interviewed by different medical anthropologists in two different languages. These sources of potential bias could not be eliminated because of logistical and funding constraints, but they must be acknowledged in our assessment of the comparison. Finally, our study only addressed the experiences of those who had succeeded in obtaining MEF and were willing to be interviewed.

Having said this, our study offers a valuable lens into the needs for patient-centered MEF approaches, whether MEF is being offered in a nation’s public or private healthcare system. We predict that more and more women around the world will be referred for MEF over time, as has been suggested in recent global assessments [32–34]. Thus, it is very important to examine the experiences of this first generation of MEF users. As seen in this study, women who completed MEF were extremely grateful for the technology’s existence. They considered themselves to be the “lucky ones” who were able to complete at least one MEF cycle. Furthermore, they articulated aspects of patient-centered care that were meaningful to them, and made subtle suggestions for changes that would improve the quality of MEF care overall. As such, women themselves can offer useful guidance in promoting a particular brand of fertility preservation—namely, patient-centered MEF—as has been outlined in Table 2. We urge IVF clinicians to make use of this knowledge and framework in

offering truly patient-centered fertility preservation to patients, who are facing fertility-threatening, and often life-threatening, medical crises.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committees and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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