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Perceptions of risk for infertility among male survivors of childhood cancer: A report from the Childhood Cancer Survivor Study

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Abstract

Background—The objective of this investigation was to characterize and identify factors associated with perceptions of risk for infertility among adult male childhood cancer survivors.

Methods—Adult male survivors (N=1233) from the Childhood Cancer Survivor Study, without a history of recurrence or subsequent malignancy, reported their perceptions of risk for infertility relative to men never diagnosed with cancer. Survivors were a median age of 37.8 years (range: 22.0–58.7 years) and 28.4 years from diagnosis (range 21.4–39.2 years). Multivariable logistic regression evaluated factors associated with perceptions of risk.

Results—Overall, 35.9% (n=443/1233) of survivors reported perceptions of risk for 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

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(36.3%, n=311/857) and men with no history of gonatoxotic exposure (35.1%, n=132/376). Survivors who fathered children (OR=4.14, 95% CI 2.74–6.24), had no survivor-focused healthcare (OR=3.07, 95% CI 1.57–5.99), were nonwhite (OR=2.28, 95% CI 1.10–4.75), and were lower income were more likely to report no increased risk of infertility following gonadotoxic treatment. Perceptions of increased risk for 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 healthcare (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 reproductive health, underscoring the need for all patients to receive education about risk for infertility throughout the continuum of cancer care.

Keywords

Childhood Cancer; Survivors; Infertility; Health Knowledge

Introduction

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

The objective of this investigation was to address this gap in the literature by determining associations between discordant perceptions of risk for infertility and sociodemographic characteristics, medical, and treatment data among a large sample of adult male survivors of childhood cancer. Previous research indicates that lower educational attainment predicts lower awareness of personal risks for late effects among survivors, while engagement in education during long-term follow-up (LTFU) care visits can increase survivors' knowledge of risk for late effects[10, 13]. Younger age of diagnosis has been significantly associated with survivors' poorer specific knowledge of their chemotherapy and/or radiation treatment histories[14–16]. Earlier work from the Childhood Cancer Survivor Study (CCSS) showed that 37% of adult male survivors who met the definition for infertility also reported fathering at least one 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 risk for 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 time of diagnosis, lower educational achievement, and lack of participation in survivor care. Additionally, 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.

Methods

Childhood Cancer Survivor Study

Participants were recruited from the Childhood Cancer Survivor Study (CCSS) cohort of ≥5-year survivors of childhood cancer from 26 institutions in the United States and Canada. Details of the CCSS study design and cohort have been previously published[17, 18]. Data on participants' self-reported demographic characteristics and history of fathering pregnancies were obtained from the CCSS baseline and follow-up questionnaires. For the purposes of this analysis, participants who reported having fathered at least one pregnancy resulting in a live birth were classified as having fathered a child. Data on participants' self-reported problems with learning or memory (e.g., "Have you ever been told by a doctor or other healthcare professional that you have, or have had, problems with learning or memory?") and participation in long-term follow-up care (e.g., "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 about male reproductive health and perceptions of the impact of childhood cancer on male health. Male survivors who were ≥18 years old when they participated in CCSS' Follow-up 4 questionnaire (2007–2008, N=4,000) were asked to consider completing a separate survey to "better understand fertility and sexual function in males". Overall, N=2,961 agreed to receive the MHQ (Supplementary Figure 1). As part of the MHQ, participants rated their risk for infertility as compared to "other men [their] age never diagnosed with cancer or a disease like cancer". Participants were given a five-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 on chemotherapy exposures, radiation treatments, and surgeries were abstracted from participants' original medical records. Estimated organ- 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 Pediatric Adolescent and Young

Adults Cancer (COG LTFU Guidelines) (Version 3.0) were used to categorize participants' risk for infertility[20]. Participants were classified as at increased risk for infertility if they received any of the following: alkylating agents or heavy metals, direct radiation to the testes or pelvis, ≥50 cGy scatter radiation to the testes from other fields, >40 Gy cranial radiation, orchiectomy, spinal cord neurosurgery, pelvic surgery, and/or cystectomy.

