02-02

CHILDHOOD CANCER SURVIVOR STUDY
Analysis Concept Proposal

1. **Title**: Education, Employment, Insurance and Marital Status Among Survivors of Pediatric Lower Extremity Bone Tumors.

2. **Working Group and Investigators**: Chronic Disease Committee
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3. **Background and Rationale:**

One particular group of survivors with potentially increased sequelae are adult survivors of pediatric lower extremity bone tumors. Those with bone tumors are not only exposed to significant amounts of chemotherapy, but also require extensive surgery (amputation or limb sparing procedures) and/or high doses of radiotherapy. Evidence of the extensive treatment can be quite noticeable (limp, inability to be fully active and amputation) and can alter one's self image since bone tumors predominantly occur in the extremities (lower > upper). The impact these treatments have on an individual are compounded by varying levels of emotional maturity (pre-adolescence and adolescence) and skeletal maturity of the child at the time of diagnosis. Emotional maturity may play an important role in psychosocial functioning because of one's development of body image, independence and relationships during adolescence. Skeletal maturity is another potential determinant of psychosocial sequelae because of its importance in determining the type of surgical local control (amputation/rotationplasty/expanding prosthesis vs. limb sparing surgeries) which can alter one's body image and infringe on self-reliance.

There are very few studies that attempt to describe and analyze psychosocial functioning of survivors of pediatric bone tumors. These studies provide some insight into the psychosocial issues in lower extremity tumors but are not limited to lower extremities, have small sample sizes, and are restricted to a limited number of institutions. With the establishment of the Childhood Cancer Survivor Study (CCSS), we have the opportunity to explore these issues in a large number of adult survivors of pediatric lower extremity bone tumors who are over 10 years out from their diagnosis.

4. **Specific Aims/Research Hypotheses:**

We plan to use the CCSS cohort to investigate those who have undergone an amputation or limb salvage for a lower extremity bone tumor to determine predictors of educational attainment, employment, health insurance, and marriage. Specific subgroups (age-surgery groups) designated

based on age (under or over 12 years at the time of diagnosis) and treatment (amputation or non-amputation). The age of 12 years as a cut off was picked because it serves as an approximate marker dividing adolescence and preadolescence and also divides those with and without significant growth potential.

	Amputation	Limb Salvage
<= 12 years old	≤12/Amp	≤12/LS
> 12 years old	>12/Amp	>12/LS

a. Primary hypothesis:
   I. There will be differences in psychosocial functioning between those who underwent limb-sparing surgeries (w+y) versus amputation (x+z) with age playing a significant role in the outcomes.

b. Secondary hypotheses:
   I. Psychosocial functioning will be highest in those who underwent a limb sparing procedure over the age of 12 years.
   II. Those under the age of 12 at the time of diagnosis who were treated with a limb sparing procedure will have the most difficulties.

5. **Analysis Framework:**
   a. Outcomes of interest: (Data collected from the baseline questionnaire)
      I. Marriage: Questions L1 and L2
      II. Education: O1 – High school graduate or College graduate
      III. Employment: O5 and O6
      IV. Health Insurance: Q1 and Q2

   b. Subject Population: All CCSS cases that have undergone a lower extremity limb surgery for osteogenic sarcoma or Ewing's sarcoma.
      I. There are 1042 survivors within the CCSS cohort who had a bone tumor(diagnosis code 8) who completed a baseline questionnaire and are either currently alive or died after completion. Of these 1009 were ≥18 years old at the time of completion and 718 had a diagnosis of osteosarcoma or Ewing's sarcoma of the lower extremity (ICD-0 codes of c40.2 and 41.2). 694 had an amputation (with or without a medical record abstracted) or a limb salvage procedure with a medical record abstraction. Preliminary assessment revealed that 243 (35%) patients were ≤ years of age at diagnosis and 471 (68%) underwent an amputation.
      II. The sibling cohort will also be analyzed for comparison to the subjects.

