INTRODUCTION
A major limitation of studies of the psychosocial consequences of childhood cancer is that they usually do not recruit numbers of participants which allow reliable subanalyses to address issues of the potential impact of age at onset/diagnosis controlling also for different types of cancer, different treatments, varied psychosocial factors (such as family income, ethnicity, gender, etc.). Our aim is to begin to fill this developmental gap in the existing literature by focusing on cancer diagnosed and treated in infancy (<6 years) versus later years (2-4 years, 5-10 years, 10+ years). We used the Childhood Cancer Survivor Study (CCSS) to examine the effects of specific periods in childhood of the onset or diagnosis of cancers for psychosocial sequelae. The main questions are two:

1. Controlling for medical and psychosocial factors, is cancer in infancy still a specific risk for adverse cognitive development?
2. If yes, what is a specific cognitive risk covering only hardwired cognition (i.e., defects in neural maturation) or at least less of a scale-size effect, covering also learning and academic achievement problems?

We also identified which types of cancer in infancy may predict the worst outcomes and in controlling for problems in cognitive functioning in our survivors’ sample by comparing their outcomes with the outcomes of a control group of siblings.

METHOD

Participants
The CCSS is a multi-institutional study, funded by the National Cancer Institute, of individuals who survived five or more years following treatment for cancer, leukemia, tumor or similar illness diagnosed during childhood or adolescence. Members of the CCSS cohort younger than 21 years at diagnosis, who were treated at one of 20 institutions, who were not Hispanic, and who had completed their education by age 18 years were included in this analysis. Children with non-Hodgkin's lymphoma, or bone cancer, were not included in the study. Table 1 presents the demographics, diagnostic, and treatment data for the 9,891 survivors and 5,635 siblings with complete data who were used in the study.

Procedures
Outcome Measures of Mental Retardation and Learning Disability.
- Whether members of the study cohort had ever been diagnosed as having had mental retardation or having been in a learning disabled or special education program.
- The measure of learning disability was recoded to exclude those respondents who had never been diagnosed as otherwise mentally retarded or learning disabled.
- Whether members of the study cohort had ever been diagnosed as having had mental retardation or being otherwise mentally retarded.

Predictors of Mental Retardation and Learning Disability.
- Group membership (survivors or siblings).
- The age of initial diagnosis of cancer.
- Gender (male vs. female).
- Treatment by chemotherapy or treatment by radiotherapy.
- Treatment by chemotherapy or treatment by radiotherapy.

Table 1 presents the data for these predictors as well as gender, household income, ethnicity, and age at follow-up which were used as covariates.

Analytic Plan
- All models were fit using binary logistic regression.
- Final models met the assumptions of additivity, linearity, and no influential outliers and included only the significant two-way interactions of the focal predictor with other predictors and the interaction of Age at follow-up vs. income.
- Predictive ability of models was assessed, and all models were validated using enhanced bootstrapping with 500 samples. Predictive ability of the models was generally acceptable: Nagelkerke R² ranged from .885 to .951, D₂ ranged from .677 to .789, and OR ranged from .000 to .009.
- Validation statistics indicated minimal to little over-fitting in the original models with minimal differences in the statistics for the validation model and the original model.

Table 1: Demographic, diagnostic, and treatment data.

Table 3: Predictors of mental retardation in survivors by diagnosis and treatment, N=7,383.

Table 4: Predictors of learning disability in survivors vs. siblings, N=10,783.

For more information, address correspondence to:
Marc H. Bornstein, Child and Family Research
NICHD, NHLBI Suite 6561, 3150 Research Drive,
Bethesda, MD 20892-7501, U.S.A.
Email: Marc_H_Bornstein@nih.gov.