Ovarian tissue cryopreservation (OTC) in prepubertal girls and young women: an analysis of parents' and patients' decision-making

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Abstract

Purpose The purpose of this study was to explore the decision-making influences, perceived level of control over decision-making, and mood states of parents and patients who were offered OTC prior to gonadotoxic therapy.

Methods Parents and patients, at least 12 years old, who required gonadotoxic therapy and were offered OTC prior to therapy, were asked to complete questionnaires. Two validated instruments were also used: the Decision-Making Control Instrument (DMCI) and the Profile of Mood States (POMS). The factors that influenced decision-making were compared using Student's *t* test, and the scores of DMCI and POMS were compared using the Mann-Whitney test.

Results Thirty-six parents and 16 patients who elected ovarian tissue cryopreservation (OTC) completed questionnaires. Five parents who declined OTC also completed questionnaires. Accepters thought OTC was a good idea and that, in the future, science would enable cryopreserved ovarian tissue to be used to restore fertility (100% parents, 93.8% patients). Among accepters, the desire for genetically related children and prevention of the stress of infertility drove parents' and patients' decisions (90.9 and 100%, respectively). The desire to prevent the stress of infertility was important to parents, but patients were less likely to report that a desire to prevent the stress of infertility factored into their decision-making (66.7 vs. 50.0%; $p < 0.001$). All respondents felt in control of their decision and displayed low levels of mood disturbance.

Conclusions Though the decision to undergo experimental OTC is difficult and often urgent, this study suggests that families feel in control of their decision-making and report little emotional disturbance.

Keywords Oncofertility · Fertility preservation · Ovarian tissue cryopreservation · Prepubertal · Decision-making

Introduction

Advances in the early detection of cancer and curative therapies have led to an overall increase in the number of cancer survivors in the USA [1]. The overall incidence of cancer in children and adolescents has increased slightly by 0.6% per year since 1975 and approximately 10,270 new cancer cases

will be diagnosed among children 0–14 years old in the USA in 2017. Despite an increasing incidence, the 5-year relative survival for children and adolescents is 83% depending on certain characteristics [2]. By the end of 2016, there were an estimated 708,650 cancer survivors under the age of 40 living in the USA, of these, 33,130 were females 0–14 years, 23,570 were females 15–19 years, 96,760 were females 20–29 years, and 242,620 were females between 30 and 39 years of age [1]. As a result, care for young patients with cancer must now focus on long-term health outcomes and issues surrounding quality of life, including reproduction. One unfortunate consequence of multimodal cancer treatments, particularly alkylating agents, radiation therapy, and stem cell conditioning regimens, is loss of ovarian function leading to infertility. The ovary is sensitive to the adverse effects of cancer treatment because ovaries contain a finite number of germ cells at birth that once lost are not regained [3]. Fertility preservation prior to undergoing gonadotoxic cancer treatment is therefore an important consideration for patients and their providers [4].

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Embryo cryopreservation and oocyte cryopreservation are the main options for fertility preservation in adult females, but these treatments require time for hormonal stimulation and oocyte retrieval and are not options for prepubertal females or those requiring imminent treatment [5]. Expanding the fertility preservation options available to both adult and pediatric patients in imminent need of lifesaving, but gonadotoxic therapy is therefore of great interest. Ovarian tissue cryopreservation (OTC) requires laparoscopy to obtain the tissue, but eliminates the need for hormonal stimulation or a sperm source and is the only method of fertility preservation available to prepubertal females at high risk of premature ovarian insufficiency [6, 7]. Though OTC is currently considered an experimental technique, over 130 births have been reported after OTC and autologous transplantation worldwide [8–15]. The success of OTC along with low rates of complication has led many experts to contend that the experimental label should now be removed [16, 17].

The decision-making process surrounding experimental fertility preservation technology in the pediatric population has not been well studied, and the studies that exist are in boys [18, 19]. Young female patients facing imminent gonadotoxic therapy are at risk of infertility and should be offered experimental OTC. However, OTC requires a laparoscopic procedure in which a portion of an ovary or a whole ovary is removed and this may deter some parents. No data exists on the decision-making process of parents and/or patients when faced with the decision about whether to undergo OTC in the face of gonadotoxic therapy. The purpose of the current study was, therefore, to explore the decision-making influences, perceived level of control over decision-making, and mood states of parents and/or patients who were offered OTC for fertility preservation prior to gonadotoxic therapy.

