

**Childhood Cancer Survivor Study  
Study Proposal: Male Health Questionnaire (MHQ)  
December 11, 2011**

1. **STUDY TITLE:** Male sexual health in childhood and adolescent cancer survivors diagnosed from 1970-1986: A report from the Childhood Cancer Survivor Study
  
2. **WORKING GROUP AND INVESTIGATORS:** This proposed publication will be within the Chronic Disease Working Group. Proposed investigators will include:

Chad Ritenour	criteno@emory.edu
Lillian Meacham	lillian_meacham@oz.ped.emory.edu
Margarett Shnorhavorian	margarett.shnorhavorian@seattlechildrens.org
Karen Wasilewski-Masker	karen.wasilewski@choa.org
Ann Mertens	ann.mertens@choa.org
Chuck Sklar	sklarc@mskcc.org
Jennifer Ford	fordj@mskcc.org
Wendy Leisenring	wleisenr@fhcrc.org
Kristy Seidel	kseidel@fhcrc.org
John Whitton	jwhitton@fhcrc.org
Marilyn Stovall	mstovall@mdanderson.org
Greg Armstrong	greg.armstrong@stjude.org
Les Robison	les.robison@stjude.org

### 3. BACKGROUND AND RATIONALE

Sexual health is influenced by previous experiences. Moreover, cancer and its subsequent treatment can have profound results on future sexual functioning [1]. When cancer occurs early in life, the cancer experience may have an adverse affect on an individual's sexual functioning in the formative years that may persist throughout their lifetime. As survival from pediatric cancer has significantly increased, more individuals may experience sexual dysfunction. Nonetheless, this topic has been poorly characterized in this particular survivor group. In this study, we specifically seek to characterize sexual health outcomes in adult males treated for childhood and adolescent cancers.

A detailed questionnaire designed to better understand psychosexual effects on male survivors following childhood cancer treatment was administered. The Male Health Questionnaire (MHQ), funded by the Lance Armstrong Foundation, was created to obtain detailed information on sexual function, infertility, testicular function, and perceptions of the impact of cancer diagnosis and treatment on sexual function among this cohort. A similar questionnaire was previously sent to female survivors in the CCSS cohort. Since little data exist on male sexual function after childhood cancer, we hope to first characterize frequency of sexual dysfunction as well as any treatments these survivors are receiving for such disorders.

Multiple factors, including aging and chronic medical conditions, affect sexual performance. Particular situations also affect men's sexual functioning, such that it may be better at some times than others. Therefore, self-reported questionnaires are often used to measure sexual function. These questionnaires allow patients to report on collective experiences rather than single encounters. Two questionnaires, the International Index of Erectile Function (IIEF) [2] and the Sexual Function Questionnaire (SFQ) [3], utilized in this study have both been validated for use as measures of sexual function among men. We will stratify results of these assessments by type of cancer and treatment, as well as characterize treatment of sexual dysfunction among groups.

Men place significant importance on sexual functioning [4], yet they often fail to discuss it with their physicians [5]. Additionally, physicians frequently do not ask about sexual concerns [6], so many disorders go untreated. As cancer patients survive years beyond treatment of their life-threatening disease, quality of life issues become increasingly important. Understanding sexual concerns of male childhood cancer survivors will allow treating clinicians to better predict effects for future generations as well as provide treatment for those who experience difficulties. Improved assessment will also potentially allow earlier treatment that may help to mitigate or prevent dysfunction.

#### 4. AIMS:

##### Aim 1:

To determine frequency and type of sexual activities, along with overall sexual function scores on a validated questionnaire, in male childhood and adolescent cancer survivors compared to sibling controls as well as to identify specific demographic, socioeconomic and health status factors associated with worse outcomes in the survivors

Hypothesis—Male survivors of childhood cancers engage in fewer and less frequent sexual experiences than sibling controls.

##### Aim 2:

To determine prevalence of erectile dysfunction, as defined by validated self-reported questionnaire, among male survivors of childhood and adolescent cancer in comparison to sibling controls

Hypothesis—Male survivors of childhood cancers experience higher rates of self-reported erectile dysfunction than their sibling controls.

##### Aim 3:

To determine the effect of childhood and adolescent cancer treatment and other sociodemographic, health or cancer-related variables on sexual function, including erectile function, in male survivors

Hypothesis—Male survivors of childhood cancers who received “at risk” therapy by long term follow-up COG guidelines have higher rates of sexual dysfunction than those survivors who did not receive such therapy.

##### Aim 4:

To determine the frequency and types of therapies used to treat sexual dysfunction in male childhood cancer survivors (a) as compared to sibling controls and (b) by treatment exposure

Hypothesis—Male survivors of childhood cancers require higher rates of treatment for sexual dysfunction than sibling controls.

#### 5. DATA ANALYSIS:

- *Aim 1: FREQUENCY OF SEXUAL ACTIVITIES*
  - Population:
    - All male survivors responding to MHQ
  - Comparison population
    - Male siblings responding to MHQ
      - Exclude siblings who have had cancer
  - Primary Outcome Variables
    - Previous sexual experiences (C4≠“none of the above”)
      - Exclude “no reply”
    - Sexual intercourse (C3)
  - Secondary Outcome Variables
    - Ejaculation
    - Orgasm
    - Libido
    - Sexually active

- Frequency of activity in past month (G8)
  - Sexual Function Questionnaire Scores
- Explanatory Variables
  - Ethnicity (baseline)
  - Age at assessment (date of MHQ-dob)
  - Marital status (M2 – LTFU)
  - Smoking status (N7 - LTFU)
  - Alcohol status (N1, N6 – LTFU)
  - Physical activity (N15, N17/N20 – LTFU)
  - Education level (A3 – LTFU)
  - Employment (A4 – LTFU)
  - Income (A6/A8 – LTFU)
  - Insurance (B9 – LTFU)
  - General health (D1)
  - Other medical conditions (B1, B2)
- Exposure Variables (Survivors only)
  - Age at diagnosis
  - Cancer diagnosis
- Statistical analysis—Descriptive statistics of subject characteristics and outcome variables will be summarized using standard measures. Odds ratios for engaging in sexual experiences and sexual intercourse for survivors, compared to siblings, will be computed using logistic regression models with generalized estimating equations and robust variance estimates to account for intra-family correlation. In addition, we will examine the explanatory factors singly in models with the survivor vs. sibling indicator to examine potential confounding effects of the explanatory variables listed. Those factors that modify the survivor vs. sibling association by more than 10% will be included in an initial multivariable regression model. Factors will be removed if their exclusion does not modify the survivor /sibling association with outcome. Within the survivor group, an additional multivariable model will be constructed to identify specific demographic, socioeconomic, and health status factors associated with worse sexual outcomes. The frequency of individual sexual activities, including summaries by age at diagnosis and primary diagnosis for survivors, will be included as a descriptive analysis.
- *Aim 2: PREVALENCE OF ERECTILE DYSFUNCTION*
  - Inclusion population:
    - All male survivors responding to the MHQ and responding positively to question G1
      - Total survivors
  - Comparison population:
    - All male siblings responding to the MHQ and responding positively to question G1
      - Exclude siblings who have had cancer
  - Primary outcome variable
    - Organic erectile dysfunction by validated questionnaire
      - IIEF Erectile Function Domain score
        - No dysfunction (EF score > 25)
        - Dysfunction (EF score ≤ 25)
  - Secondary outcome variable
    - Self-reported erectile dysfunction by single qualitative question
      - MHQ G12a ≠ “not at all” AND/OR
      - MHQ G12c ≠ “not at all”

- Explanatory Variables
  - Ethnicity (baseline)
  - Age at assessment (date of MHQ-dob)
  - Marital status (M2 – LTFU)
  - Smoking status (N7 - LTFU)
  - Alcohol status (N1, N6 – LTFU)
  - Physical activity (N15, N17/N20 – LTFU)
  - Education level (A3 – LTFU)
  - Employment (A4 – LTFU)
  - Income (A6/A8 – LTFU)
  - Insurance (B9 – LTFU)
  - Age at diagnosis
  - Cancer diagnosis
  - General health (D1)
  - Other medical conditions (B1, B2)
  
- Statistical analysis— Descriptive analyses of subject characteristics and outcome variables will be summarized using standard measures. Odds ratios for erectile dysfunction in survivors, compared to siblings, will be computed using logistic regression models with generalized estimating equations and robust variance estimates to account for intra-family correlation. In addition, we will examine the explanatory factors singly in models with the survivor vs. sibling indicator to examine potential confounding effects of the explanatory variables listed. Those factors that modify the survivor vs. sibling association by more than 10% will be included in an initial multivariable regression model. Factors will be removed if their removal does not modify the survivor /sibling association with outcome. An important corollary of this analysis will be to examine the concordance rate of the primary and secondary outcomes, both measures of erectile dysfunction, within the cohort to examine for differences in how individuals report this condition.
  