Statistical analyses

Participants with a history of relapse or subsequent malignancy (N=269) were excluded, as treatment data for these events was unavailable and may have included gonadotoxic therapy. Participants who did not rate their perception of risk for infertility on the MHQ (N=31) or were missing treatment data (N=89) were also 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 risk for infertility and their actual risk based on their gonadotoxic treatment exposure status. For men with a history of gonadotoxic treatment exposure, factors associated with their report of being "not at increased risk" for infertility at the $p<0.10$ level on univariable analysis were assessed in multivariable models. The final multivariable model included treatment exposure factors, plus demographic and long-term follow-up characteristics that showed statistically significant associations with the outcome or whose omission would impact other estimates from the model by more than 10%. A separate analysis was conducted among male survivors who were not exposed to infertility-risk-conferring cancer therapy, yet perceived themselves to be at elevated risk for infertility. Survivors' history of fathering one or more children was included in both multivariable models to allow for evaluation of the relationships between infertility risk perception and characteristics of interest while controlling for fatherhood status as a potential confounding factor. P-values <0.05 were considered statistically significant.

Results

Participants and non-participants

The MHQ was completed and returned by 1,622 survivors (55.1% response rate- see Supplemental Figure 1). Demographics and treatment characteristics for participants and non-participants in these analyses are presented in Table 1 and Supplementary Table 1. Participants were slightly older and more likely to be white, have been married or lived as married, and report higher educational achievement as compared to non-participants. Rates of participation in long-term follow-up (LTFU) care were similar between participants and non-participants. At 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 diagnosis (range: 21.4–39.2 years). A large majority of participants (80.5%) were previously exposed to potentially gonadotoxic therapies, and 40.1% reported a history of fathering children.

Survivors' perceptions of risk for infertility

Overall, 35.9% (n=443/1233) of survivors reported perceptions of risk for infertility that were discordant with their previous cancer treatment exposures (Table 2). Stratifying by exposure status, 36.3% of survivors exposed to gonadotoxic treatments perceived no

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

Perceptions of risk for infertility following exposure to gonadotoxic therapy

As expected, men who fathered children were significantly more likely to report no increased risk for infertility (OR=4.14, 95% CI 2.74–6.24; Table 3). There were no statistically significant interactions 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 were also a significantly more likely to incorrectly report no increased risk for 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 for infertility as compared survivors with yearly income over $100,000 (see Table 3). Younger age at cancer diagnosis and lower educational achievement were significantly associated with discordant perceptions of risk for infertility in univariate analyses; however, neither was significant in the multivariable model.

Survivors who had never participated in LTFU care were more likely to report no increased risk for infertility (OR=3.07, 95% CI 1.57–5.99) as compared to survivors who reported LTFU care within the past three 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 risk for infertility. Cranial radiation exposure ≥40 Gy was associated with discordant perceptions of risk for 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 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 risk for infertility. Participants with a history of multiple treatment exposures conferring risk for infertility were less likely to report discordant perceptions (25%) than participants with only one 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 for infertility, regardless of what other treatment exposures occurred.

Predicting discordant perceptions of risk for infertility among survivors not exposed to gonadotoxic therapy

Table 4 shows that perceptions of increased risk for infertility among survivors not exposed to gonoadotoxic 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 between a history of fathering a child and educational outcomes or engagement in LTFU care.

Discussion

Few large studies have assessed childhood cancer survivors' perceptions of risks for infertility. 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 for infertility. Consistent with previously published studies[9, 10], our results demonstrate that over one-third of adult male survivors (35.9%) report perceptions of risks for infertility that are discordant with their childhood cancer treatment histories. Discordant perceptions about personal risk for infertility appear to be equally common among men exposed to therapies that put them at risk (36.3%) as compared to 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 seek out reproductive assistance in a timely manner, which could reduce their chances of future reproductive success. Additionally, male survivors who mistakenly believe that they are at risk for infertility may not engage in consistent contraceptive use with female partners, which could result in unplanned pregnancy. These data are concerning as inaccurate beliefs about 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 received exposure to multiple types of cancer treatments conferring risk for infertility were less likely to report discordant perceptions of risk for infertility. 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 for infertility were notably higher among survivors who received cranial radiation exposure ≥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 high levels of cranial radiation may require more intensive educational supports to understand their risks for infertility.

As previous study of adult male survivors of childhood cancer suggests that survivors can experience episodes of both fertility and infertility[2], we wanted to better understand how history of fathering children influenced survivors' perceptions of risk for infertility. As expected, fatherhood status had a differential impact on male survivors' perceptions of risk for 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 for clinical infertility (e.g., 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 (e.g., lifestyle factors, female-factor infertility in partner, etc.). These data highlight the importance for all male survivors to understand their actual risks based on treatment exposures, regardless of prior history of fathering children, in order to be able to make well-informed family planning decisions in the future.