Methods

Institutional Review Board (IRB) approval for an experimental ovarian tissue cryopreservation study was obtained at the Hospital of the University of Pennsylvania (HUP) in April 2007 and at the Children's Hospital of Philadelphia (CHOP) in May 2009. The experimental protocol and criteria for inclusion and exclusion have been previously described [20]. IRB approval was also obtained for the administration of a questionnaire to assess decision-making factors that determined whether they consented to undergo OTC. At HUP, patients were considered eligible for OTC if they were generally healthy females between 11 and 42 years of age with both ovaries and in need of imminent medical or surgical treatment that would likely result in permanent loss of subsequent ovarian function. Patients were excluded if they were at high risk for surgical complications, had laboratory evidence of ovarian insufficiency with serum FSH levels above 20 mIU/mL in the

absence of recent administration of chemotherapy, BRCA gene mutation, suspected ovarian malignancy, and/or the presence of large ovarian masses. Eligible patients were approached by a member of the OTC study team, who was not directly involved in their clinical care, educated about OTC, and offered oophorectomy or ovarian biopsy in consultation with a reproductive endocrinologist. Patient education included a discussion that while there have been live births from ovarian tissue, numbers are small and there are no guarantees that the tissue would be useful in the future. The details of the process of OTC and how tissue may be used in the future was also described to patients. Furthermore, patients were informed that the use of the tissue was outside the scope of this study and that use of the tissue will be based on the knowledge at the time the patient desires to use it. At CHOP, IRB approval was initially restricted to females at least 10 years of age and later expanded to include females at least 1 year of age and was limited to ovarian biopsy only. Eligible pediatric patients were also limited to those at highest risk for long-term ovarian dysfunction based on planned cumulative dose of alkylating agents, radiation plan, or stem cell transplant conditioning. Previous therapy was not an exclusion criterion. At CHOP, parents were educated as described and prior to signing the consent form, needed to provide written confirmation that they understood that the use of OTC for fertility preservation was experimental, that they understood that only their daughter could make decisions about her cryopreserved ovarian tissue or have access to it in the future, and that there is no guarantee that the tissue would be useful in the future. Patients who opted to undergo OTC were taken for surgery once their hematologic parameters had stabilized after their last chemotherapy dose or prior to chemotherapy or stem cell transplantation (SCT). To avoid an additional exposure to anesthesia, the OTC procedure took place at the time of another procedure, such as central line placement, or at the time of a marrow or tumor resection. The ovarian surgery, cryopreservation, and storage were performed at no cost to the participants. At the time of data collection for this study, 80 OTC cases had been performed: 27 at HUP and 53 at CHOP.

Parents as well as patients who were at least 12 years old and who desired to participate in the study were asked to consent for the completion of a questionnaire within one month of undergoing the OTC procedure. Parents and patients who declined OTC were also approached within a month of initial contact to consent to the completion of a questionnaire. Paper questionnaires were distributed either in person or by mail from May 2012 to October 2016. The questionnaires were designed to characterize the demographics of the cohort and to explore factors that were considered in the decision-making process in those who underwent OTC and those who declined (Online Resources 1 and 2). The questionnaire contained multiple sections as follows: Part I consisted of 15 items focused on demographic data including current age of

patient, religion, marital status, race, ethnicity, occupation, and educational level of parent or patient completing the questionnaire, household income, previous knowledge of fertility technologies, previous participation in clinical research, timing of approach regarding participation in this study, and who made the decision to participate or not; Part II Attitudes/Beliefs with six items scored on a 4-point Likert scale from “strongly agree” to “strongly disagree”; Part III Child’s Role with four items, scored on a 4-point Likert scale from “strongly agree” to “strongly disagree”; Part IV Decision Influences/Considerations with 17 items scored on a 4-point Likert scale from “A lot” to “Not at All”; Part V, Attitudes/Beliefs and VI focused on Study Improvement for those who actually have the ovarian tissue biopsy, consisted eight items combining both 4-point Likert scale from “strongly agree” to “strongly disagree” as well as Yes/No questions with opportunity for free text. The questions were similar to those used in a prior study of testicular tissue cryopreservation [18]. Questionnaires assessed the influence of the following factors on decision-making: religion, family opinion, desire for genetic preservation, concern for psychological distress from infertility diagnosis or treatment, desire to benefit society or science, desire to preserve their bloodline, ethical/moral objections, financial considerations, limited time to make the decision, lack of knowledge about the procedure, fear the procedure may complicate treatment or delay therapy, risks of the procedure, procedure being too futuristic or experimental, fear of tissue damage, potential disputes over the tissue, and concerns about tissue disposition. Questionnaires were not administered to patients who underwent OTC prior to the addition of the survey to the study. Otherwise, worsening illness, death, language barrier, and psychosocial reasons precluded the distribution of the survey to four other patients who underwent OTC.