- *Aim 3: EFFECT OF CANCER THERAPY ON RATES OF DYSFUNCTION*
  - Population
    - Inclusion criterion
      - All male survivors responding to the MHQ and responding positively to question G1
    - Exclusion criterion
      - Recurrence
      - SMN
  
  - Primary Outcome Variables
    - International Index of Erectile Function (IIEF)
      - Erectile Function Domain
      - Orgasmic Function Domain
      - Sexual Desire Domain
      - Intercourse Satisfaction Domain
      - Overall Satisfaction
    - Sexual Function Questionnaire (SFQ)
      - Sexual Functioning Scale
        - Interest
        - Desire
        - Arousal
        - Orgasm
        - Satisfaction
        - Activity

- Relationship
  - Masturbation
  - Problems
- Secondary Outcome Variables (Self-report single questions)
  - Erectile difficulty (G12a ≠ “not at all” AND/OR G12c ≠ “not at all”)
  - Lack of sexual interest or desire(G12b ≠ “not at all”)
  - Delayed ejaculation(G12d ≠ “not at all”)
  - Anxiety about sexual performance(G12e ≠ “not at all”)
  - Inability to achieve orgasm(G12f ≠ “not at all”)
  - Pain during penetration(G12g ≠ “not at all”)
  - Other problems(G12h ≠ “not at all”)
- Exposure Variables
  - Oncology
    - Age at diagnosis (MRAF)
    - Primary diagnosis (MRAF)
    - At risk based on the COG Long-Term Follow-Up Guidelines (Yes/No) – Summary category with any of the following exposures:
      - Alkylating agents (including heavy metals) - any
      - Cranial radiation (> 40 Gy)
      - Testicular radiation - any
      - TBI
      - Orchiectomy
    - Alkylator exposure (MRAF)
      - Summed AAD (0-11) – per Green et al. JCO June 2009, 27 (16):2677-2685
      - *Cyclophosphamide equivalent scores if available for analysis*
    - Radiation exposure by dosimetry (MRAF & Dosimetry)
      - Hypothalamic/pituitary (Cranial) in Gy
      - Testicular radiation in Gy
      - TBI
    - Surgery
      - Testicular surgery (MHQ-B3d with additional data from MRAF; FU 2007 J35, J36)
        - Unilateral orchiectomy
        - Bilateral orchiectomy
        - Other testicular surgery
      - Prostate surgery (MHQ-B3a)
      - Pelvic surgery (MHQ-B3b)
      - Penis surgery (MHQ-B3c)
      - Operations on the Nervous System (MRAF; Baseline; FU 2007)
        - 0.3X – Operations on spinal cord and spinal canal structures
        - 0.5X – Operations on sympathetic nerves or ganglia
- Explanatory Variables
  - General
    - Ethnicity (baseline)
    - Age at assessment (date of MHQ-dob)
    - Marital status (M2 – LTFU)
    - Smoking status (N7- LTFU)
    - Alcohol status (N1, N6 – LTFU)
    - Physical activity (N15, N17/20 – LTFU)
    - Education level (A3 – LTFU)
    - Employment (A4 – LTFU)

- Income (A6/8 – LTFU)
- Insurance (B9 – LTFU)
- General health status (MHQ – D1)
- Personal care (N22;23 – LTFU)
- Pain (L21 – L23 – LTFU)
- Other medical conditions (MHQ – B1, B2)
- Cognitive/Psychological
  - Problems with learning or memory (K1 – LTFU)
  - Anxiety/fears as a result of cancer/treatment (L20 – LTFU)
  - Concern of ability to have children (O2 – LTFU)
- Neurological
  - Weakness or inability to move legs (K12; K14e - LTFU)
- Endocrine
  - Timing of puberty (C1)
  - Testosterone treatment (B4, B6)
  - Erectile dysfunction treatment (B11)
- Statistical analysis—Median scores for each of the domains and subscales of the IIEF and SFQ will be reported descriptively and summarized by exposure variable. Since survivors who have experienced an SMN or recurrence are to be excluded due to the lack of treatment information available for those subjects, we will generate tables for the full population of survivors to compare and understand the difference between those subjects excluded and those included in the analytic data set.

Odds ratios for the association between exposure variables and an abnormal Erectile Function Domain (score  $\leq 25$ ) of the IIEF will be evaluated using logistic regression models, initially in univariable models and subsequently in multivariable models. Candidate risk factors from the list above will be included in an initial multivariable model if they had a p-value  $< 0.2$  in univariable models. They will be dropped from the model if they are not significant at  $\alpha=0.05$  and if their exclusion does not modify another OR in the model by more than 10%. Due to collinearity between some exposure variables, such as the COG Long-Term Follow-Up Guidelines risk categorization and exposure to individual agents, separate models will be built and best fitting models selected for publication.

Because several of the LTFU explanatory variables are potentially associated both with cancer treatments received during childhood and with the development of erectile dysfunction, their presence within a multivariable model could interfere with discerning the effects of the cancer treatments. To deal with this situation, a multivariable model using only cancer treatment variables will first be constructed. Potential downstream mediator variables will then be added to examine (i) how significant the mediator variables are in their own right and (ii) how much their presence in the model changes the relative risk estimates and significance level for cancer treatment variables.

- *Aim 4: FREQUENCY AND TYPE OF THERAPY FOR SEXUAL DYSFUNCTION*

- Population
  - All male survivors responding to the MHQ and responding positively to question G1
    - All survivors
    - Survivors without recurrence or SMN
- Comparison population
  - All male siblings responding to the MHQ and responding positively to question G1
- Primary outcome variable

- Treatment for sexual dysfunction
  - Qualitative (ever) (B11)
  - Qualitative (current) (B12b)
  - Medical treatment (B11)
  - Other medical (device) treatment (B14)
  - Surgical treatment (B13)
- Explanatory variables
  - General
    - Ethnicity (baseline)
    - Age at assessment (date of MHQ-dob)
    - Marital status (M2 – LTFU)
    - Smoking status (N7 - LTFU)
    - Alcohol status (N1, N6 – LTFU)
    - Physical activity (N15, N17/N20 – LTFU)
    - Education level (A3 – LTFU)
    - Employment (A4 – LTFU)
    - Income (A6/A8 – LTFU)
    - Insurance (B9 – LTFU)
    - General health (D1)
    - Other medical conditions (B1, B2)
  - Cancer-related Demographics (SURVIVORS ONLY)
    - Era of treatment
    - Age at diagnosis
    - Primary diagnosis
    - General health status (MHQ – D1)
    - Personal care (N22;23 – LTFU)
    - Pain (L21 – L23 – LTFU)
    - Problems with learning or memory (K1 – LTFU)
    - Anxiety/fears as a result of cancer/treatment (L20 – LTFU)
    - Concern of ability to have children (O2 – LTFU)
    - Weakness or inability to move legs (K12; K14e - LTFU)
    - Timing of puberty (C1)
    - Testosterone treatment (B4, B6)
  - Exposure Variables (SURVIVORS ONLY)
    - At risk based on the COG Long-Term Follow-Up Guidelines (Yes/No) – Summary category with any of the following exposures
      - Alkylating agents (including heavy metals) - any
      - Cranial radiation (> 40 Gy)
      - Testicular radiation - any
      - TBI
      - Orchiectomy
    - Alkylator exposure (MRAF)
      - Summed AAD (0-11) – per Green et al. JCO June 2009, 27 (16):2677-2685
      - *Cyclophosphamide equivalent scores if available for analysis*
        - Hypothalamic/pituitary (Cranial) in Gy
        - Testicular radiation in Gy
        - TBI
    - Surgery
      - Testicular surgery (MHQ-B3d with additional data from MRAF; FU 2007 J35, J36)
        - Unilateral orchiectomy
        - Bilateral orchiectomy
        - Other testicular surgery

