Original Article

Perceptions of Risk of Infertility Among Male Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study

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BACKGROUND: The objective of the current study was to characterize and identify factors associated with perceptions of risk of infertility among adult male survivors of childhood cancer. **METHODS:** A total of 1233 adult male survivors from the Childhood Cancer Survivor Study who were without a history of disease recurrence or subsequent malignancy reported their perceptions of their risk of infertility compared with men never diagnosed with cancer. Survivors were a median age of 37.8 years (range, 22.0-58.7 years) and were 28.4 years from their diagnosis (range, 21.4-39.2 years). Multivariable logistic regression evaluated factors associated with perceptions of risk. **RESULTS:** Overall, 35.9% of the survivors (443 of 1233 survivors) reported perceptions of their risk of infertility that were discordant with their actual risk based on previous cancer treatment exposures. Discordant perceptions were equally common among men exposed to gonadotoxic therapies (36.3%; 311 of 857 men) and those with no history of gonadotoxic exposure (35.1%; 132 of 376 men). Survivors who fathered children (odds ratio [OR], 4.14; 95% confidence interval [95% CI], 2.74-6.24), had no survivor-focused health care (OR, 3.07; 95% CI, 1.57-5.99), were nonwhite (OR, 2.28; 95% CI, 1.10-4.75), and were of lower income were more likely to report no increased risk of infertility after gonadotoxic treatment. Perceptions of increased risk of infertility among men with no history of gonadotoxic treatment were predicted by never having fathered a child (OR, 1.88; 95% CI, 1.17-3.03), recent participation in survivor-focused health care (OR, 2.11; 95% CI, 1.01-4.42), and higher educational achievement. **CONCLUSIONS:** Many male survivors of childhood cancer are unaware of how their cancer treatments could impact their reproductive health, underscoring the need for all patients to receive education regarding their risk of infertility throughout the continuum of cancer care. ***Cancer*** **2018;124:2447-55**.

KEYWORDS: childhood cancer, health knowledge, infertility, survivors.

INTRODUCTION

The adverse effects of childhood cancer treatment on male reproductive health have been well documented,[1-3] and clinical practice guidelines have been established to assist providers in the identification and education of patients who are at increased risk of infertility based on cancer treatment exposures.[4,5] Despite these advances, to the best of our knowledge little research has been conducted evaluating survivors' knowledge of their risk of infertility. The available literature has suggested that survivors often are worried and/or uncertain about their fertility status,[6,7] and are incorrect in their estimates of their risk of infertility based on treatment history.[8-10] Furthermore, many adult survivors are unable to recall any discussion of reproductive health risks with their health care providers or parents,[6,11] and even when information was recalled, survivors' beliefs regarding their risk of infertility did not always relate to the information presented.[12] These findings indicate that many survivors do not possess accurate knowledge of their risks of infertility; however, to our knowledge, it remains unknown what factors predict perceptions of risk of infertility among adult male survivors of childhood cancer.

The objective of the current investigation was to address this gap in the literature by determining associations between discordant perceptions of risk of infertility and sociodemographic characteristics and medical and treatment data among a large sample of adult male survivors of childhood cancer. Previous research has indicated that lower educational attainment predicts a lower awareness of personal risks of late effects among survivors, whereas engagement in education

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during long-term follow-up (LTFU) care visits can increase survivors' knowledge of their risk of late effects.[10,13] Younger age at the time of diagnosis has been found to be significantly associated with survivors' poorer specific knowledge of their chemotherapy and/or radiotherapy histories.[14-16] Earlier work from the Childhood Cancer Survivor Study (CCSS) demonstrated that approximately 37% of adult male survivors who met the definition for infertility also reported fathering at least 1 child, thus indicating that fertility and infertility are not dichotomous experiences in survivorship.[2] In terms of our hypotheses, we assumed that survivors' personal history of fathering children would significantly impact their perceptions of their risk of infertility and sought to explore these relationships. After controlling for this important factor, we hypothesized that discordant perceptions of infertility risk due to cancer therapy would be associated with younger age at the time of diagnosis, lower educational achievement, and a lack of participation in survivor care. In addition, we hypothesized that perception of infertility risk would be significantly related to specific gonadotoxic treatment exposures and/or treatment for low testosterone or erectile dysfunction.