Two validated instruments were also used: the Decision-Making Control Instrument (DMCI) as a measure of the strength of control in decision-making and the Profile of Mood States (POMS) to describe mood states in participants who chose to cryopreserve ovarian tissue [18, 21, 22]. The DMCI is a nine-item questionnaire that measures self-control, absence of control, and others’ control. All nine items are rated on a 6-point Likert scale from “strongly disagree” to “strongly agree” and scored accordingly. The sum of all nine items results in the total score (Online Resource 3). The higher the DMCI score, the greater the perceived level of control over the decision. The POMS is a 30-item questionnaire, validated in adolescents and adults, with words describing common emotions and measures six different dimensions of mood: tension-anxiety, depression, anger-hostility, vigor-activity, fatigue, and confusion. Items are scored on a 5-point Likert scale from “not at all” to “extremely” (Online Resource 4). The six dimensions of mood are scored separately and a higher score in a given mood dimension indicates a greater level of

disturbance in that particular mood state. The total score is the sum of all the mood states and determines overall level of mood disturbance [23].

Demographic characteristics were summarized using descriptive statistics. The factors that influenced decision-making were compared using Student’s *t* test. The total score of the DMCI and POMS were compared between parents and patients who filled out the questionnaires using the Mann-Whitney test. Fisher’s exact test was used to analyze categorical data.

Results

Twenty-seven eligible patients from HUP and 53 from CHOP underwent OTC. From CHOP, the questionnaires from 38 parents and/or patients who underwent OTC were available for analysis. At HUP, where all patients seen were post-pubertal, fewer patients underwent OTC as the options of oocyte and/or embryo cryopreservation were the preferred methods of fertility preservation. Six patients who underwent OTC at HUP completed the study questionnaire. Five parents who declined OTC also completed questionnaires and were included in this analysis. Only one patient who declined treatment completed a questionnaire and was excluded from the analysis.

In total, 52 questionnaires were collected on 44 patients who underwent OTC. This included 36 parents or guardians of minors who consented to OTC for their daughters, and an additional 7 patients, 18 years or older, who also consented to the procedure themselves. All 36 parents or guardians filled out a questionnaire, and 16 patients who were at least 12 years of age filled out a questionnaire. Of the 16 patients who completed a questionnaire, 8 of their parents also completed a questionnaire. The overall response rate was 93.6%. Demographic characteristics of the parents who desired to pursue OTC for their daughters are shown in Table 1. Parents who elected OTC for their daughters reported being mostly Caucasian, well-educated, married, and Christian. The most common diagnoses for which patients underwent OTC were relapsing leukemia (38.6%) and refractory lymphoma (20.5%). The majority of patients who underwent OTC were approached for the study more than one week after their diagnosis as patients were only approached if their therapy was thought to be high risk for gonadotoxicity and the therapy after initial diagnosis in many cases may not be as high risk. Thus, many patients were approached in the setting of recurrent or relapsing disease requiring SCT. Side effects were reported by 32.4% of parents and 30.8% of patients surveyed. These side effects were largely postoperative pain and bloating after laparoscopy. One parent reported a wound hematoma, and another incisional irritation. There were no other reported postoperative complications. Patients who completed

Table 1 Demographic characteristics of parents who opted for their daughter to undergo OTC and who completed questionnaires