- Prostate surgery (MHQ-B3a)
  - Pelvic surgery (MHQ-B3b)
  - Penis surgery (MHQ-B3c)
  - Operations on the Nervous System (MRAF; Baseline; FU 2007)
    - 0.3X – Operations on spinal cord and spinal canal structures
    - 0.5X – Operations on sympathetic nerves or ganglia
- Statistical analysis—Descriptive summaries of the outcome variables, similar to those described for other Aims, will be included. Logistic regression models will be fit to evaluate odds ratios for the association of survivor vs. sibling with treatment of sexual dysfunction. Similar methods as described above for previous Aims will be utilized to evaluate confounding variables for multivariable models. In addition, among survivors, associations between cancer therapy exposures and treatment of sexual dysfunction will be evaluated in univariable models, and then multivariable models will be built using procedures previously described. Due to collinearity between some exposure variables, such as the COG Long-Term Follow-Up Guidelines scoring system and exposure to individual agents, separate models will be built.

## PUBLICATION STRATEGY

The vast data relative to male sexual health that was collected by the MHQ allow for numerous important analyses to be performed. Multiple papers can likely be generated from these analyses. However, we wish to maintain the combination of high impact journal submissions and quality high-level reporting when planning for data dissemination. We, therefore, propose the following publication strategy and order, recognizing that it may change once data are reviewed:

1. Overview report to high-impact medical journal—Summary publication listing findings of the study with important points covering the four aims along with summary tables of high-level results
2. Report of erectile dysfunction prevalence and treatment among survivors to high-impact specialty journal (more detailed report of Aims 2 and 4)
3. Report of more detailed effects of cancer therapy on sexual behaviors and function in the childhood survivor cohort to high-impact oncology journal

## REFERENCES

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2. Rosen, R.C., et al., The international index of erectile function (IIEF); a multidimensional scale for assessment of erectile dysfunction. *Urology*, 1997. **49**(6): p. 822-30.
3. Syrjala, K., et al., Sexual function measurement and outcomes in cancer survivors and matched controls. *Journal Sex Research*, 2000. **37**(3): p. 213-25.
4. Gray, R., Fitch, M. and Davis, C., Breast cancer and prostate cancer self-help groups: Reflections on differences. *Psycho-Oncology*, 1996. **5**(2): p. 137-42.
5. Marwick, C., Survey says patients expect little physician help on sex. *JAMA*, 1999. **281**(23): p. 2173-4.
6. Metz, M.E. and M.H. Seifert, Jr., Men's expectations of physicians in sexual health concerns. *J Sex Marital Ther*, 1990. **16**(2): p. 79-88.



## APPENDIX: TABLES

*Please note: we have provided “skeleton” tables first to provide an overview of the format we have in mind. The skeleton tables are followed by the same tables with all of the variables listed acknowledging that not all would be used in a publication but are included to show the descriptive analysis that will be carried out in the initial steps of the review*

**Table 1 (AIM 1): Prevalence of Sexual Experiences by demographic characteristics of cohort**

	All Survivors	All Survivors with previous sexual experiences	All Survivors with no previous sexual experiences	All Survivors with previous sexual intercourse	All Siblings	All Siblings with previous sexual experiences	All Survivors with no previous sexual experiences	All Siblings with previous sexual intercourse
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
<b>TOTAL COHORT</b>								
<b>Ethnicity</b>								
<b>Age at Assessment</b>								
<b>Marital Status</b>								
<b>Substance use</b>								
<b>Physical Activity</b>								
<b>Highest Level of Education</b>								
<b>Employment</b>								
<b>Income</b>								
<b>Insurance</b>								
<b>Age at Diagnosis</b>								
<b>Cancer Diagnosis</b>								
<b>General Health</b>								
<b>psychiatric illness</b>								
<b>Spinal Injury</b>								
<b>Prostate Disease</b>								

**Table 2 (AIM 1): Comparison of sexual practices in survivors and their male siblings**

	<b>All MHQ Survivors (Number)</b>	<b>All MHQ Survivors (%)</b>	<b>MHQ Siblings (Number)</b>	<b>MHQ Siblings (%)</b>	<b>p- Value</b>
<b>TOTAL COHORT</b>					
<b>State of health</b>					
<b>Onset of puberty</b>					
<b>Ejaculation Y/N age</b>					
<b>Sexual Intercourse Y/N age</b>					
<b>Recent Sexual Experiences</b>					
<b>Previous Sexual Experiences</b>					
<b>Sexually active in past year</b>					
<b>Sexually active in past month</b>					
<b>Frequency of thoughts, urges, fantasies, dreams in past month</b>					
<b>Frequency of interest or desire by sexual activity in past month</b>					
Dreams or fantasy					
Masturbation					
Touching, hugging, holding, kissing					
Petting or foreplay					
Intercourse					
Other sexual activity					
<b>Frequency of arousal by sexual activity in past month</b>					
Dreams or fantasy					
Masturbation					
Touching, hugging, holding, kissing					
Petting or foreplay					
Intercourse					
Other sexual activity					
<b>Pleasure from any sexual activity in past month</b>					
<b>Frequency of activities in past month (G8)</b>					
Dreams or fantasy					
Masturbation					
Touching, hugging, holding, kissing					
Petting or foreplay					
Intercourse					
Other sexual activity					
<b>Reached orgasm (ejaculation) in past month</b>					
<b>Intensiveness of orgasms in past month (</b>					
<b>Ease of orgasms in past</b>					

<b>month</b>					
<b>SFQ Score</b>					
Total Score					
--Interest subscale					
--Desire subscale					
--Arousal subscale					
--Orgasm subscale					
--Satisfaction subscale					
--Activity subscale					
--Relationship subscale					
--Masturbation subscale					
--Problems subscale					

**Table 3 (AIM 1): Multivariable analysis**

**Table 3a**

Previous sexual experiences in survivors and their male siblings (multivariable analysis)

**Table 3b**

Previous sexual intercourse in survivors and their male siblings (multivariable analysis)

		Odds Ratio	95% Confidence Intervals	p- Value
Siblings				
Survivors				
Age at asesment	20-29 y			
	30-39 y			
	40-49 y			
	50-59 y			
	60+ y			
Age at diagnosis	< 5 y			
	5-9 y			
	10-14 y			
	15-21 y			
Physical activity	Yes			
	No			
Smoking	Never			
	Current			
	Former			

\*Other factors found to be important will be shown

**Table 4 (AIM 2): Erectile function, as reported on IIEF questions 1-5 and 15 (Erectile Function domain), in all survivors by demographics, including age at diagnosis and primary diagnosis (reported as medians)**

	1 (H1) How often were you able to get an erection during sexual activity?	2 (H2) When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	3 (H3) When you attempted sexual intercourse, how often were you able to penetrate your partner?	4 (H4) During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner?	5 (H5) During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	15 (H15) How do you rate your confidence that you could get and keep an erection?	<b>Erectile Function Domain of the IIEF (Sum score of questions 1-5, 15) MHQ H1-H5, H15</b>	
	Median	Median	Median	Median	Median	Median	Median	Range
<b>TOTAL COHORT</b>								
<b>Ethnicity</b>								
<b>Age at Assessment</b>								
<b>Marital Status</b>								
<b>Substance use</b>								
<b>Physical Activity</b>								
<b>Highest Level of Education</b>								
<b>Employment</b>								
<b>Income</b>								
<b>Insurance</b>								
<b>Age at Diagnosis</b>								
<b>Cancer Diagnosis</b>								
<b>General Health</b>								
<b>Psychiatric illness</b>								
<b>Spinal Injury</b>								
<b>Prostate Disease</b>								

