Long-term Surveillance of Exposed Patient Populations:
Experience with Pediatric/Adolescent Cancer Survivors

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Long-term Surveillance of Exposed Patient Populations: Experience with Pediatric/Adolescent Cancer Survivors

- Childhood Cancer Survivor Cohorts
- Prospective vs. Retrospective
- Ascertainment of Long-term Outcomes
  - Patient-reported vs. Clinical Assessment
  - Cumulative Burden
  - Record Linkage
  - mHealth
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Childhood Cancers in the US: Survivorship Statistics

- Estimate 13,500 newly diagnosed cases annually
- >83% achieve five-year survival
- End of 2013, estimated number surpass 420,000
- 1 in 750 in the US is a childhood cancer survivor
- Number of survivors will approach 500,000 by 2020
Pediatric Cancer Survivor Cohorts

**CCSS**
Childhood Cancer Survivor Study Cohort
U24 CA55727 (PI: Armstrong)
35,937 Survivors (24,500+ participants)

**SJLIFE**
St. Jude Lifetime Cohort
U01 CA195547 (MPI: Hudson/Robison)
8245 Survivors (6000+ clinically assessed)
## Pediatric Cancer Survivor Cohorts

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CCSS (Dx 1970 - 1999)</th>
<th>SJLIFE (Dx 1962 - 2012)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort size</td>
<td>35,937 (24,000+ active participants)</td>
<td>8,245 (4,688 participants to date)</td>
</tr>
<tr>
<td>Entry criteria</td>
<td>≥5 years from diagnosis</td>
<td>≥5 years from diagnosis</td>
</tr>
<tr>
<td>Age at cancer diagnosis</td>
<td>&lt;21 years</td>
<td>&lt;25 years</td>
</tr>
<tr>
<td>Cancers</td>
<td>Leukemia, CNS, HL, NHL, neuroblastoma, soft tissue sarcoma, Wilms, bone tumors</td>
<td>All diagnoses</td>
</tr>
<tr>
<td>Study design</td>
<td>Retrospective cohort with prospective follow-up, hospital-based</td>
<td>Retrospective cohort with prospective follow-up, hospital-based</td>
</tr>
<tr>
<td>Methods of contact</td>
<td>Surveys</td>
<td>Clinic visits and surveys</td>
</tr>
<tr>
<td>Comparison population</td>
<td>Siblings, general population</td>
<td>Frequency-matched community controls, general population</td>
</tr>
<tr>
<td>Therapeutic exposures</td>
<td>&gt;90%</td>
<td>100%</td>
</tr>
<tr>
<td>Ascertainment methods</td>
<td>Self-report, pathology reports, NDI</td>
<td>Med. assessment, self-report, med. record, NDI</td>
</tr>
<tr>
<td>Collection of germline DNA</td>
<td>&gt;60%</td>
<td>&gt;95%</td>
</tr>
</tbody>
</table>
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Recruitment of the Initial CCSS Cohort

- Registered: 21,655
  - Eligible: 20,270
    - Ineligible: 1,385
    - Required Tracing: 7,913
      - In Process: 94
      - Lost to Follow-up: 2,996
  - Current Address: 12,363
  - Successful Contact: 17,280 (85%)
    - Located: 4,917
Recruitment of the Initial CCSS Cohort

- Successful Contact ($n=17,280$)
  - Baseline Data (Participant) $n=14,054$
  - Baseline Data (Non-Participant) $n=3,132$
  - Medical Release $n=12,752$
  - No Medical Release $n=1,302 (37\%$ Refused)
  - Medical Record Abstraction $n=12,455$
    - No Medical Record Abstraction $n=297$
      - Records Unavailable $n=0$
      - In Process $n=297$
    - Fully Evaluable Participant $n=12,455 (72\%)$
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Spectrum of Health-related and Quality of Life Outcomes

Robison and Hudson. Nat Rev Cancer, 2014
Engagement with Medical Care within Past 2-Years

Childhood Cancer Survivor Study

Oeffinger et al. Ann Fam Med, 2004
Prevalence - Yield of Risk-based Screening

**Abnormal Pulmonary Function**
- **At Risk = 417**

**Hearing Loss**
- **At Risk = 251**

**Breast Cancer**
- **At Risk Females= 133**

**At Risk Criteria**
- Bleomycin, Carmustine/Lomustine, Busulfan, Lung RT, or thoracotomy
- Cisplatin/Carboplatin or Ear RT
- >20 Gy RT to the breast
Prevalence - Yield of Risk-based Screening

![Graphs showing cumulative prevalence of Cardiomyopathy, Heart Valve Disorder, and Pituitary Dysfunction over age, with at risk numbers and conditions specified.]