Demographic characteristics	<i>n</i> = 33
Parental age, mean $\pm$ SD (range), years	42.1 $\pm$ 6.5 (28–56)
Age of patients, mean $\pm$ SD (range), years	9.2 $\pm$ 4.2 (3–17)
Race, <i>n</i> (%)	
Caucasian	27 (77.1)
African American	7 (20.0)
Asian	1 (2.9)
Ethnicity, <i>n</i> (%)	
Hispanic	3 (8.3)
Non-Hispanic	33 (91.7)
Religion, <i>n</i> (%)	
Christian	28 (80.0)
Jewish	4 (11.4)
Other	3 (9.1)
Relationship status, <i>n</i> (%)	
Single, never married	4 (11.1)
Single, divorced	5 (13.9)
Married	26 (72.2)
Separated	1 (2.8)
Education level, <i>n</i> (%)	
Graduated HS	2 (5.6)
Some college or technical school after HS	9 (25.0)
Graduated college	11 (30.6)
Some postgraduate education	2 (5.6)
Graduate degree obtained	12 (33.3)
Annual income, <i>n</i> (%)	
Less than \$60,000	12 (36.4)
Greater than or equal to \$60,000	21 (63.6)
When approached about study, <i>n</i> (%)	
Less than 1 week after diagnosis	2 (6.7)
More than 1 week after diagnosis ^a	28 (93.3)
Patient diagnoses, <i>n</i> (%)	
Leukemias ^b	17 (38.6)
Lymphomas ^b	9 (20.5)
Sarcomas	7 (15.9)
Solid tumors ^b	7 (15.9)
Non-cancer hematologic disease ^b	4 (9.1)

^a Most patients were approached after disease relapse requiring stem cell transplantation

^b All leukemia patients, patients with non-cancer hematologic disease, eight lymphoma patients, and two patients with solid tumors (neuroblastoma) were planning to undergo stem cell transplantation

questionnaires had a mean age of 18.6 ± 5.0 , were mostly Caucasian (75.0%), and Christian (78.6%).

Questionnaires explored the attitudes and beliefs of patients and parents regarding cancer treatment and OTC (Fig. 1). Most parents (66.7%) and patients (68.8%) were aware that cancer treatment could affect fertility. In terms of options for

fertility preservation, both parents and patients were largely unaware of the option of OTC prior to being approached about the study, with only 30.3% of parents and 6.3% of patients reporting previous knowledge of this fertility preservation procedure. However, patients and parents who opted for OTC thought it was a good idea (100% of parents and patients) and that in the future, science would enable the use of cryopreserved ovarian tissue to restore fertility (parents 100% vs. patients 93.8%). Both parents and patients who accepted the procedure (100% of patients and parents) believed that they made the right decision by undergoing OTC and only few reported that they would regret having done the procedure if the tissue was not usable in the future (3% parents and 12.5% patients). All parents who declined OTC thought that it was a somewhat good idea and desired for their daughters to have genetically related children, but risks of the biopsy and desire not to complicate treatment drove their decisions to decline.

Parents and patients were asked to indicate the people they included in the decision-making process. Parents and patients alike enlisted the help of healthcare workers, specifically physician(s), nurses, or social workers, to make their decision, and infrequently involved other family members or religious advisors. The decision-making factors for parents compared to patients are shown in Fig. 2. The desire for genetically related children drove the decision for both parents and patients (90.9 vs. 100%; $p = 0.37$). Parents were more likely to report that the desire to prevent the psychological stress associated with infertility factored into their decision-making (66.7 vs. 50.0%; $p < 0.001$). Other factors that weighed in the decision-making process included the potential benefit to society (parents 72.7% vs. patients 53.3%; $p = 0.31$), family opinion (parents 42.4% vs. patients 62.5%; $p = 0.11$), the desire to not complicate treatment (parents 30.3% vs. patients 20.0%; $p = 0.24$), risks of the procedure (parents 28.1% vs. patients 6.7%; $p = 0.22$), desire to preserve bloodline (parents 27.3% vs. patients 53.3%; $p = 0.11$), limited time to decide (parents 24.2% vs. patients 46.7%; $p < 0.05$), religious beliefs (parents 18.2% vs. 6.3%; $p = 0.59$), moral objections to assisted reproductive technology (parents 15.2% vs. 0% patients; $p = 0.16$), concern about the risks of damage to ovarian tissue during storage (parents 18.2% vs. patients 14.3%; $p = 0.62$), potential disputes about tissue disposition (parents 12.5% vs. patients 14.3%; $p = 0.62$), the experimental nature of OTC (parents 18.2% vs. patients 20.0%; $p = 0.88$), concern that OTC was too futuristic (parents 9.1% vs. patients 6.7%; $p = 0.70$), lack of knowledge about OTC (parents 9.1% vs. patients 6.7%; $p = 0.55$), or financial implications (parents 7.1% vs. patients 0%; $p = 0.33$). A sub-group analysis of the parent-patient dyads showed no difference between parents and their children in terms of decision-making influences. There was also no difference in decision-making influences between patients ages 12–18 years old and those who were 18 years and older.