MATERIALS AND METHODS

Childhood Cancer Survivor Study

Participants were recruited from the CCSS cohort of ≥5-year survivors of childhood cancer from 26 institutions in the United States and Canada. Details regarding the CCSS study design and cohort have been published previously.[17,18] Data regarding participants' self-reported demographic characteristics and history of fathering pregnancies were obtained from the CCSS baseline and follow-up questionnaires. For the purposes of the current study, participants who reported having fathered at least 1 pregnancy resulting in a live birth were classified as having fathered a child. Data regarding participants' self-reported problems with learning or memory (eg, "Have you ever been told by a doctor or other health care professional that you have, or have had, problems with learning or memory?") and participation in LTFU care (eg, "When was your most recent routine check-up where a doctor examined you and did tests to see if you had any health problems from your cancer or your cancer treatment?") were obtained from the CCSS follow-up questionnaires.

Men's Health Questionnaire

The Men's Health Questionnaire (MHQ) was developed to obtain information regarding male reproductive health and perceptions of the impact of childhood cancer on male health. Male survivors who were aged ≥18 years when they participated in the CCSS' Follow-Up 4 questionnaire (2007-2008; 4000 participants) were asked to consider completing a separate survey to "better understand fertility and sexual function in males." Overall, a total of 2961 male survivors agreed to receive the MHQ (see Supporting Fig. 1). As part of the MHQ, participants rated their risk of infertility as compared with "other men (their) age never diagnosed with cancer or a disease like cancer." Participants were given a 5-item response including the items: "much less risk," "slightly less risk," "about the same risk," "slightly more risk," or "much more risk." For analysis, perception of increased risk was defined as a response of "slightly more" or "much more" risk. Additional self-reported data collected included dichotomous "yes" or "no" responses to history of depression, spinal cord injury, prostate disease, testosterone treatment, and treatment for erectile dysfunction. The complete MHQ can be found at: https://ccss.stjude.org/content/dam/en_US/shared/ccss/documents/survey/survey-mens-health-2007.pdf.

Medical Record Review

Information regarding chemotherapy exposures, radiotherapy, and surgeries were abstracted from the participants' original medical records. Estimated organ-absorbed and tissue-absorbed doses of radiation were obtained using methods previously reported.[18,19] The Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancers (version 3.0) were used to categorize participants' risk of infertility.[20] Participants were classified as being at an increased risk of infertility if they received any of the following: alkylating agents or heavy metals, direct radiation to the testes or pelvis, ≥50 centigrays of scatter radiation to the testes from other fields, >40 grays (Gy) of cranial radiation, orchiectomy, spinal cord neurosurgery, pelvic surgery, and/or cystectomy.

Statistical Analyses

Participants with a history of disease recurrence or subsequent malignancy (269 participants) were excluded because treatment data for these events were unavailable and may have included gonadotoxic therapy. Participants who did not rate their perception of risk of infertility on the MHQ (31 participants) or who were missing treatment data (89 participants) also were excluded. Participant characteristics and outcome variables were summarized with descriptive statistics. Logistic regression was used to evaluate factors associated with discordance between survivors' perceptions of their risk of infertility and their actual risk based on their gonadotoxic treatment exposure status. For men with a history of gonadotoxic treatment

TABLE 1. Demographic and Treatment Characteristics for Adult Male Survivors of Childhood Cancer (N = 1233)[a]