At Risk Criteria
- Anthracycline/Anthraquinone or heart RT
- Heart RT
- ≥18 Gy RT hypothalamus-pituitary
Cumulative Prevalence of Chronic Health Conditions

Common Terminology Criteria, Version 4.03

Cumulative Prevalence of Chronic Health Conditions over Age (years) and Time from Diagnosis (years).
Long-term Survivors of Childhood Cancer
Cumulative Burden of Grade 3-5* Chronic Health Conditions

*Grade 3-5 Conditions
(Serious/disabling, Life-threatening or Fatal)

Importance of a comparison (referent) population

Bhakta et al. Lancet, 2017
Long-term Survivors of Childhood Cancer
Grade 3-5 Cumulative Burden By Organ System

Bhakta et al. Lancet, 2017
Record Linkage

- National Death Index
- Virtual Pooled Cancer Registry
- Administrative (Medicare, Medicaid)
- Others (Organ transplant, Assisted Reproduction)
Mobil Health (mHealth) Approaches

Welcome & Consent

Let’s get started by learning more about symptoms you may have had. This study is about checking your symptoms on a regular basis, which will help us design a better way to collect symptom data and find ways to help improve your symptoms.

Your Past Symptoms & Treatments

This section asks about how you have managed symptoms you may have experienced in the past. For each symptom, please select any treatment strategy you have used in the past 3 months.

Have you experienced ANY of these symptoms in the past 3 months? (Mark all that apply)

- Headache
- Body Aches/Pains
- Fatigue
- Difficulty Falling or Staying Asleep at Night
- Anxiety
- Poor Memory
- Lack of Concentration
- None

Next

Daily Assignment

Great job! You’re caught up on your activities. We’ll contact you when you have new things to do.

Month 1 Amazon Gift Code

Month 1 Amazon Gift Code: 12345-6789-0123
Go here to redeem: https://www.amazon.com/go/redeem

Symptom Checklist

Symptom Severity

How severe was your poor coordination over the past 24 hours?
- Mild
- Moderate
- Severe
Mobil Health (mHealth) Approaches

- CCSS SAM Pilot Design and Response Rate
  - Collect real-time PRO data via mobile phone, tablet & computer
  - Daily symptom (1 minute) & monthly QOL impact (5 minutes) report

<table>
<thead>
<tr>
<th>Month 1</th>
<th>Month 2</th>
<th>Month 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Week 1</strong></td>
<td><strong>Week 5</strong></td>
<td><strong>Week 9</strong></td>
</tr>
<tr>
<td>$S_1$ $S_2$ $S_3$ $S_4$ $Q_1$</td>
<td>$S_1$ $S_2$ $S_3$ $S_4$ $S_5$ $Q_1$</td>
<td>$S_1$ $S_2$ $S_3$ $S_4$ $S_5$ $Q_1$</td>
</tr>
<tr>
<td>41 enrolled/60 invited 68% response rate</td>
<td>88% completed ≥4 symptom &amp; QOL impact reports</td>
<td>83% completed ≥4 symptom &amp; QOL impact reports</td>
</tr>
</tbody>
</table>

Automatic text/email reminders: daily & break between months
Gaps in Knowledge Regarding Long-term Outcomes: Theoretical Framework

![Diagram showing cumulative incidence of cancer survivor population vs. general population over age (Years), with advanced onset of morbidity associated with cancer and therapy and excess lifetime morbidity associated with cancer and therapy marked.](image)
Gaps in Knowledge Regarding Long-term Outcomes: Theoretical Framework

- **Treated Population**
- **Expected in General Population**

Advanced Onset of Morbidity Associated with Therapy

Excess Lifetime Morbidity Associated with Therapy

Time Since Treatment Exposure (Years)

Cumulative Incidence

0 10 20 30 40 50 60 70