Fig. 1 Bar graph showing the distribution of attitudes and beliefs of both parents and patients who accepted the OTC procedure to preserve fertility

High DMCI scores indicated that both parents and patients who chose to undergo oocyte tissue cryopreservation felt in control of their decision, though parents reported higher mean DMCI scores compared to patients (mean parent DMCI 45.8 ± 3.4 , mean patient DMCI 43.8 ± 4.0 ; $p = 0.03$) (Table 2). Of the three items of the DMCI, a significant difference was seen in the absence of control domain (parents 16.2 ± 2.4 vs. patients 14.3 ± 2.9 ; $p = 0.01$). There was no significant

difference between parent and patient DMCI in the domains of self-control (parents 17.5 ± 1.1 vs. patients 12.7 ± 0.7 ; $p = 0.72$) and others' control (parents 12.2 ± 1.3 , patients 16.8 ± 1.8 ; $p = 0.15$).

Emotional disturbance was also measured in parents and patients by the POMS questionnaire (Table 3). There was no difference between parents and patients in terms of overall level of emotional disturbance (parents 11.2 ± 14.3 vs. patients

Fig. 2 Bar graph showing the decision-making influences of parents and patients who accepted the OTC procedure to preserve fertility

Table 2 Scores of Decision-Making Control Instrument (DMCI)

DMCI variable	Parents (mean $\pm$ SD)	Patients (mean $\pm$ SD)
Self-control	17.5 $\pm$ 1.1	12.7 $\pm$ 0.7
Absence of control	16.2 $\pm$ 2.4*	14.4 $\pm$ 3.0*
Others' control	12.2 $\pm$ 1.3	16.8 $\pm$ 1.8
DCMI total score	45.8 $\pm$ 3.4*	43.8 $\pm$ 4.0*

* $p < 0.05$

19.5 $\pm$ 15.3; $p = 0.17$) or in the level of tension-anxiety (parents 4.3 $\pm$ 4.1 vs. patients 5.8 $\pm$ 3.9; $p = 0.50$), depression (parents 2.7 $\pm$ 3.3 vs. patients 3.6 $\pm$ 3.8; $p = 0.65$), anger-hostility (parents 0.97 $\pm$ 2.0 vs. patients 2.2 $\pm$ 3.5; $p = 0.20$), vigor (parents 4.1 $\pm$ 5.0 vs. patients 2.2 $\pm$ 2.8; $p = 0.12$), fatigue (parents 3.8 $\pm$ 4.5 vs. patients 4.6 $\pm$ 4.0; $p = 0.77$), and confusion (parents 4.4 $\pm$ 2.5 vs. patients 5.4 $\pm$ 2.3; $p = 0.10$).

Discussion

Infertility is an unfortunate consequence of many lifesaving cancer therapies in children and young adults. As patients survive well into their reproductive years and beyond, it is critical to explore fertility preservation options. While embryo cryopreservation and oocyte cryopreservation are established treatments for fertility preservation in post-pubertal females, these options are not available to prepubertal females and may not be an option for females needing imminent cytotoxic treatment. Ovarian tissue cryopreservation, though considered to be an experimental procedure, is the only option for these patients. Few studies have been published on the decision-making process surrounding experimental fertility preservation technology in the pediatric population, and the studies that exist are in testicular tissue cryopreservation in boys [18, 19]. In this study, we report the attitudes, beliefs, and decision-making factors that are important to the parents and female patients who made the decision to undergo OTC.

This study showed that patients' and parents' decisions were largely influenced by the desire for genetically related children in the future. The desire to have genetically related children (86.7%) and to prevent the psychological distress of

infertility (66.7%) largely drove parents' decisions. Similarly, in a prior study of testicular tissue cryopreservation in prepubertal male patients prior to gonadotoxic therapy, parents who accepted testicular tissue cryopreservation for their sons indicated that their decisions were largely influenced by the hope that their child could have genetically related children in the future (85.7%) and a desire to prevent the psychological stress of infertility if rendered infertile by his treatment (60%) [18]. The similarity in the decision-making influences between the prior testicular tissue cryopreservation study and the current OTC study indicates the high value that many parents facing this decision place on preserving their child's ability to produce genetically related offspring and prevent future emotional issues surrounding infertility. Patient questionnaires were not available from the testicular tissue cryopreservation study, but patients in the current OTC study were also largely driven by the desire for genetically related children (100%), while only 50% of patients considered the psychological distress of infertility in their decision. This may reflect the fact that children are less likely than adults to understand or have experience with infertility.