**Table 5 (AIM 2): Characteristics of cohort reporting difficulty in either obtaining or maintaining erections**

	Total Survivors in MHQ	Survivors reporting Erectile Difficulty	Survivors not reporting Erectile Difficulty	Total Siblings in MHQ	Siblings reporting Erectile Difficulty	Siblings not reporting Erectile Difficulty
<b>TOTAL COHORT</b>						
<b>Ethnicity</b>						
<b>Age at Assessment</b>						
<b>Marital Status</b>						
<b>Substance use</b>						
<b>Physical Activity</b>						
<b>Highest Level of Education</b>						
<b>Employment</b>						
<b>Income</b>						
<b>Insurance</b>						
<b>Age at Diagnosis</b>						
<b>Cancer Diagnosis</b>						
<b>General Health</b>						
<b>psychiatric illness</b>						
<b>Spinal Injury</b>						
<b>Prostate Disease</b>						

**Table 6 (AIM 3): Psychosexual function, as reported on standardized questionnaires, in survivors by age at diagnosis, primary diagnosis and treatment exposure**

**Table 6a (International Index of Erectile Function)**

	<b>IIEF Total Score (H1-H15 totalled)</b>	<b>Erectile Function Domain (H1-5+ H15 totalled)</b>	<b>Abnormal Erectile Function Domain (EF score &lt;26)</b>	<b>Orgasmic Function Domain (H9+H10)</b>	<b>Sexual Desire Domain (H11+ H12)</b>	<b>Intercourse Satisfaction Domain (H6+H7+H8)</b>	<b>Overall Satisfaction Domain (H13+H14)</b>
	Median	Median		Median	Median	Median	Median
<b>TOTAL COHORT (All survivors no recurrence /SMN)</b>							
<b>Age at Diagnosis</b>							
<b>Cancer Diagnosis</b>							
<b>COG LTFUG- Defined Exposure Risk</b>							
<b>Alkylator exposure Summed AAD Or cyclophosphamide equivalents</b>							
<b>Radiation (in Gy)</b>							
Cranial							
Testicular Radiation							
TBI							
<b>Surgery GU or spinal</b>							
<b>General Health</b>							
<b>Need Help with Personal Care</b>							
<b>Need Help with Routine Activities</b>							
<b>Somatic Pain</b>							
<b>Interference of Pain with Normal Work</b>							
<b>Location of Pain</b>							
<b>Current Problem with Learning or Memory</b>							
<b>Anxiety/Fears about Cancer History</b>							
<b>Concerns of Ability to Have Children</b>							
<b>Weakness of inability to move legs</b>							
<b>Timing of Puberty</b>							
<b>Testosterone Treatment</b>							
<b>Erectile Dysfunction Treatment</b>							

**Table 6b (Sexual Function Questionnaire)**

	SFQ Total Score	Interest	Desire	Arousal	Orgasm	Satisfaction	Activity	Relationship	Masturbation	Problems
<b>TOTAL COHORT (All survivors no recurrence /SMN))</b>										
<b>Age at Diagnosis</b>										
<b>Cancer Diagnosis</b>										
<b>COG LTFUG- Defined Exposure Risk</b>										
<b>Alkylator exposure Summed AAD Or cyclophosphamide equivalents</b>										
<b>Radiation (in Gy)</b>										
Cranial										
Testicular Radiation										
TBI										
<b>Surgery GU or spinal</b>										
<b>General Health</b>										
<b>Need Help with Personal Care</b>										
<b>Need Help with Routine Activities</b>										
<b>Somatic Pain</b>										
<b>Interference of Pain with Normal Work</b>										
<b>Location of Pain</b>										
<b>Current Problem with Learning or Memory</b>										
<b>Anxiety/Fears about Cancer History</b>										
<b>Concerns of Ability to Have Children</b>										
<b>Weakness of inability to move legs</b>										
<b>Timing of Puberty</b>										
<b>Testosterone Treatment</b>										
<b>Erectile Dysfunction Treatment</b>										





**Table 7 (AIM 3): Effects of Cancer Treatment on Male Sexual Function in Childhood Cancer Survivors by Self-Reported answers on the MHQ**

	Total in MHQ	Survivors reporting Erectile Difficulty	Survivors reporting Lack of sexual interest or desire	Survivors reporting Delayed Ejaculation	Survivors reporting Anxiety about sexual performance	Survivors reporting Inability to achieve orgasm	Survivors reporting Pain during penetration or intercourse	Survivors reporting Other problem with sexuality
	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)
<b>TOTAL COHORT (All survivors)</b>								
<b>General Health</b>								
<b>Need Help with Personal Care</b>								
<b>Need Help with Routine Activities</b>								
<b>Pain</b>								
<b>Current Problem with Learning or Memory</b>								
<b>Anxiety/Fears about Cancer History</b>								
<b>Concerns of Ability to Have Children</b>								
<b>Weakness of inability to move legs</b>								
<b>Timing of Puberty</b>								
<b>Testosterone Treatment</b>								
<b>Erectile Dysfunction Treatment</b>								
<b>Primary Diagnosis</b>								
<b>Age at Diagnosis</b>								
<b>COG LTFUG-Defined Exposure Risk</b>								
<b>Alkylator exposure (Summed AAD Or cyclophosphamide equivalents)</b>								
<b>Radiation (in Gy)</b>								
Cranial								
Testicular Radiation								
TBI								
<b>Surgery GU or spinal</b>								

**Table 8 (AIM 4): Frequency of ED treatment in survivors versus siblings**

	<b>MHQ Survivors</b>	<b>MHQ Siblings</b>
<b>TOTAL COHORT</b>		
<b>Treatment for ED</b>		
<b>Current treatment for ED</b>		
<b>Medical treatment for ED</b>		
<b>Other medical therapy for sexual dysfunction (e.g. mechanical pump)</b>		
<b>Surgical therapy for sexual dysfunction</b>		

**Table 9 (AIM 4): Frequency of ED treatments in Survivors**

	<b>Ever treated for ED</b>	<b>Medical therapy (PDE5i or other) for</b>	<b>Other medical therapy for sexual dysfunction (device)</b>	<b>Surgical therapy for sexual dysfunction</b>
	N(%)	N(%)	N(%)	N(%)
<b>TOTAL COHORT (All survivors)</b>				
<b>Era of treatment</b>				
<b>Age at Diagnosis</b>				
<b>Cancer Diagnosis</b>				
<b>COG LTFUG- Defined Exposure Risk</b>				
<b>Alkylator exposure (Summed AAD Or cyclophosphamide equivalents)</b>				
<b>Radiation (in Gy)</b>				
Cranial				
Testicular Radiation				
TBI				
<b>Surgery GU or spinal</b>				
<b>General Health</b>				
<b>Need Help with Personal Care</b>				
<b>Need Help with Routine Activities</b>				
<b>Somatic Pain</b>				
<b>Interference of Pain with Normal Work</b>				
<b>Location of Pain</b>				
<b>Current Problem with Learning or Memory</b>				
<b>Anxiety/Fears about Cancer History</b>				
<b>Concerns of Ability to Have Children</b>				
<b>Weakness of inability to move legs</b>				
<b>Timing of Puberty</b>				
<b>Testosterone Treatment</b>				

## The second set of Detailed Tables

Note: The following tables are constructed with the acknowledgement that not all would be used in a publication but are included to show the descriptive analysis that will be carried out in the initial steps of the review

**Table 1 (AIM 1): Prevalence of Sexual Experiences by demographic characteristics of cohort**

	All Survivors	All Survivors with previous sexual experiences (C4#"none of the above")	All Survivors with no reply to previous sexual experiences (C4#"no reply")	All Survivors with previous sexual intercourse (C3=yes)	All Siblings	All Siblings with previous sexual experiences (C4#"none of the above")	All Survivors with no reply to previous sexual experiences (C4#"no reply")	All Siblings with previous sexual intercourse (C3=yes)
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
<b>TOTAL COHORT</b>								
<b>Ethnicity</b>								
Non-Hispanic White								
Hispanic								
Non-Hispanic Black								
Other								
<b>Age at Assessment</b>								
Mean (range)								
20-29								
30-39								
40-49								
50-59								
60+								
<b>Marital Status</b>								
Single; never married								
Married								
Living as married								
Widowed								
Divorced								
Separated								
<b>Smoking Status (N7)</b>								
Never								
Current								
Former								
<b>Alcohol Use (N1)</b>								