While controlling for fertility status as a potentially biasing factor, non-white 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 found that non-white race and lower educational attainment predicted lower awareness of personal risks for late effects among survivors[10]. These outcomes indicate that demographic subgroups of survivors may be less likely to receive education about risks for late effects or may experience difficulties understanding or recalling health risk information presented. Oncology and survivor programs should consider specialized outreach to these populations to increase knowledge about risks for infertility, and patient education regarding risk for infertility late effects must start before patients are lost-to-follow-up for cancer care. Pediatric oncology professionals can provide age appropriate education about infertility risks and future family planning options to patients as they are transitioning off therapy. Previous research has demonstrated that a significant subset of pre-teen female survivors and over half of female adolescent survivors are able to accurately report their risk for infertility before reaching young adulthood[8]. As the literature indicates that accurate parent knowledge of late effect risks can translate into more accurate knowledge for survivors[8, 14], providers can also help 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.

Our study also found that men who were not at increased risk for 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 about risks for infertility is 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 amongst survivors[7] (Bring-up the topic; Explain rationale and allow patients to voice concerns). Survivors should be encouraged to choose when and with whom they would like to discuss risks for infertility in order to optimize receptivity to and retention of information (Time discussions to reflect patients' preferences). Providers can be prepared to offer appropriate referrals for semen analysis, consultation with reproductive endocrinology, or behavioral health for distress related to fertility challenges (Tell patients about resources). Survivor healthcare providers can educate survivors about their risk for infertility utilizing the evidence outlined in the COG LTFU Guidelines[5] and may consider utilizing teach back techniques recommended by the Agency

for Healthcare Research and Quality (AHRQ) to ensure education has been effective[25] (Educate 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 misunderstanding to ensure patients' perceptions are accurate. Lastly, providers can utilize survivors' medical records to document when male health consultations are performed and what level of risk for infertility was communicated (Record 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 a relapse or subsequent malignancy, and thus, those survivors were excluded from analyses. Exclusion of survivors who were more heavily treated, and more likely to experience increased risks for 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 about infertility and sexual functioning may have deterred some survivors from participation. Moving forward, future research should attempt to assess reasons for participation refusal in studies focused on male reproductive health perceptions. Lastly, our 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 were also unable to explore the potential contributions of neurocognitive functioning to survivors' risk perception beyond one 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 for reproductive health problems.

Conclusions

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 intervention. 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 about infertility risks throughout the continuum of cancer care from diagnosis to survivorship.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographic and Treatment Characteristics for Adult Male Survivors of Childhood Cancer*

		N=1233	Percent(%)
Age at primary cancer diagnosis	<=4 years	416	33.7
	5–9 years	277	22.5
	10–14 years	293	23.8
	15–20 years	247	20.0
Age at Men's Health Questionnaire	20–29 years	214	17.4
	30–39 years	530	43.0
	40–49 years	436	35.4
	50–59 years	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#	Yes	857	69.5
	No	376	30.5
History of fathering children	Yes	499	40.5
	No	734	59.5
Education achievement	Did not attend college	172	13.9
	Some college	281	22.8
	College graduate	521	42.3
	Post graduate level	259	21.0
Personal income	Less than $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
	Over $100,000	199	16.8
Most recent participation in survivor-focused healthcare	Less than 3 years	581	52.4

		N=1233	Percent(%)
	3 or more years	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

[*] Percentages provided for those with known demographic or treatment status

[#] Exposure to alkylators or heavy metals, direct radiation to testes or pelvis, ≥50 cGy absorbed radiation to the testes, orchiectomy, spinal cord neurosurgery, pelvic surgery, cystectomy, and/or >40 Gy cranial radiation.

Table 2

Perception of Risk for Infertility by Gonadotoxic Therapeutic Exposure Status and History of Fathering Children

