



Conducting reproductive research during a new childhood cancer diagnosis: ethical considerations and impact on participants

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Abstract

Purpose Research among adults shows benefits and low perceived burden of engaging in behavioral research. However, questions remain regarding the ethics of conducting behavioral research in pediatric populations during sensitive situations, including during a new life-threatening diagnosis or at end-of-life. We examined reactions to participating in a behavioral reproductive research study among male adolescents newly diagnosed with cancer and their parents, as a step towards optimizing fertility preservation utilization in a population where future infertility is common.

Methods Pediatric literature regarding the ethics of behavioral research was reviewed. In our pilot, forty-four participants (19 mothers, 11 fathers, 14 male adolescents newly diagnosed with cancer) from 20 families completed demographic questionnaires and a fertility preservation decision tool developed by the study team. Qualitative interviews exploring the impact of study participation were subsequently conducted. Verbatim transcripts were coded for thematic content using the constant comparison method.

Results Literature review showed positive reactions to research participation among youth/caregivers. In our pilot study, 89% ($n = 17$) of mothers, 64% ($n = 7$) of fathers, and 71% ($n = 10$) of adolescents reported at least one benefit of participating. Eleven percent ($n = 2$) of mothers, 36% ($n = 4$) of fathers, and 29% ($n = 4$) of adolescents said they were not affected; none of the participants reported a negative effect.

Conclusion Consistent with prior literature, our study suggests behavioral reproductive research prior to cancer treatment can offer direct benefits to participants and society, without increasing burden. These findings will inform future interventions to improve long-term psychosocial and reproductive outcomes for youth with cancer.

Keywords Cancer · Fertility · Ethics · Participant burden

Introduction

Each year in the USA, approximately 16,000 youth under the age of 20 are diagnosed with cancer [1]. Medical advances have resulted in improved 5-year survival rates which now exceed 80% [2]. Despite this success, over two-thirds of survivors will experience a chronic health condition or late effects related to cancer treatment [3, 4]. Specifically, more than half of males experience infertility after cancer therapy [3–6]. Previous research has shown infertility can impair psychosexual development, diminish overall well-being, and impact romantic relationships in survivors [7–10].

Sperm banking is an established, effective, and generally noninvasive fertility preservation (FP) option for pubertal males. Despite the long-standing availability of this technology, rates of fertility counseling and sperm banking remain

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strikingly low at many pediatric cancer centers [11–13]. Healthcare providers have raised ethical concerns about initiating fertility-related discussions among youth newly diagnosed with cancer, due to worries about potentially delaying treatment and/or upsetting patients and parents by prioritizing FP over survival/treatment, contributing to this discrepancy [14–16]. Reproductive health research in this setting has also been limited due to ethical concerns about approaching youth and families for behavioral research at sensitive time points such as a new cancer diagnosis [17]. When asked, however, youth have reported that fertility is a priority [18, 19] and that fertility counseling at the time of a new cancer diagnosis actually buffered the emotional impact of cancer by reducing fears and providing hope for the future [20, 21]. Adolescents have also reported a desire to participate in discussions and decisions about FP [22].

An expanding body of literature has thus supported counseling all pubertal males, regardless of age and/or infertility risk [23–25] about sperm banking prior to cancer treatment [25]. However, a recent study showed that only 50% of adolescent males advised to bank sperm actually attempted it, and parents had a significant influence on this decision [26, 27]. In order to develop novel family-centered FP interventions, more research is needed to understand how adolescent males and their parents jointly make FP decisions before cancer treatment. Prior to designing a behavioral study in this area, it is important to ask—*Does the benefit of the research outweigh the potential harms or burden? Would the research only offer benefits to society or is there potential for direct benefit to participants as well?* In this manuscript, we will review salient ethical and logistical considerations in designing mixed method, reproductive research among youth and families at the time of a new childhood cancer diagnosis. We highlight findings from relevant behavioral studies with youth and families at sensitive time points and report the impact of participation in a pilot study examining FP decisions in adolescent males newly diagnosed with cancer.