Yes								
No								
<b>Alcohol Abuse (5+ drinks) (N6)</b>								
One day/week or more								
Less than one day per week								
<b>Physical Activity (N15)</b>								
Yes								
No								
<b>Moderate or Vigorous activity (N17; N20)</b>								
< 3 days per week								
3+ days per week								
<b>Highest Level of Education (A3)</b>								
Did not complete HS								
Completed HS or GED								
Non-college training after HS								
Some college								
College graduate								
Post graduate								
<b>Employment (A4)</b>								
Full time (30+ hours/wk)								
Part time (< 30 hr/wk)								
Caring for home/family								
Unemployed looking for work								
Unable to work								
Retired								
Student								
<b>Household Income (A6)</b>								
< \$20,000								
\$20,000-39,999								
\$40,000-59,999								
\$60,000-79,999								

\$80,000-99,999								
>\$100,000								
Don't know								
<b>Individual Income (A8)</b>								
None								
< \$20,000								
\$20,000-39,999								
\$40,000-59,999								
\$60,000-79,999								
\$80,000-99,999								
>\$100,000								
Don't know								
<b>Insurance (B9)</b>								
Yes								
No								
Canadian resident								
<b>Age at Diagnosis</b>								
< 5 years								
5-9 years								
10-14 years								
15-21 years								
<b>Cancer Diagnosis</b>								
Acute lymphoblastic leukemia								
Acute myeloid leukemia								
Other leukemia								
Astrocytoma								
Medulloblastoma								
PNET								
Other CNS tumor								
Hodgkins lymphoma								
Non-Hodgkins lymphoma								
Kidney tumor								
Neuroblastoma								
Soft tissue sarcoma								
Ewings sarcoma								
Osteosarcoma								
Other bone tumors								
<b>General Health</b>								

<b>(D1)</b>								
Excellent								
Very good								
Good								
Fair								
Poor								
<b>Depression (B1a)</b>								
Yes								
No								
<b>Obsessive Compulsive Disorder (B1b)</b>								
Yes								
No								
<b>Other major psychiatric illness (B1c)</b>								
Yes								
No								
<b>Spinal Injury (B1d)</b>								
Yes								
No								
<b>Prostate Disease (B1e)</b>								
Yes								
No								
<b>Addiction (B2)</b>								
Yes								
--Alcohol								
--Drugs								
No								



**Table 2 (AIM 1): Comparison of sexual practices in survivors and their male siblings**

	All MHQ Survivors (Number)	All MHQ Survivors (%)	MHQ Siblings (Number)	MHQ Siblings (%)	p- Value
<b>TOTAL COHORT</b>					
<b>State of health (D1)</b>					
Excellent					
Very good					
Good					
Fair					
Poor					
<b>Onset of puberty (C1)</b>					
Early					
Normal					
Late					
<b>Ejaculation (C2)</b>					
Yes					
--Age (mean)		y		y	
--Age (median)		y		y	
--Age (mode)		y		y	
No					
<b>Sexual Intercourse (C3)</b>					
Yes					
--Age (mean)		y		y	
--Age (median)		y		y	
--Age (mode)		y		y	
No					
<b>Recent Sexual Experiences (C4)</b>					
The opposite gender - women					
The same gender – men					
I have only masturbated					
I use sexual videos, internet, etc.					
None of the above					
No reply					
<b>Previous Sexual Experiences (C5)</b>					
The opposite gender - women					
The same gender – men					
I have only masturbated					
I use sexual videos, internet, etc.					
None of the above					
No reply					
<b>Sexually active in past year (G1)</b>					
Yes					

No					
<b>Sexually active in past month (G3)</b>					
Yes					
No					
<b>Frequency of thoughts, urges, fantasies, dreams in past month (G4)</b>					
Not at all					
Once					
2 or 3 times					
Once a week					
2 or 3 times a week					
Once a day					
More than once a day					
<b>Frequency of interest or desire by sexual activity in past month (G5)</b>					
Dreams or fantasy					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
Masturbation					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
Touching, hugging, holding, kissing					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
Petting or foreplay					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					

--Once a day					
--More than once a day					
Intercourse					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
Other sexual activity					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
<b>Frequency of arousal by sexual activity in past month (G6)</b>					
Dreams or fantasy					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
Masturbation					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
Touching, hugging, holding, kissing					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
Petting or foreplay					
--Not at all					

--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
<b>Intercourse</b>					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
<b>Other sexual activity</b>					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
<b>Pleasure from any sexual activity in past month (G7)</b>					
I have had no sexual activity					
I have not felt any pleasure					
Seldom, less than 25% of time					
Sometimes, about 50% of time					
Usually, about 75% of time					
Always felt pleasure					
<b>Frequency of activities in past month (G8)</b>					
<b>Dreams or fantasy</b>					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
<b>Masturbation</b>					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					

Touching, hugging, holding, kissing					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
Petting or foreplay					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
Intercourse					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
Other sexual activity					
--Not at all					
--Once					
--2 to 3 times					
--Once a week					
--2 to 3 times per week					
--Once a day					
--More than once a day					
<b>Reached orgasm (ejaculation) in past month (G9)</b>					
I have had no sexual activity					
I have not experienced orgasm					
Seldom, less than 25% of time					
Sometimes, about 50% of time					
Usually, about 75% of time					
Always experienced orgasm					
<b>Intensiveness of orgasms in past month (G10)</b>					
No sexual activity					
No orgasms					
Very mild					
Fairly mild					
Fairly strong					

Very strong					
<b>Ease of orgasms in past month (G11)</b>					
No sexual activity					
No orgasms					
Very difficult					
Fairly difficult					
Fairly easy					
Very easy					
<b>SFQ Score</b>					
Total Score					
--Interest subscale					
--Desire subscale					
--Arousal subscale					
--Orgasm subscale					
--Satisfaction subscale					
--Activity subscale					
--Relationship subscale					
--Masturbation subscale					
--Problems subscale					

**Table 3 (AIM 1): Multivariable analysis**

**Table 3a**

**Previous sexual experiences in survivors and their male siblings (multivariable analysis)**

		Odds Ratio	95% Confidence Intervals	p- Value
Siblings				
Survivors				
Age at asesment	20-29 y			
	30-39 y			
	40-49 y			
	50-59 y			
	60+ y			
Age at diagnosis	< 5 y			
	5-9 y			
	10-14 y			
	15-21 y			
Physical activity	Yes			
	No			
Smoking	Never			
	Current			
	Former			

\*Other factors found to be important will be shown

**Table 3b**  
**Previous sexual intercourse in survivors and their male siblings (multivariable analysis)**

		Odds Ratio	95% Confidence Intervals	p- Value
Sibling				
Survivor				
Age at asesment	20-29 y			
	30-39 y			
	40-49 y			
	50-59 y			
	60+ y			
Age at diagnosis	< 5 y			
	5-9 y			
	10-14 y			
	15-21 y			
Physical activity	Yes			
	No			
Smoking	Never			
	Current			
	Former			

\*Other factors found to be important will be shown



**Table 4 (AIM 2): Erectile function, as reported on IIEF questions 1-5 and 15 (Erectile Function domain), in all survivors by demographics, including age at diagnosis and primary diagnosis (reported as medians)**