Characteristic		No.	%
Age at primary cancer diagnosis, y	≤4	416	33.7
	5-9	277	22.5
	10-14	293	23.8
	15-20	247	20.0
Age at Men's Health Questionnaire, y	20-29	214	17.4
	30-39	530	43.0
	40-49	436	35.4
	50-59	53	4.3
Race/ethnicity	White, non-Hispanic	1099	93.9
	Black, non-Hispanic	23	2.0
	Hispanic	34	2.9
	Other	15	1.3
Diagnosis type	Leukemia	383	31.1
	CNS tumor	107	8.7
	Hodgkin lymphoma	187	15.2
	Non-Hodgkin lymphoma	154	12.5
	Wilms tumor	105	8.5
	Neuroblastoma	66	5.4
	Soft tissue sarcoma	116	9.4
	Bone cancer	115	9.3
Gonadotoxic treatment exposure[b]	Yes	857	69.5
	No	376	30.5
History of fathering children	Yes	499	40.5
	No	734	59.5
Educational achievement	Did not attend college	172	13.9
	Some college	281	22.8
	College graduate	521	42.3
	Postgraduate level	259	21.0
Personal income	<$20,000	171	14.4
	$20,000-$39,999	277	23.4
	$40,000-$59,999	266	22.5
	$60,000-$79,999	177	14.9
	$80,000-$99,999	94	7.9
	>$100,000	199	16.8
Most recent participation in survivor-focused health care	<3 y	581	52.4
	≥3 y	407	36.7
	Never	121	10.9
Problems with learning or memory	Yes	149	12.3
	No	1062	87.7
History of depression	Yes	165	13.6
	No	1044	86.4
History of spinal injury	Yes	61	5.2
	No	1117	94.8
History of prostate disease	Yes	23	1.9
	No	1157	98.1
History of testosterone treatment	Yes	83	6.9
	No	1113	93.1
History of erectile dysfunction treatment	Yes	64	5.2
	No	1163	94.8

Abbreviation: CNS, central nervous system.
[a] Percentages were provided for those patients with known demographic or treatment status.
[b] Exposure to alkylators or heavy metals, direct radiation to the testes or pelvis, ≥50 centigrays of absorbed radiation to the testes, orchiectomy, spinal cord neurosurgery, pelvic surgery, cystectomy, and/or >40 grays of cranial radiation.

exposure, factors associated with their report of being "not at increased risk" for infertility at the $P<.10$ level on univariable analysis were assessed in multivariable models. The final multivariable model included treatment exposure factors plus demographic and LTFU characteristics that demonstrated statistically significant associations

TABLE 2. Perception of Risk of Infertility by Gonadotoxic Therapeutic Exposure Status and History of Fathering Children

Total Population (N = 1233)		
Gonadotoxic Cancer Therapy Exposure Status		
Exposed (n = 857)	Not Exposed (n = 376)	Overall Perception of Risk
Self-identifies as "not at increased risk" of infertility[a] 311 (36.3%)	Self-identifies as "at increased risk" of infertility[a] 132 (35.1%)	Perception of risk was discordant with exposure 443 (35.9%)
Self-identifies as "at increased risk" of infertility[a] 546 (63.7%)	Self-identifies as "not at increased risk" of infertility[a] 244 (64.9%)	Perception of risk was concordant with exposure 790 (64.1%)
Men With No History of Fathering Children (N = 734)		
Gonadotoxic Cancer Therapy Exposure Status		
Exposed (n = 523)	Not Exposed (n = 211)	Overall Perception of Risk
Self-identifies as "not at increased risk" of infertility[a] 141 (27.0%)	Self-identifies as "at increased risk" of infertility[a] 87 (41.2%)	Perception of risk was discordant with exposure 228 (31.1%)
Self-identifies as "at increased risk" of infertility[a] 382 (73.0%)	Self-identifies as "not at increased risk" of infertility[a] 124 (58.8%)	Perception of risk was concordant with exposure 506 (68.9%)
Men With a History of Fathering Children (N = 499)		
Gonadotoxic Cancer Therapy Exposure Status		
Exposed (n = 334)	Not Exposed (n = 165)	Overall Perception of Risk
Self-identifies as "not at increased risk" of infertility[a] 170 (50.9%)	Self-identifies as "at increased risk" of infertility[a] 45 (27.3%)	Perception of risk was discordant with exposure 215 (43.1%)
Self-identifies as "at increased risk" of infertility[a] 164 (49.1%)	Self-identifies as "not at increased risk" of infertility[a] 120 (72.7%)	Perception of risk was concordant with exposure 284 (56.9%)

[a] Compared with men of the same age who have not been diagnosed with cancer.

with the outcome or whose omission would impact other estimates from the model by >10%. A separate analysis was conducted among male survivors who were not exposed to cancer therapy that conferred a risk of infertility yet perceived themselves to be at an elevated risk of infertility. A survivor's history of fathering ≥1 children was included in both multivariable models to allow for the evaluation of the relationships between infertility risk perception and characteristics of interest while controlling for fatherhood status as a potential confounding factor. *P* values <.05 were considered statistically significant.