Barriers to conducting behavioral research in pediatric populations

To date, few studies have examined reproductive health and FP decision-making among adolescent males and their parents in real time as these decisions are made. This gap is largely due to the short time frame between diagnosis and treatment initiation. Following confirmation of a new cancer diagnosis, the oncologist must complete the medical evaluation, review the treatment plan and potential adverse effects, and order many pre-treatment consults, including a fertility consult (at sites where a fertility team is available). The fertility specialist then reviews the risk for infertility and FP options, including logistics and cost with the patient and family, and then coordinates a

FP attempt with the storage facility. The time allotted for these steps is generally 24–48 h and often occurs while the patient is hospitalized. Thus, conducting behavioral reproductive research in this setting is understandably difficult. We have previously described strategies that can facilitate successful recruitment and retention of these families, including strong collaboration with the healthcare team [28].

Beyond the logistical barriers to recruitment, many clinicians, investigators, and Institutional Review Boards (IRBs) have questioned whether it is ethical to approach certain medically ill youth and their parents for behavioral research [29]. Data from adult studies have suggested low perceived burden and high potential for benefit of engaging in behavioral research [30]. However, there are different considerations for youth, who may have unique developmental challenges and thus varying capacity to assent. In a study where injured youth and their parents were asked about their experiences surrounding research participation, both patients and parents had positive reactions, and most saliently felt good about helping others [31]. Another study showed that adolescents felt proud that they could participate in research just to help others; the majority said they would even be willing to undergo extra lab draws or skin biopsies for this purpose [32]. While these findings are generally reassuring, the question remains as to whether positive reactions to research are also seen in more serious situations such as a new diagnosis of a life-threatening medical condition or at the end-of-life.

In a recent study among families of 271 children, 7–21 years of age, undergoing treatment for many different conditions including cancer, neurofibromatosis type 1, sickle cell disease, HIV, primary immune deficiencies, and Li Fraumeni syndrome, investigators assessed whether participation was burdensome and/or beneficial to the youth and their caregivers [17]. The study involved a series of self-report questionnaires, and the visit duration ranged from 20 to 40 min (including informed consent/assent and data collection). Responses on a burden and benefit scale showed that most participants (85% of patients and 95% of caregivers) reported at least some benefit of participation [17]. Furthermore, 83% of patients and 93% of caregivers did not find participation to be burdensome [17]. Of those who reported feeling burdened, 81% of patients and 78% of caregivers still reported benefit from participation [17].

Similarly, perceived burden and benefit were examined among bereaved parents who had participated in research regarding their child's end-of-life experience [33]. Of one hundred seventy-eight bereaved caregivers of children with cancer who initiated the survey, 120 completed the eight burden and benefit items at the end. Half of the participants reported “no burden at all,” and less than 2% reported it was “very”

burdensome. Most (73%) reported some degree of benefit. In another study of bereaved parents, 100% said they were pleased and thankful to have participated in the study > 6 months after the death of their child; they perceived both personal benefits of participation (connecting with their child) and the benefit of helping others [34].

While self-selection is a factor, these findings suggest few adolescents or parents perceive participation in behavioral research as burdensome even at sensitive time points. Furthermore, altruism or the potential to help others is often a perceived benefit. However, reactions to behavioral reproductive research have not yet been examined among youth and parents at the time of a new cancer diagnosis. Thus, as part of a pilot study at a large pediatric cancer center, we assessed the impact of participating in behavioral reproductive research on adolescent males newly diagnosed with cancer and their families.

Methods

Following IRB approval, males (12–25 years old, all offered FP) and their parents were recruited at the time of a new cancer diagnosis (before treatment initiation) just after the fertility consult was completed. Following informed consent/assent, a questionnaire (developed by the study team based on the health belief model and previous literature [19, 35, 36] was administered with the entire visit lasting about 10–15 min. Approximately 1 to 2 months later, families were invited to complete brief questionnaires examining parent-adolescent communication and decision quality regarding FP; one-on-one qualitative interviews were also conducted to explore perspectives on their FP decision (lasting approximately 15–30 min). Twenty-one families have been approached

for the study thus far; 95% have participated in visit 1 and 100% of those have participated in visit 2 [28].