c. Explanatory Variables: Sex (A2), diagnosis (osteosarcoma or Ewing's), site of primary tumor (extremity or pelvis), age at diagnosis (≤12 years vs.> 12 years), age at baseline completion, time from diagnosis to baseline completion, type of surgery (amputation vs. non-amputation), age-surgery group (≤12/Amp, ≤12/LS, >12/LS, and >12/Amp).
   I. Principal investigator and an orthopedic surgeon using the ICD-9 designations and items I1, I4, I5 and I6 will determine type of surgery.
   II. Questions relating the "mental well Being": J16-J37 and N15 will be looked at for any correlations.

d. Specific Tables:
   I. Patient characteristics (overall, by amputation status (amputation vs. non-amputation), by age group (≤12 years vs.> 12 years), by age-surgery group (≤12/Amp, ≤12/LS, >12/LS, and >12/Amp)): sex, diagnosis x site of primary tumor, radiation use to primary site, age at diagnosis, age at baseline completion, and time since diagnosis to baseline completion.
   II. Outcome: Odds rations for education attainment, employment, health insurance, and marriage.
   III. For any comparisons between means of age, years of follow up, etc... I will be using t-test statistics.
   IV. In the univariate analysis, I plan on applying logistic regression (or I could use chi-square) by using the psychosocial variables as the dichotomous dependent variable and using the following as the dichotomous independent variables: gender (m/f), age at diagnosis (< 12,>12), amputation status (Amp/No amp), tumor type (Osteosarcoma/Ewing's), Site of tumor (pelvis/extremity), pelvic radiation (yes/no), college graduate (yes/no), married (yes/no) and work the past year (yes/no). For independent continuous variables current age and years of follow-up, I would use logistic regression.
   V. For the multivariate analysis, I also plan on applying logistic regression by using the same dichotomous dependent variables while adjusting for current age, years of follow and other appropriate variables (e.g. adjusting for college graduation and marital status when examining health insurance).
   VI. In the sibling analysis, I will be using the Generalized Estimating Equation (GEE) [Proc GLM] to calculate estimates of odds ratios for analyses comparing subjects and sibling.

Table 1: Demographics by amputation status and age at diagnosis. Over12 – Over the age of 12 years at diagnosis. Under12 – 12 years and younger at diagnosis.

Parameters # (%)	All 694 (100%)	Amputee 471 (67.9%)	Non-amputee	Over 12 451 (65.0%)	Under12 243 (35.0%)
Type/site of primary tumor:					
Osteosarcoma: Pelvic					
Osteosarcoma: Extremity					
Ewing's Sarcoma: Pelvic					
Ewing's Sarcoma: Extremity					
Radiation use to primary site:					
Limb Radiation					
Pelvic Radiation					
Age at Diagnosis					
Mean Years from Diagnosis to Baseline Questionnaire					
Age at Baseline Questionnaire					

Sex:
Male
Female

Table 2: Demographics by age-surgery group. ≤12/Amp: those under the age of 12 years at diagnosis with an amputation, >12/Amp: those over the age of 12 years at diagnosis with an amputation, ≤12/LS: those under the age of 12 years with a limb sparing treatment, and Over LS: those over the age of 12 years with a limb sparing treatment.

Parameters # (%)	All 694 (100%)	≤12/Amp 172 (24.8%)	≤12/LS 71 (10.2%)	>12/Amp 299 (43.1%)	>12/LS 152 (21.9%)
Type/site of primary tumor:					
Osteosarcoma: Pelvic					
Osteosarcoma: Extremity					
Ewing's Sarcoma: Pelvic					
Ewing's Sarcoma: Extremity					
Sex:					
Male					
Female					
Radiation use to primary site:					
Limb Radiation					
Pelvic Radiation					
Age at Diagnosis					
Mean Years from Diagnosis to Baseline Questionnaire					
Age at Baseline Questionnaire					