RESULTS

Participants and Nonparticipants

The MHQ was completed and returned by 1622 survivors (55.1% response rate) (see Supporting Fig. 1). Demographics and treatment characteristics for participants and nonparticipants in these analyses are presented in Table 1 and Supporting Table 1. Participants were slightly older and more likely to be white, to have been married or lived as married, and to report higher educational achievement compared with nonparticipants. Rates of participation in LTFU care were similar between participants and nonparticipants. At the time of survey completion, survivors were a median of 37.8 years of age (range, 22.0-58.7 years) and 28.4 years from their diagnosis (range, 21.4-39.2 years). A large majority of participants (80.5%) previously were exposed to potentially gonadotoxic therapies, and 40.1% reported a history of fathering children.

Survivors' Perceptions of Risk of Infertility

Overall, 35.9% of survivors (443 of 1233 survivors) reported perceptions of their risk of infertility that were discordant with their previous cancer treatment exposures

TABLE 3. Factors Associated With Discordant Perceptions of Risk of Infertility Among Survivors Exposed to Gonadotoxic Therapy

Factors	Categories	Adjusted OR (95% CI)	*P*
Age at primary cancer diagnosis, y	≤4	1.00 (reference)	-
	5-9	0.91 (0.53-1.57)	.73
	10-14	0.80 (0.47-1.37)	.42
	15-21	1.20 (0.70-2.07)	.51
Race/ethnicity	White non-Hispanic	1.00 (reference)	-
	Other	2.28 (1.10-4.75)	.03
History of fathering children	Yes	4.14 (2.74-6.24)	<.001
	No	1.00 (reference)	-
Educational achievement	Did not attend college	1.94 (0.99-3.79)	.05
	Some college	1.71 (0.95-3.08)	.08
	College graduate	1.37 (0.82-2.28)	.23
	Postgraduate level	1.00 (reference)	-
Personal income	<20,000	3.23 (1.53-6.82)	<.01
	$20,000-$39,999	2.61 (1.34-5.09)	<.01
	$40,000-$59,999	2.62 (1.39-4.92)	<.01
	$60,000-$79,999	2.00 (1.03-3.87)	.04
	$80,000-$99,999	0.89 (0.37-2.17)	.80
	>$100,000	1.00 (reference)	-
Most recent participation in long-term follow-up care	<3 y	1.00 (reference)	-
	≥3 y	0.85 (0.57-1.28)	.45
	Never	3.07 (1.57-5.99)	<.01
History of testosterone treatment	Yes	0.41 (0.17-0.98)	<.05
	No	1.00 (ref. level)	-
History of erectile dysfunction treatment	Yes	0.32 (0.13-0.80)	.01
	No	1.00 (reference)	-
≥40 Gy cranial radiation[a]	Yes	2.88 (1.41-5.88)	<.01
	No	1.00 (reference)	-
Pelvic or testicular radiation[a]	Yes	0.33 (0.19-0.59)	<.001
	No	1.00 (reference)	-
TBI	Yes	0.36 (0.04-3.52)	.38
	No	1.00 (reference)	-
Exposure to alkylator agents	Yes	0.32 (0.16-0.64)	<.01
	No	1.00 (reference)	-
Orchiectomy	Yes	0.10 (0.01-1.00)	<.05
	No	1.00 (reference)	-

Abbreviations: 95% CI, 95% confidence interval; Gy, gray; OR, odds ratio; TBI, total body irradiation.
[a] Did not include TBI.

(Table 2). Stratifying by exposure status, approximately 36.3% of survivors who were exposed to gonadotoxic treatments perceived no increased risk of infertility (311 of 857 survivors), whereas 35.1% of unexposed survivors perceived they were at increased risk of infertility due to their cancer or its treatment (132 of 376 unexposed survivors). To investigate potential bias incurred by previous fertility, we further stratified based on history of fathering children. Among men with no history of fathering children, 27.0% of survivors who were exposed to gonadotoxic treatments perceived no increased risk of infertility (141 of 523 survivors), whereas 41.2% of unexposed survivors perceived they were at increased risk of infertility due to their cancer or its treatment (87 of 211 unexposed survivors). Among men with a history of fathering children, approximately 50.9% of survivors who were exposed to gonadotoxic treatments perceived no increased risk of infertility (170 of 334 survivors), whereas 27.3% of unexposed survivors perceived they were at increased risk of infertility due to their cancer or its treatment (45 of 165 unexposed survivors).