	1 (H1) How often were you able to get an erection during sexual activity?	2 (H2) When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	3 (H3) When you attempted sexual intercourse, how often were you able to penetrate your partner?	4 (H4) During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner?	5 (H5) During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	15 (H15) How do you rate your confidence that you could get and keep an erection?	<b>Erectile Function Domain of the IIEF (Sum score of questions 1-5, 15) MHQ H1-H5, H15</b>	
	Median	Median	Median	Median	Median	Median	Median	Range
<b>TOTAL COHORT</b>								
<b>Ethnicity</b>								
Non-Hispanic White								
Hispanic								
Non-Hispanic Black								
Other								
<b>Age at Assessment</b>								
Mean (range)								
20-29								
30-39								
40-49								
50-59								
60+								
<b>Marital Status</b>								
Single; never married								
Married								
Living as married								
Widowed								
Divorced								
Separated								
<b>Smoking Status (N7)</b>								
Never								
Current								
Former								
<b>Alcohol Use (N1)</b>								
Yes								
No								
<b>Alcohol Abuse (5+ drinks) (N6)</b>								
One day/week or more								
Less than one day								

per week								
<b>Physical Activity (N15)</b>								
Yes								
No								
<b>Moderate or Vigorous activity (N17; N20)</b>								
< 3 days per week								
3+ days per week								
<b>Highest Level of Education (A3)</b>								
Did not complete HS								
Completed HS or GED								
Non-college training after HS								
Some college								
College graduate								
Post graduate								
<b>Employment (A4)</b>								
Full time (30+ hours/wk)								
Part time (< 30 hr/wk)								
Caring for home/family								
Unemployed looking for work								
Unable to work								
Retired								
Student								
<b>Household Income (A6)</b>								
< \$20,000								
\$20,000-39,999								
\$40,000-59,999								
\$60,000-79,999								
\$80,000-99,999								
>\$100,000								
Don't know								
<b>Individual Income (A8)</b>								
None								
< \$20,000								
\$20,000-39,999								
\$40,000-59,999								
\$60,000-79,999								
\$80,000-99,999								
>\$100,000								
Don't know								
<b>Insurance (B9)</b>								

Yes								
No								
Canadian resident								
<b>Age at Diagnosis</b>								
< 5 years								
5-9 years								
10-14 years								
15-21 years								
<b>Cancer Diagnosis</b>								
Acute lymphoblastic leukemia								
Acute myeloid leukemia								
Other leukemia								
Astrocytoma								
Medulloblastoma								
PNET								
Other CNS tumor								
Hodgkins lymphoma								
Non-Hodgkins lymphoma								
Kidney tumor								
Neuroblastoma								
Soft tissue sarcoma								
Ewings sarcoma								
Osteosarcoma								
Other bone tumors								
<b>General Health (D1)</b>								
Excellent								
Very good								
Good								
Fair								
Poor								
<b>Depression (B1a)</b>								
Yes								
No								
<b>Obscensive Compulsive Disorder (B1b)</b>								
Yes								
No								
<b>Other major psychiatric illness (B1c)</b>								
Yes								
No								
<b>Spinal Injury (B1d)</b>								
Yes								

No								
<b>Prostate Disease (B1e)</b>								
Yes								
No								
<b>Addiction (B2)</b>								
Yes								
--Alcohol								
--Drugs								
No								

**Table 5 (AIM 2): Characteristics of cohort reporting difficulty in either obtaining or maintaining erections**

	Total Survivors in MHQ	Survivors reporting Erectile Difficulty (G12a ≠ "not at all" AND/OR G12c ≠ "not at all")	Survivors not reporting Erectile Difficulty (G12a = "not at all" AND G12c = "not at all")	Total Siblings in MHQ	Siblings reporting Erectile Difficulty (G12a ≠ "not at all" AND/OR G12c ≠ "not at all")	Siblings not reporting Erectile Difficulty (G12a = "not at all" AND G12c = "not at all")
<b>TOTAL COHORT</b>						
<b>Ethnicity</b>						
Non-Hispanic White						
Hispanic						
Non-Hispanic Black						
Other						
<b>Age at Assessment</b>						
Mean (range)						
20-29						
30-39						
40-49						
50-59						
60+						
<b>Marital Status</b>						
Single; never married						
Married						
Living as married						
Widowed						
Divorced						
Separated						
<b>Smoking Status (N7)</b>						
Never						
Current						
Former						
<b>Alcohol Use (N1)</b>						
Yes						
No						
<b>Alcohol Abuse (5+ drinks) (N6)</b>						
One day/week or						

more						
Less than one day per week						
<b>Physical Activity (N15)</b>						
Yes						
No						
<b>Moderate or Vigorous activity (N17; N20)</b>						
< 3 days per week						
3+ days per week						
<b>Highest Level of Education (A3)</b>						
Did not complete HS						
Completed HS or GED						
Non-college training after HS						
Some college						
College graduate						
Post graduate						
<b>Employment (A4)</b>						
Full time (30+ hours/wk)						
Part time (< 30 hr/wk)						
Caring for home/family						
Unemployed looking for work						
Unable to work						
Retired						
Student						
<b>Household Income (A6)</b>						
< \$20,000						
\$20,000-39,999						
\$40,000-59,999						
\$60,000-79,999						
\$80,000-99,999						
>\$100,000						
Don't know						
<b>Individual Income (A8)</b>						

None						
< \$20,000						
\$20,000-39,999						
\$40,000-59,999						
\$60,000-79,999						
\$80,000-99,999						
>\$100,000						
Don't know						
<b>Insurance (B9)</b>						
Yes						
No						
Canadian resident						
<b>Age at Diagnosis</b>						
< 5 years						
5-9 years						
10-14 years						
15-21 years						
<b>Cancer Diagnosis</b>						
Acute lymphoblastic leukemia						
Acute myeloid leukemia						
Other leukemia						
Astrocytoma						
Medulloblastoma						
PNET						
Other CNS tumor						
Hodgkins lymphoma						
Non-Hodgkins lymphoma						
Kidney tumor						
Neuroblastoma						
Soft tissue sarcoma						
Ewings sarcoma						
Osteosarcoma						
Other bone tumors						
<b>General Health (D1)</b>						
Excellent						
Very good						
Good						
Fair						

Poor						
<b>Depression (B1a)</b>						
Yes						
No						
<b>Obsessive Compulsive Disorder (B1b)</b>						
Yes						
No						
<b>Other major psychiatric illness (B1c)</b>						
Yes						
No						
<b>Spinal Injury (B1d)</b>						
Yes						
No						
<b>Prostate Disease (B1e)</b>						
Yes						
No						
<b>Addiction (B2)</b>						
Yes						
--Alcohol						
--Drugs						
No						



**Table 6 (AIM 3): Psychosexual function, as reported on standardized questionnaires, in survivors by age at diagnosis, primary diagnosis and treatment exposure**

**Table 6a (International Index of Erectile Function)**

	<b>IIEF Total Score (H1-H15 totaled)</b>	Erectile Function Domain (H1-5+ H15 totaled)	Abnormal Erectile Function Domain (EF score <26)	Orgasmic Function Domain (H9+H10)	Sexual Desire Domain (H11+ H12)	Intercourse Satisfaction Domain (H6+H7+H8)	Overall Satisfaction Domain (H13+H14)
	Median	Median	Percentage	Median	Median	Median	Median
<b>TOTAL COHORT (All survivors without recurrence or SMN)</b>							
<b>Age at Diagnosis</b>							
< 5 years							
5-9 years							
10-14 years							
15-21 years							
<b>Cancer Diagnosis</b>							
Acute lymphoblastic leukemia							
Acute myeloid leukemia							
Other leukemia							
Astrocytoma							
Medulloblastoma							
PNET							
Other CNS tumor							
Hodgkins lymphoma							
Non-Hodgkins lymphoma							
Kidney tumor							
Neuroblastoma							
Soft tissue sarcoma							
Ewings sarcoma							
Osteosarcoma							
Other bone tumors							
<b>COG LTFUG-Defined Exposure Risk</b>							
Yes							
No							
<b>Alkylator exposure Summed AAD Or cyclophosphamide equivalents</b>							
0							

