

Proposal No: 98-20  
Topic: Physical Disabilities

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Lead CCSS Investigator: Melissa Hudson

Collaborators:

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98-20

CHILDHOOD CANCER SURVIVOR STUDY  
Analysis Concept Proposal

Submitted: August 10, 1998

1. **Title:** Physical Disabilities After Treatment for Pediatric Hodgkin's Disease
2. **Working Group and Investigators:** This proposed publication will be within the Neurological/Psychosocial and Chronic Disease Working Group. Proposed investigators (name/e-mail/fax) will include:

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3. **Background and Rationale:** Appreciation of the late sequelae following pediatric Hodgkin's disease has been made possible by the development of curative therapy over the past 30 years. Currently, 85% to 90% of children and adolescents with Hodgkin's disease will be cured with radiation therapy, combination chemotherapy, or combined modality therapy using chemotherapy and radiation therapy. Treatment programs developed from the 1960s to the 1980s intensified therapy with the objective of improving disease-free survival. These treatments prescribed the delivery of high-dose (3500 - 4400 cGy) radiation therapy to extended volumes, and high cumulative dosages of alkylating agent chemotherapy. Late effects resulting from these therapies include musculoskeletal growth impairment, cardiopulmonary toxicity, thyroid dysfunction, infertility and the development of subsequent malignancies. The frequency and severity of some sequelae have been correlated with the gender, age at diagnosis, and the intensity and type of treatment. Modifications of contemporary treatment regimens for pediatric Hodgkin's disease, which have reduced radiation volumes and dosages and chemotherapeutic exposures, have diminished the incidence of serious treatment sequelae. However, subclinical organ dysfunction and the carcinogenic effects of therapy may not become clinically apparent until many years after treatment. This study will describe the general functional status of children and adolescents treated for Hodgkin's disease and its relationship to clinical diagnostic parameters, treatment modality and intensity, the presence of organ dysfunction, and health practices. Successful completion of this study may identify groups of Hodgkin's survivors with a greater than expected morbidity in functional status who deserve special attention in follow-up.
4. **Specific Aims/Objectives/Research Hypothesis:** This publication is designed to investigate the general physical functioning of survivors of pediatric Hodgkin's disease. The two main objectives are to 1) describe the physical functioning by

demographic and clinical treatment characteristics and 2) to identify vulnerable subgroups who have significant problems in physical functioning.

**Hypotheses:**

- The level of physical functioning will depend on the age at diagnosis, time since diagnosis, gender, and exposure to specific treatment modalities.
- Survivors of pediatric Hodgkin's disease who were female, younger at diagnosis, or have a longer time since diagnosis will have a higher risk of poor physical functioning.
- Survivors who were treated with higher doses of radiation therapy and chemotherapy and combined modality therapy will have a higher risk of poor physical functioning.
- Physical disabilities will be correlated with medical conditions.

**5. Analysis Framework:**

- a. Outcomes of interest include: medical care (B.1 – B.8), physical activity (N.9 – N.15), educational attainment (O.1 – O.4), employment history (O.5 – O.11);
- b. Subject population: all CCSS cases with Hodgkin's disease
- c. Explanatory variables:
  - constant demographic variables: gender, race, age at study entry;
  - demographic variables modified through the cancer experience: marital status (L-1 – L13), income (Q.8 – Q.9) tobacco use (N.1 – N. 2), alcohol use (N.3 – N.8), health practices (N.15 – N.22), and concern for future health (R-1);
  - treatment/medical variables: age at diagnosis, time since diagnosis, recurrence, type of therapy, extent (local, mantle, mantle/para-aortic, total nodal) and dose ( $< 30$  Gy,  $\geq 30$  Gy) of radiation, type and cumulative doses of chemotherapy drugs (MOPP, COPP, ABVD, MOPP/ABVD, COPP/ABVD, other), number of relapses, number of additional cancer diagnoses, presence of chronic disease (cardiovascular, respiratory, neurologic, gastrointestinal, hormonal, and sensory). Note that effects of radiation or chemotherapy may be modified by the age at diagnosis and/or gender.
- d. Specific tables for manuscript:
  1. Table describing demographic and treatment characteristics of Hodgkin's patients in the CCSS cohort

Gender (% male; % female)  
 Age at diagnosis (median, range)  
 Age at follow-up (mean, standard deviation, median, range)  
 Mean time since diagnosis (standard deviation)  
 Race (white, African American, Hispanic, native American, Asian, other)  
 Staging laparotomy + splenectomy (yes, no)  
 Type of treatment  
     Chemotherapy only  
     Radiation therapy only  
     Chemotherapy + radiation therapy  
 Cumulative radiation doses (< 30 Gy, ≥ 30 Gy)  
 Extent of radiation volume (local, mantle, mantle/para-aortic, total nodal)  
 Type of chemotherapy (non-cross resistant alkylating agent – MOPP, COPP, CVPP;  
 ABVD, alternating non-cross resistant – MOPP/ABVD, COPP/ABVD)

- Table showing frequency of organ dysfunction (number/%) in Hodgkin's survivors in CCSS cohort by gender, age at diagnosis, race, and type of treatment (Categorization by treatment will depend on number of events. To start with breakdown by chemotherapy alone, radiation therapy alone, and chemotherapy plus radiation therapy), time since diagnosis, and history of recurrence.

Organ dysfunction will be captured by the following health outcomes in the questionnaire:

Neurosensory (C.1, C.2, C.3, C.8, C.9, C.10)  
 Renal (D.1, D.2, D.3, D.4)  
 Endocrine (E.1 - E.8, E.10, E.11)  
 Cardiovascular (F.2 - F.6, F.8-F.10)  
 Pulmonary (G.6, G.9 - G.12)  
 Gastrointestinal (H.1, H.2, H.4 - H.6)  
 Neurologic (J.2, J.4, J.5, J.6, J.13, J.14)

- Table describing frequency of selected outcomes of health utilization, physical activity, educational attainment, and employment history by constant demographic variables (c.1) and demographic variables modified through the cancer experience (c.2) and the frequency of organ dysfunction (d.2).