Perceptions of Risk of Infertility After Exposure to Gonadotoxic Therapy

As expected, men who fathered children were significantly more likely to report no increased risk of infertility (odds ratio [OR], 4.14; 95% confidence interval [95% CI], 2.74-6.24) (Table 3). There were no statistically

TABLE 4. Factors Associated With Discordant Perceptions of Risk of Infertility Among Survivors With No History of Gonadotoxic Therapy

Factors	Categories	Adjusted OR (95% CI)	*P*
History of fathering children	Yes	1.00 (reference)	-
	No	1.88 (1.17-3.03)	.01
Educational achievement	Did not attend college	1.00 (reference)	-
	Some college	3.81 (1.41-10.3)	.01
	College graduate	3.18 (1.24-8.16)	.02
	Postgraduate level	5.61 (2.07-15.2)	<.001
Most recent participation in long-term follow-up care	<3 y	2.11 (1.01-4.42)	.05
	≥3 y	1.51 (0.71-3.21)	.29
	Never	1.00 (reference)	-

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio.

significant interactions observed between a history of fathering a child and any of the other factors in the multivariable model presented in Table 3. Men of minority race/ethnicity also were found to be significantly more likely to incorrectly report no increased risk of infertility (all other race/ethnicities vs white, non-Hispanic: OR, 2.28 [95% CI, 1.10-4.75]). Survivors with lower income were more likely to incorrectly report no increased risk of infertility compared with survivors with a yearly income >$100,000 (Table 3). Younger age at the time of a cancer diagnosis and lower educational achievement were found to be significantly associated with discordant perceptions of risk of infertility in univariate analyses; however, neither was noted to be significant in the multivariable model.

Survivors who had never participated in LTFU care were more likely to report no increased risk of infertility (OR, 3.07; 95% CI, 1.57-5.99) compared with survivors who reported LTFU care within the past 3 years. Participants with histories of testosterone (OR, 0.41; 95% CI, 0.17-0.98) or erectile dysfunction (OR, 0.32; 95% CI, 0.13-0.80) treatments were less likely to report discordant perceptions of their risk of infertility. Cranial radiation exposure ≥40 Gy was associated with discordant perceptions of risk of infertility (OR, 2.88; 95% CI, 1.41-5.88). In contrast, survivors with a history of pelvic or testicular radiation (OR, 0.33; 95% CI, 0.19-0.59), alkylator agent exposure (OR, 0.32; 95% CI, 0.16-0.64), or orchiectomy (OR, 0.10; 95% CI, 0.10-1.00) were less likely to report discordant perceptions of their risk of infertility. Participants with a history of multiple treatment exposures conferring a risk of infertility were less likely to report discordant perceptions (25%) compared with participants with only 1 type of exposure (39%). However, discordance between perception of infertility risk and treatment exposure was notably higher among survivors who received cranial radiation exposure ≥40 Gy, who were more likely to report no increased risk of infertility, regardless of what other treatment exposures occurred.

Predicting Discordant Perceptions of Risk of Infertility Among Survivors Not Exposed to Gonadotoxic Therapy

Table 4 shows that perceptions of increased risk of infertility among survivors not exposed to gonadotoxic therapy were more likely among survivors who reported never having fathered a child (OR, 1.88; 95% CI, 1.17-3.03), attended college, or reported recent LTFU care participation (OR, 2.11; 95% CI, 1.01-4.42). There were no statistically significant interactions noted between a history of fathering a child and educational outcomes or engagement in LTFU care.