Study respondents were hopeful that in the future, successful pregnancy could be attained using cryopreserved ovarian tissue. Recent reports of over 130 live births from ovarian tissue cryopreservation of the post-pubertal ovary validate patients' optimism in their decision to undergo OTC [8–15]. However, there is relatively little data on birth from the autotransplantation of prepubertal ovarian tissue, though prepubertal tissue has been shown to induce puberty after gonadotoxic therapy [24, 25]. In one study, a 27-year-old woman with sickle cell anemia underwent autotransplantation of ovarian tissue that had been cryopreserved when she was 13 years old prior to menarche and prior to hematopoietic stem cell transplantation [26]. Menstruation resumed after autotransplantation and, two years later, she had an unassisted pregnancy and delivered a healthy infant [26]. These reports demonstrate the potential utility of OTC for prepubertal children undergoing gonadotoxic treatment and highlight the need for further research in refining techniques to maximize patient outcomes.

While OTC holds promise, it is considered an experimental procedure at this time and must be conducted as part of a

Table 3 Scores of Profile of Mood States (POMS) in parents and patients

POMS variable	Parents (mean $\pm$ SD)	Patients (mean $\pm$ SD)
Tension-anxiety	4.3 $\pm$ 4.1	5.8 $\pm$ 3.9
Depression	2.7 $\pm$ 3.3	3.6 $\pm$ 3.8
Anger-hostility	0.97 $\pm$ 2.0	2.2 $\pm$ 3.5
Vigor	4.1 $\pm$ 5.0	2.2 $\pm$ 2.8
Fatigue	3.8 $\pm$ 4.5	4.6 $\pm$ 4.0
Confusion	4.4 $\pm$ 2.5	5.4 $\pm$ 2.3
Total mood disturbance	11.2 $\pm$ 14.3	19.5 $\pm$ 15.3

research study with IRB approval [27]. It is particularly important to consider that children offered OTC are a vulnerable population with a limited ability to understand, weigh the risks and benefits, and provide informed consent. The risks, benefits, and alternatives of the procedure should to be explained to the patient's legal representatives and to patients in language they can understand so that representative(s) can provide informed consent with assent of the child, when possible [28]. Consent for OTC is being offered often at a time when parents and patients are often grappling with a new diagnosis and also making important decisions regarding lifesaving medical treatment. Even in this situation, the DMCI data demonstrate that parents and patients felt in control of their decision and were not deterred by the experimental nature of the procedure or the limited time they had to decide.

Data on the attitudes of prepubertal females and their parents toward OTC is lacking in the USA. The strength of this study lies in the fact that we were able to capture the unique attitudes of a cohort of prepubertal females and their parents toward OTC. This study is one of few that investigate decision-making in experimental fertility preservation technologies [18, 19]. The current study has shown that OTC is acceptable to parents of prepubertal children as well as children and young women after puberty. Despite knowing that OTC is an experimental procedure, parents and patients were hopeful that the cryopreserved tissue would enable them to restore fertility in the future if they developed ovarian insufficiency after their gonadotoxic therapy. The study is limited by a small sample size and is therefore not reflective of the general population and limits the generalizability of the conclusions that may be drawn. Finances did not factor greatly in the decision-making for OTC; however, there was no fee for the OTC procedure, which potentially enabled families to decide whether to undergo OTC independent of financial concerns. It is possible that if families have to pay for the procedure as OTC becomes more widely accepted outside of a research setting, finance may become more of a factor in the decision-making process. There were also very few refusers in the study; therefore, the study is inevitably biased toward participants who accepted OTC and conclusions cannot be made regarding the attitudes of families who declined OTC. Another limitation includes the fact that the POMS questionnaire, though validated in adolescents 13 years and older, was administered to participants who were 12 years old or older. In the cohort of adolescents and young adult patients who filled out the POMS questionnaire, only one was under the age of 13. When the analysis of the POMS questionnaire was repeated without the single 12-year-old patient, the results are unchanged. The DMCI has been validated in parents of ill children, but in this study, the DMCI was administered to both parents and patients at least 12 years of age in order to compare responses; the results from patient responses must therefore be interpreted with caution. More research is needed

before OTC is widely adopted outside of a research setting, but we have shown that OTC is acceptable to patients and parents of prepubertal females and young women in whom oocyte cryopreservation or embryo cryopreservation is not an option. Parents and patients feel in control of their decision-making and report little emotional disturbance despite limited time to make their decision.

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Compliance with ethical standards

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

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

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