	Graduated High School (≤ 18 years old at diagnosis)		Graduated College (>25 years old at questionnaire completion)	
	# Respondents (% Graduated)	OR (95% C.I.)	# Respondents (% Graduated)	OR (95% C.I.)
Sex				
Female				
Male				
Age at Diagnosis				
> 12 years				
≤ 12 years				
Amputation				
No				
Yes				
Age-Surgery Group				
> 12/LS				
≤ 12/LS				
≤ 12/Amp				
> 12/Amp				
Tumor Type				
Ewings Sarcoma				
Osteosarcoma				
Primary Site				
Extremity				
Pelvic				
Pelvic Radiation				
No				
Yes				
Current Age				
Years from Diagnosis				

Table 3: Univariate Analysis of high school and college graduation

	Ever had a job		Employed Past Year	
	# Respondents (% employed)	OR (95% C.I.)	# Respondents (% employed)	OR (95% C.I.)
Sex				
Female				
Male				
Age at Diagnosis				
> 12 years				
≤ 12 years				
Amputation				
No				
Yes				
Age-Surgery Group				
> 12/LS				
≤ 12/LS				
≤ 12/Amp				
> 12/Amp				
Tumor Type				
Ewings Sarcoma				
Osteosarcoma				
Primary Site				
Extremity				
Pelvic				
High School Graduate				
No				
Yes				
College Graduate				
No				
Yes				
Current Age				
Years from Diagnosis				

Table 4: Univariate Analysis of Employment Issues

	Currently Have Health Insurance		Difficulty Obtaining Health Insurance	
	# Respondents (% insured)	OR (95% C.I.)	# Respondents (%having difficulty)	OR (95% C.I.)
Sex				
Female				
Male				
Age at Diagnosis				
> 12 years				
≤ 12 years				
Amputation				
No				
Yes				
Age-Surgery Group				
> 12/LS				
≤ 12/LS				
≤ 12/Amp				
> 12/Amp				
Tumor Type				
Ewings Sarcoma				
Osteosarcoma				
Primary Site				
Extremity				
Pelvic				
College Graduate				
No				
Yes				
Worked Past Year				
No				
Yes				
Current Marital Status				
Not Married				
Married				
Current Age				
Years from Diagnosis				

Table 5: Univariate Analysis of Health Insurance Issues

	Ever Married		Currently in First Marriage	
	# Respondents (% Married)	OR (95% C.I.)	# Respondents (% 1st Marriage)	OR (95% C.I.)
Sex				
Female				
Male				
Age at Diagnosis				
> 12 years				
≤ 12 years				
Amputation				
No				
Yes				
Age-Surgery Group				
> 12/LS				
≤ 12/LS				
≤ 12/Amp				
> 12/Amp				
Tumor Type				
Ewings Sarcoma				
Osteosarcoma				
Primary Site				
Extremity				
Pelvic				
Pelvic Radiation				
No				
Yes				
College Graduation				
No				
Yes				
Current Age				
Years from Diagnosis				

Table 6: Univariate Analysis of Marital Issues

OR (95% C.I.)	High School	College	Ever had a Job	Work the Past Year	Health Insurance	Health Insurance Problems	Ever Married	Currently in 1st Marriage
>12/LS (Reference)								
≤12/LS								
≤12/Amp								
>12/Amp								
Education								
High School								
College								
Sex (males vs. Females)								
Site (Pelvic vs. extremity)								
Currently Married								

Table 7: Multivariate Analysis – all analysis adjusted for current age and years since diagnosis. High school analysis includes only cases ≤ 18 years old at diagnosis. College analysis only includes siblings and cases over the age of 25 at questionnaire completion.
** P<0.005
* P<0.05

OR (95% C.I.)	High School	College	Ever had a job	Work the past year	Currently have health insurance	Health insurance problems	Ever been married	Currently in first marriage
All Cases (n=694)								
>12/LS (n=152)								
≤12/LS (n=71)								
>12/Amp (n=299)								
≤ 12/Amp (n=172)								

Table 8: Comparison to sibling cohort: High school analysis includes only cases ≤ 18 years old at diagnosis. College analysis only includes siblings and cases over the age of 25 years at questionnaire completion

** P<0.005

* P<0.05