DISCUSSION

To the best of our knowledge, few large studies to date have assessed the perceptions of survivors of childhood cancer regarding their risk of infertility. We believe the current investigation is unique in its focus on male survivors of childhood cancer and comprehensive examination of sociodemographic and treatment factors predicting perceptions of risk of infertility. Consistent with previously published studies,[9,10] the results of the current study demonstrated that greater than one-third of adult male survivors (35.9%) reported perceptions of risks of infertility that were discordant with their childhood cancer treatment histories. Discordant perceptions regarding one's personal risk of infertility appeared to be equally common among men exposed to therapies that put them at risk (36.3%) compared with men with no history of such exposures (35.1%). Men who are unaware of treatment-related infertility risks may be less likely to undergo fertility testing or to seek out reproductive assistance in a timely

manner, which could reduce their chances of future reproductive success. In addition, male survivors who mistakenly believe that they are at risk of infertility may not engage in consistent contraceptive use with female partners, which could result in unplanned pregnancy. These data are concerning because inaccurate beliefs regarding reproductive health may negatively impact sexual health behavior and/or family planning for adult male survivors and their partners.[6,7]

In general, male survivors who were exposed to multiple types of cancer treatments conferring a risk of infertility were less likely to report discordant perceptions of that risk. Survivors with complex gonadotoxic exposure histories may be more likely to have been referred to an endocrinologist, perhaps resulting in detailed discussions of fertility risk. An important caveat to these conclusions was our finding that discordant perceptions of risk of infertility were notably higher among survivors who received cranial radiation exposure $\geq$40 Gy, regardless of other exposures. Given that cranial radiation is associated with neurocognitive late effects such as problems with memory and learning,[5,20] survivors with a history of receipt of high levels of cranial radiation may require more intensive educational supports to understand their risks of infertility.

Because a previous study of adult male survivors of childhood cancer suggested that survivors can experience episodes of both fertility and infertility,[2] we wanted to better understand how a history of fathering children influenced survivors' perceptions of their risk of infertility. As expected, fatherhood status had a differential impact on male survivors' perceptions of their risk of infertility based on their treatment exposure status. These findings likely reflect confirmation biases in information processing, or the human tendency to interpret evidence in support of our existing beliefs and discount evidence opposing our beliefs.[21,22] Survivors with a history of gonadotoxic treatment were more likely to have discordant perceptions if they had fathered a child (OR, 4.14). Male survivors in this group who previously fathered a child may view their offspring as evidence that their gonadotoxic therapy did not confer any risk of clinical infertility (eg, inability to conceive after 12 months of trying to become pregnant). In contrast, survivors with no gonadotoxic treatment exposures were more likely to have discordant perceptions if they had never fathered a child (OR, 1.88). Men in this group may consider their lack of offspring as evidence of infertility and mistakenly attribute it to their childhood cancer treatment instead of other potential causes (eg, lifestyle factors, female factor infertility in a partner, etc). These data highlight the importance for all male survivors to understand their actual risks based on treatment exposures, regardless of a prior history of fathering children, to be able to make well-informed family planning decisions in the future.

While controlling for fertility status as a potentially biasing factor, nonwhite race, lower personal income, and never having participated in LTFU care also predicted discordant perceptions of risk among men with a history of gonadotoxic treatment exposure. Previous research has found that nonwhite race and lower educational attainment are predictive of a lower awareness of personal risks of late effects among survivors.[10] These outcomes indicate that demographic subgroups of survivors may be less likely to receive education regarding the risks of late effects or may experience difficulties in understanding or recalling health risk information that has been presented. Oncology and survivor programs should consider specialized outreach to these populations to increase knowledge regarding risks of infertility, and patient education regarding risks of infertility late effects must start before patients are lost to follow-up for cancer care. Pediatric oncology professionals can provide age-appropriate education regarding infertility risks and future family planning options to patients as they are transitioning off therapy. Previous research has demonstrated that a significant subset of preteen female survivors and greater than one-half of female adolescent survivors are able to accurately report their risk of infertility before reaching young adulthood.[8] Because the literature indicates that accurate parental knowledge of the risks of late effects can translate into more accurate knowledge for survivors,[8,14] providers also can help to narrow knowledge gaps by ensuring that the parents of pediatric oncology patients of all ages understand the reproductive risks conferred by their child's cancer therapy.