Total Population (N=1233)		
Gonadotoxic cancer therapy exposure status		**Overall Perception of Risk**
Exposed (n=857)	Not exposed (n=376)	
Self-identifies as “Not at increased * risk” for infertility 311 (36.3%)	Self-identifies as “At increased * risk” for infertility 132 (35.1%)	Perception of Risk Discordant with Exposure 443 (35.9%)
Self-identifies as “At increased * risk” for infertility 546 (63.7%)	Self-identifies as “Not at increased * risk” for infertility 244 (64.9%)	Perception of Risk Concordant with Exposure 790 (64.1%)
Men with no history of fathering children (N=734)		
Gonadotoxic cancer therapy exposure status		**Overall Perception of Risk**
Exposed (n=523)	Not exposed (n=211)	
Self-identifies as “Not at increased * risk” for infertility 141 (27.0%)	Self-identifies as “At increased * risk” for infertility 87 (41.2%)	Perception of Risk Discordant with Exposure 228 (31.1%)
Self-identifies as “At increased * risk” for infertility 382 (73.0%)	Self-identifies as “Not at increased * risk” for infertility 124 (58.8%)	Perception of Risk Concordant with Exposure 506 (68.9%)
Men with a history of fathering children (N=499)		
Gonadotoxic cancer therapy exposure status		**Overall Perception of Risk**
Exposed (n=334)	Not exposed (n=165)	
Self-identifies as “Not at increased * risk” for infertility 170 (50.9%)	Self-identifies as “At increased * risk” for infertility 45 (27.3%)	Perception of Risk Discordant with Exposure 215 (43.1%)
Self-identifies as “At increased * risk” for infertility 164 (49.1%)	Self-identifies as “Not at increased * risk” for infertility 120 (72.7%)	Perception of Risk Concordant with Exposure 284 (56.9%)

* in comparison to men of the same age who have not had cancer

Table 3

Factors Associated with Discordant Perceptions of Risk for Infertility Among Survivors Exposed to Gonadotoxic Therapy

Factors	Categories	Adjusted Odds Ratio	*p*-value
Age at primary cancer diagnosis	<=4 yrs	1.00 (ref. level)	--
	5–9 yrs	0.91 (0.53–1.57)	0.73
	10–14 yrs	0.80 (0.47–1.37)	0.42
	15–21 yrs	1.20 (0.70–2.07)	0.51
Race /Ethnicity	White non-Hispanic	1.00 (ref. level)	--
	Other	2.28 (1.10–4.75)	**0.03**
History of fathering children	Yes	4.14 (2.74–6.24)	**<0.001**
	No	1.00 (ref. level)	--
Education achievement	Did not attend college	1.94 (0.99–3.79)	0.05
	Some college	1.71 (0.95–3.08)	0.08
	College graduate	1.37 (0.82–2.28)	0.23
	Post graduate level	1.00 (ref. level)	--
Personal income	Less than $20,000	3.23 (1.53–6.82)	**<0.01**
	$20,000 – $39,999	2.61 (1.34–5.09)	**<0.01**
	$40,000 – $59,999	2.62 (1.39–4.92)	**<0.01**
	$60,000 – $79,999	2.00 (1.03–3.87)	**0.04**
	$80,000 – $99,999	0.89 (0.37–2.17)	0.80
	Over $100,000	1.00 (ref. level)	--
Most recent participation in long-term follow-up care	Less than 3 years	1.00 (ref. level)	--
	3 or more years	0.85 (0.57–1.28)	0.45
	Never	3.07 (1.57–5.99)	**<0.01**
History of testosterone treatment	Yes	0.41 (0.17–0.98)	**<0.05**
	No	1.00 (ref. level)	--
History of erectile dysfunction treatment	Yes	0.32 (0.13–0.80)	**0.01**
	No	1.00 (ref. level)	--
>40 Gy cranial radiation[†]	Yes	2.88 (1.41–5.88)	**<0.01**
	No	1.00 (ref. level)	--
Pelvic or testicular radiation[†]	Yes	0.33 (0.19–0.59)	**<0.001**
	No	1.00 (ref. level)	--
Total body irradiation (TBI)	Yes	0.36 (0.04–3.52)	0.38
	No	1.00 (ref. level)	--
Alkylator agent exposure	Yes	0.32 (0.16–0.64)	**<0.01**
	No	1.00 (ref. level)	--

Factors	Categories	Adjusted Odds Ratio	*p*-value
Orchiectomy	Yes	0.10 (0.01–1.00)	**<0.05**
	No	1.00 (ref. level)	--

† does not include TBI

Table 4

Factors Associated with Discordant Perceptions of Risk for Infertility Among Survivors with No History of Gonadotoxic Therapy

Factors	Categories	Adjusted Odds Ratio	*p*-value
History of fathering children	Yes	1.00 (ref. level)	--
	No	1.88 (1.17–3.03)	**0.01**
Educational Achievement	Did not attend college	1.00 (ref. level)	--
	Some college	3.81 (1.41–10.3)	**0.01**
	College graduate	3.18 (1.24–8.16)	**0.02**
	Post graduate level	5.61 (2.07–15.2)	**<0.001**
Most recent participation in long-term follow-up care	Less than 3 years	2.11 (1.01–4.42)	**0.05**
	3 or more years	1.51 (0.71–3.21)	0.29
	Never	1.00 (ref. level)	--