1							
2							
3							
4							
5							
6+							
<b>Radiation (in Gy)</b>							
Cranial (Hypothalamic/ pituitary Radiation)							
None							
<20							
20-20.99							
≥ 30							
Testicular Radiation							
None							
<4							
≥ 4							
TBI							
Yes							
No							
<b>Surgery (B3)</b>							
Unilateral Orchiectomy							
Yes							
No							
Bilateral Orchiectomy							
Yes							
No							
Other testicular surgery							
Yes							
No							
Prostate surgery (B3a)							
Yes							
No							
Pelvic surgery (B3b)							
Yes							
No							
Penis surgery (B3c)							
Yes							
No							
Operations on the Nervous System (MRAF; Baseline; FU 2007)							
03.X—Operations on spinal cord and spinal canal structures							
05.X—Operations on sympathetic nerves							

or ganglia							
<b>General Health (D1)</b>							
Excellent							
Very good							
Good							
Fair							
Poor							
<b>Need Help with Personal Care (N22)</b>							
Yes							
No							
<b>Need Help with Routine Activities (N23)</b>							
Yes							
No							
<b>Somatic Pain (L21)</b>							
None							
Very mild							
Mild							
Moderate							
Severe							
Very Severe							
<b>Interference of Pain with Normal Work (L22)</b>							
Not at all							
A little bit							
Moderately							
Quite a bit							
Extremely							
<b>Location of Pain (L23)</b>							
Head							
Neck							
Chest							
Hands/Arms							
Abdomen							
Back							
Pelvis							
Legs/Feet							
Other							
<b>Current Problem with Learning or Memory (K1)</b>							
No (Includes condition no longer present)							
Mild							
Moderate							
Severe							
Disabling							
<b>Anxiety/Fears</b>							

<b>about Cancer History (L20)</b>									
No									
Small amount									
Medium amount									
A lot									
Very many/extreme									
<b>Concerns of Ability to Have Children (O2)</b>									
Very									
Somewhat									
Concerned									
Not very									
Not at all									
<b>Weakness of inability to move legs (K12)</b>									
Yes - current									
No – includes condition no longer present									
<b>Timing of Puberty (C1)</b>									
Early									
Normal									
Late									
<b>Testosterone Treatment (B4, B6)</b>									
Yes ever (B4)									
No ever (B4)									
Yes current (B6)									
No current (B6)									
<b>Erectile Dysfunction Treatment (B11)</b>									
Yes									
No									

**Table 6b (Sexual Function Questionnaire)**

	SFQ Total Score	Interest	Desire	Arousal	Orgasm	Satisfaction	Activity	Relationship	Masturbation	Problems
<b>TOTAL COHORT (All survivors without recurrence or SMN)</b>										
<b>Age at Diagnosis</b>										
< 5 years										
5-9 years										
10-14 years										
15-21 years										

<b>Cancer Diagnosis</b>										
Acute lymphoblastic leukemia										
Acute myeloid leukemia										
Other leukemia										
Astrocytoma										
Medulloblastoma										
PNET										
Other CNS tumor										
Hodgkins lymphoma										
Non-Hodgkins lymphoma										
Kidney tumor										
Neuroblastoma										
Soft tissue sarcoma										
Ewings sarcoma										
Osteosarcoma										
Other bone tumors										
<b>COG LTFUG-Defined Exposure Risk</b>										
Yes										
No										
<b>Alkylator exposure (Summed AAD Or cyclophosphamide equivalents)</b>										
0										
1										
2										
3										
4										
5										
6+										
<b>Radiation (in Gy)</b>										
<b>Cranial (Hypothalamic/pituitary Radiation)</b>										
None										
<20										
20-30										
≥ 30										
<b>Testicular Radiation</b>										
None										
<4										
≥ 4										
<b>TBI</b>										
Yes										
No										
<b>Surgery (B3)</b>										

Unilateral Orchiectomy										
Yes										
No										
Bilateral Orchiectomy										
Yes										
No										
Other testicular surgery										
Yes										
No										
Prostate surgery (B3a)										
Yes										
No										
Pelvic surgery (B3b)										
Yes										
No										
Penis surgery (B3c)										
Yes										
No										
Operations on the Nervous System (MRAF; Baseline; FU 2007)										
03.X—Operations on spinal cord and spinal canal structures										
05.X—Operations on sympathetic nerves or ganglia										
<b>General Health (D1)</b>										
Excellent										
Very good										
Good										
Fair										
Poor										
<b>Need Help with Personal Care (N22)</b>										
Yes										
No										
<b>Need Help with Routine Activities (N23)</b>										
Yes										
No										
<b>Somatic Pain (L21)</b>										
None										
Very mild										

Mild										
Moderate										
Severe										
Very Severe										
<b>Interference of Pain with Normal Work (L22)</b>										
Not at all										
A little bit										
Moderately										
Quite a bit										
Extremely										
<b>Location of Pain (L23)</b>										
Head										
Neck										
Chest										
Hands/Arms										
Abdomen										
Back										
Pelvis										
Legs/Feet										
Other										
<b>Current Problem with Learning or Memory (K1)</b>										
No (Includes condition no longer present)										
Mild										
Moderate										
Severe										
Disabling										
<b>Anxiety/Fears about Cancer History (L20)</b>										
No										
Small amount										
Medium amount										
A lot										
Very many/extreme										
<b>Concerns of Ability to Have Children (O2)</b>										
Very										
Somewhat										
Concerned										
Not very										
Not at all										
<b>Weakness of inability to move legs (K12)</b>										
Yes - current										

No – includes condition no longer present										
<b>Timing of Puberty (C1)</b>										
Early										
Normal										
Late										
<b>Testosterone Treatment (B4, B6)</b>										
Yes ever (B4)										
No ever (B4)										
Yes current (B6)										
No current (B6)										
<b>Erectile Dysfunction Treatment (B11)</b>										
Yes										
No										



**Table 7 (AIM 3): Effects of Cancer Treatment on Male Sexual Function in Childhood Cancer Survivors by Self-Reported answers on the MHQ**

	Total in MHQ	Survivors reporting Erectile Difficulty (G12a ≠ "not at all" AND/OR G12c ≠ "not at all")	Survivors reporting Lack of sexual interest or desire (G12b ≠ "not at all")	Survivors reporting Delayed Ejaculation (G12d ≠ "not at all")	Survivors reporting Anxiety about sexual performance (G12e ≠ "not at all")	Survivors reporting Inability to achieve orgasm (G12f ≠ "not at all")	Survivors reporting Pain during penetration or intercourse (G12g ≠ "not at all")	Survivors reporting Other problem with sexuality (G12h ≠ "not at all")
	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)
<b>TOTAL COHORT (All survivors)</b>								
<b>General Health (D1)</b>								
Excellent								
Very good								
Good								
Fair								
Poor								
<b>Need Help with Personal Care (N22)</b>								
Yes								
No								
<b>Need Help with Routine Activities (N23)</b>								
Yes								
No								
<b>Somatic Pain (L21)</b>								
None								
Very mild								
Mild								
Moderate								
Severe								
Very Severe								
<b>Interference of Pain with Normal Work (L22)</b>								
Not at all								
A little bit								
Moderately								
Quite a bit								
Extremely								
<b>Location of Pain (L23)</b>								

Head								
Neck								
Chest								
Hands/Arms								
Abdomen								
Back								
Pelvis								
Legs/Feet								
Other								
<b>Current Problem with Learning or Memory (K1)</b>								
No (Includes condition no longer present)								
Mild								
Moderate								
Severe								
Disabling								
<b>Anxiety/Fears about Cancer History (L20)</b>								
No								
Small amount								
Medium amount								
A lot								
Very many/extreme								
<b>Concerns of Ability to Have Children (O2)</b>								
Very								
Somewhat								
Concerned								
Not very								
Not at all								
<b>Weakness of inability to move legs (K12)</b>								
Yes - current								
No – includes condition no longer present								
<b>Timing of Puberty (C1)</b>								
Early								
Normal								
Late								
<b>Testosterone Treatment (B4, B6)</b>								
Yes ever (B4)								