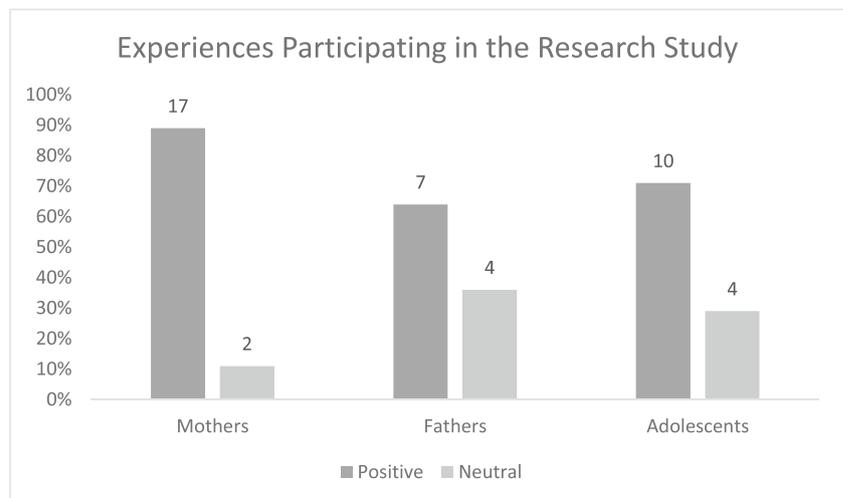
Analysis

During the interview, 44 participants ($n = 19$ mothers, $n = 11$ fathers, $n = 14$ adolescents) were asked how the study questionnaire affected their FP decision, relationships, communication with their family, and how participation in the study affected them and their family overall. Participant interviews were audiotaped, transcribed, and analyzed for thematic content. Two major themes emerged with regard to the impact of study participation/survey completion including a “positive effect/beneficial” and “neither positive nor negative effect.” For the current manuscript, two study team members (KL, TM) quantitatively coded the frequency of each theme. Frequency counts for each interview were independently coded and compared, and any discrepancies were resolved via consensus. Inter-rater reliability was excellent ($\kappa = 0.96$) [37].

Results

The majority of families were Caucasian (93% of adolescents, 95% of mothers, 82% of fathers). The most common diagnosis was lymphoma (43%, $n = 6$), followed by non-central nervous system (CNS) solid tumors (36%, $n = 5$), CNS tumors (14%, $n = 2$), and leukemia (7%, $n = 1$). Eighty-nine percent ($n = 17$) of mothers, 64% ($n = 7$) of fathers, and 71% ($n = 10$) of adolescents reported at least one benefit of participating in the study (see Fig. 1). Overall, 11% ($n = 2$) of mothers, 36% ($n = 4$) of fathers, and 29% ($n = 4$) of adolescents said they

Fig. 1 Experiences participating in the research study



were not affected by participating in the study; none of the participants reported a negative effect (Fig. 1).

Discussion

The diagnosis of childhood cancer is a source of shock and distress for both the affected youth and his or her parents. Although recruitment for clinical therapeutic trials must occur at the time of cancer diagnosis [38], behavioral research is less common and often perceived by IRBs and clinical care teams as overly burdensome [17]. While exercising sensitivity in this setting is paramount, assumptions about how certain aspects of clinical care and research affect the youth and family may be inaccurate. Our review of the recent studies among youth with life-altering conditions and bereaved parents suggest that behavioral research participation is not perceived as burdensome and actually offers some direct benefits to participants [17, 33, 34].

The rapidly expanding field of oncofertility has created new opportunities for future parenthood and is improving quality of life for many survivors [39]. It is now our responsibility to conduct ethically sound behavioral and medical research to examine the efficacy of new FP technologies and optimize the utilization of established FP methods. Although our sample was small and surveys were purposefully brief, findings from our pilot study suggest that behavioral reproductive research can offer direct benefits to participants and to the larger population, without increasing burden even at the time of a new cancer diagnosis. Future interventions informed by these findings will have high potential to improve long-term psychosocial and reproductive outcomes for adolescent males with cancer.

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