The results of the current study also demonstrated that men who were not at increased risk of infertility due to treatment exposure were more likely to perceive themselves to be at increased risk if they were more highly educated and reported recent engagement in LTFU care. Given these unexpected outcomes, it is clear that universal and individualized health education followed by correction of misinformation regarding risks of infertility are critical for all survivors of childhood cancer regardless of exposure status or previous history of fertility. The BETTER model was created to promote sexual health communication in oncology,[23,24] and oncology providers may consider using components of the model when delivering infertility risk education. Providers can begin by initiating

age-appropriate discussions of risks and normalizing infertility concerns as common among survivors[7] (*B*ring-up the topic; *E*xplain rationale and allow patients to voice concerns). Survivors should be encouraged to choose when and with whom they would like to discuss risks of infertility to optimize receptivity to and retention of information (*T*ime discussions to reflect patients' preferences). Providers can be prepared to offer appropriate referrals for semen analysis and/or consultations with reproductive endocrinology or behavioral health specialists for distress related to fertility challenges (*T*ell patients about resources). Survivor health care providers can educate survivors regarding their risk of infertility using the evidence outlined in the Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancers,[5] and may consider using teach-back techniques as recommended by the Agency for Healthcare Research and Quality to ensure education has been effective[25] (*E*ducate patients about side effects of cancer treatments). These methods invite patients to "teach back" what they have learned from providers. If there are inaccuracies in survivors' recall, providers have the opportunity to correct misunderstandings to ensure that the patient's perceptions are accurate. Last, providers can use survivors' medical records to document when male health consultations are performed and what level of infertility risk was communicated (*R*ecord assessment and interventions in the medical record).

The current study has limitations, which are important to address in future research. Treatment data were not available for survivors who experienced disease recurrence or a subsequent malignancy, and therefore those survivors were excluded from analyses. The exclusion of survivors who were more heavily treated, and therefore more likely to experience increased risks of infertility, may be a potential bias. Although we were able to recruit a large sample of adult male survivors for the MHQ, the sensitive nature of questions regarding infertility and sexual functioning may have deterred some survivors from participation. Moving forward, future research should attempt to assess reasons for refusal to participate in studies focused on male reproductive health perceptions. Last, the current study was limited by the data collected within the MHQ, and thus we were not able to examine concurrent relationships between male survivors' perceptions of risk and specific psychological factors such as health-related worry, generalized anxiety, and overall psychological distress. We also were unable to explore the potential contributions of neurocognitive functioning to survivors' risk perception beyond 1 item assessing self-reported problems with learning or memory. Future work in this area should explore these associations to inform the development of educational interventions to promote awareness of risk of reproductive health problems.

Conclusions

To our knowledge, the majority of research investigating patients' infertility experiences has been conducted with female participants, and research into men's perceptions of reproductive risks is needed.[26,27] Thus, the data from this large population of male survivors supply novel insights into perceptions of infertility risks and focuses for educational interventions. Additional research is needed to identify best-practice methods of delivering male health information to address the knowledge gaps observed in this population. Overall, the data from this investigation indicate that a substantial number of male survivors are unaware of how their childhood cancer treatment may have impacted their reproductive health, which underscores the need for all patients to have access to ongoing education regarding infertility risks throughout the continuum of cancer care from diagnosis to survivorship.

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CONFLICT OF INTEREST DISCLOSURES

Kristy D. Seidel has acted as a paid statistical consultant for C-SATS. Chad W.M. Ritenour owns stock in Stryker and has provided expert testimony for AbbVie.

AUTHOR CONTRIBUTIONS

Jordan Gilleland Marchak: Conceptualization, writing–original draft, and writing–review and editing. **Kristy D. Seidel**: Data curation, formal analysis, methodology, software, writing–original draft, and writing–review and editing. **Ann C. Mertens**: Conceptualization, project administration, methodology, and writing–review and editing. **Chad W.M. Ritenour**: Writing–review and editing. **Karen Wasilewski-Masker**: Writing–review and editing. **Wendy M. Leisenring**: Data curation, formal analysis, methodology, software and writing–review and editing. **Charles A. Sklar**: Writing–review and editing. **Jennifer S. Ford**: Writing–review and editing. **Kevin R. Krull**: Writing–review and editing. **Marilyn Stovall**: Data curation, formal analysis, methodology, software, and writing–review and editing. **Leslie L. Robison**: Data curation, methodology, software, funding acquisition, investigation, and writing–review and editing. **Gregory T. Armstrong**: Data curation, methodology, software, funding acquisition, investigation, and writing–

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