No ever (B4)								
Yes current (B6)								
No current (B6)								
<b>Erectile Dysfunction Treatment (B11)</b>								
Yes								
No								
<b>Primary Diagnosis</b>								
ALL								
AML								
Other leukemia								
Astrocytoma								
Medulloblastoma								
Other CNS								
Hodgkins								
NHL								
Kidney								
Neuroblastoma								
Soft Tissue Sarcoma								
Ewings Sarcoma								
Osteosarcoma								
Other sarcoma								
<b>Age at Diagnosis</b>								
0-4								
5-9								
10-14								
15+								
<b>COG LTFUG-Defined Exposure Risk</b>								
Yes								
No								
<b>Alkylator exposure (Summed AAD Or cyclophosphamide equivalents)</b>								
0								
1								
2								
3								
4								
5								
6+								
<b>Radiation (in Gy)</b>								
Cranial (Hypothalamic/pituitary Radiation)								

None								
<20								
20-20.99								
≥ 30								
Testicular Radiation								
None								
<4								
≥ 4								
TBI								
Yes								
No								
<b>Surgery (B3)</b>								
Unilateral Orchiectomy								
Yes								
No								
Bilateral Orchiectomy								
Yes								
No								
Other testicular surgery								
Yes								
No								
Prostate surgery (B3a)								
Yes								
No								
Pelvic surgery (B3b)								
Yes								
No								
Penis surgery (B3c)								
Yes								
No								
Operations on the Nervous System (MRAF; Baseline; FU 2007)								
03.X—Operations on spinal cord and spinal canal structures								
05.X—Operations on sympathetic nerves or ganglia								

**Table 8 (AIM 4): Frequency of ED treatment in survivors versus siblings**

	<b>MHQ Survivors</b>	<b>MHQ Siblings</b>
<b>TOTAL COHORT</b>		
<b>Treatment for ED (B11)</b>		
Yes		
No		
<b>Current treatment for ED (B12b)</b>		
Yes		
No		
<b>Medical treatment for ED (B12)</b>		
Yes		
No		
<b>Other medical therapy for sexual dysfunction (e.g. mechanical pump) (B14)</b>		
Yes		
No		
<b>Surgical therapy for sexual dysfunction (B13)</b>		
Yes		
No		

**Table 9 (AIM 4): Frequency of ED treatments by survivor and sibling demographics**

	All Survivors	All Survivors with previous ED treatment (B11=yes)	All Survivors with current treatment for ED (B12b=yes)	All Survivors with medical treatment for ED (B12=yes)	All Siblings	All Siblings with previous ED treatment (B11=yes)	All Survivors with current treatment for ED (B12b=yes)	All Siblings with medical treatment for ED (B12=yes)
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
<b>TOTAL COHORT</b>								
<b>Ethnicity</b>								
Non-Hispanic White								
Hispanic								
Non-Hispanic Black								
Other								
<b>Age at Assessment</b>								
Mean (range)								
20-29								
30-39								
40-49								
50-59								
60+								
<b>Marital Status</b>								
Single; never married								
Married								
Living as married								
Widowed								
Divorced								
Separated								
<b>Smoking Status (N7)</b>								
Never								
Current								
Former								
<b>Alcohol Use (N1)</b>								
Yes								
No								
<b>Alcohol Abuse (5+ drinks) (N6)</b>								
One day/week or more								
Less than one day per week								
<b>Physical Activity (N15)</b>								

Yes								
No								
<b>Moderate or Vigorous activity (N17; N20)</b>								
< 3 days per week								
3+ days per week								
<b>Highest Level of Education (A3)</b>								
Did not complete HS								
Completed HS or GED								
Non-college training after HS								
Some college								
College graduate								
Post graduate								
<b>Employment (A4)</b>								
Full time (30+ hours/wk)								
Part time (< 30 hr/wk)								
Caring for home/family								
Unemployed looking for work								
Unable to work								
Retired								
Student								
<b>Household Income (A6)</b>								
< \$20,000								
\$20,000-39,999								
\$40,000-59,999								
\$60,000-79,999								
\$80,000-99,999								
>\$100,000								
Don't know								
<b>Individual Income (A8)</b>								
None								
< \$20,000								
\$20,000-39,999								
\$40,000-59,999								

\$60,000-79,999								
\$80,000-99,999								
>\$100,000								
Don't know								
<b>Insurance (B9)</b>								
Yes								
No								
Canadian resident								
<b>General Health (D1)</b>								
Excellent								
Very good								
Good								
Fair								
Poor								
<b>Depression (B1a)</b>								
Yes								
No								
<b>Obsessive Compulsive Disorder (B1b)</b>								
Yes								
No								
<b>Other major psychiatric illness (B1c)</b>								
Yes								
No								
<b>Spinal Injury (B1d)</b>								
Yes								
No								
<b>Prostate Disease (B1e)</b>								
Yes								
No								
<b>Addiction (B2)</b>								
Yes								
--Alcohol								
--Drugs								
No								



**Table 10 (AIM 4): Frequency of ED treatments in Survivors**

	<b>Ever treated for ED (B11)</b>	<b>Medical therapy (PDE5i or other) for ED (B12)</b>	<b>Other medical therapy for sexual dysfunction (device) (B14)</b>	<b>Surgical therapy for sexual dysfunction (B13)</b>
	N(%)	N(%)	N(%)	N(%)
<b>TOTAL COHORT (All survivors)</b>				
<b>Era of treatment</b>				
1970-1975				
1976-1980				
1981-1986				
<b>Age at Diagnosis</b>				
< 5 years				
5-9 years				
10-14 years				
15-21 years				
<b>Cancer Diagnosis</b>				
Acute lymphoblastic leukemia				
Acute myeloid leukemia				
Other leukemia				
Medulloblastoma				
PNET				
Other CNS tumor				
Hodgkins lymphoma				
Non-Hodgkins lymphoma				
Kidney tumor				
Neuroblastoma				
Soft tissue sarcoma				
Ewings sarcoma				
Osteosarcoma				
Other bone tumors				
<b>COG LTFUG- Defined Exposure Risk</b>				
Yes				
No				
<b>Alkylator exposure (Summed AAD Or cyclophosphamide equivalents)</b>				
0				
1				
2				
3				
4				

5				
6+				
<b>Radiation (in Gy)</b>				
Cranial (Hypothalamic/ pituitary Radiation)				
None				
<20				
20-30				
≥ 30				
Testicular Radiation				
None				
<4				
≥ 4				
TBI				
Yes				
No				
<b>Surgery (B3)</b>				
Unilateral Orchiectomy				
Yes				
No				
Bilateral Orchiectomy				
Yes				
No				
Other testicular surgery				
Yes				
No				
Prostate surgery (B3a)				
Yes				
No				
Pelvic surgery (B3b)				
Yes				
No				
Penis surgery (B3c)				
Yes				
No				
Operations on the Nervous System (MRAF; Baseline; FU 2007)				
03.X—Operations on spinal cord and spinal canal structures				
05.X—Operations on sympathetic nerves or ganglia				
<b>General Health (D1)</b>				
Excellent				
Very good				
Good				
Fair				
Poor				
<b>Need Help with Personal Care (N22)</b>				

Yes				
No				
<b>Need Help with Routine Activities (N23)</b>				
Yes				
No				
<b>Somatic Pain (L21)</b>				
None				
Very mild				
Mild				
Moderate				
Severe				
Very Severe				
<b>Interference of Pain with Normal Work (L22)</b>				
Not at all				
A little bit				
Moderately				
Quite a bit				
Extremely				
<b>Location of Pain (L23)</b>				
Head				
Neck				
Chest				
Hands/Arms				
Abdomen				
Back				
Pelvis				
Legs/Feet				
Other				
<b>Current Problem with Learning or Memory (K1)</b>				
No (Includes condition no longer present)				
Mild				
Moderate				
Severe				
Disabling				
<b>Anxiety/Fears about Cancer History (L20)</b>				
No				
Small amount				
Medium amount				
A lot				
Very many/extreme				
<b>Concerns of Ability to Have Children (O2)</b>				
Very				
Somewhat				
Concerned				
Not very				
Not at all				

<b>Weakness of inability to move legs (K12)</b>				
Yes - current				
No – includes condition no longer present				
<b>Timing of Puberty (C1)</b>				
Early				
Normal				
Late				
<b>Testosterone Treatment (B4, B6)</b>				
Yes ever (B4)				
No ever (B4)				
Yes current (B6)				
No current (B6)				