With notable successes in the treatment of pediatric and adolescent cancers, research on long-term treatment-related outcomes among survivors is a priority. CCSS consists of a large, diverse and well-characterized retrospective cohort of 5-year survivors. Initial objectives of CCSS focus on mortality, second cancers, cardiopulmonary function, reproductive outcomes and health behaviors. Among the 20,276 survivors, there was a 10.8-fold excess (95% CI=10.3-11.3) in overall mortality. Cumulative mortality was 6.4%, 9.3%, 11.4% and 14.0% at 10, 15, 20 and 25 years post-diagnosis, respectively. A significant excess mortality was found for subsequent cancers [Standardized Mortality Ratio (SMR)=19.4], cardiac (SMR=8.2) and pulmonary (SMR=9.2) causes. Of 314 cases of second cancers ascertained [Standardized Incidence Ratio (SIR)=6.4; 95% CI=5.7-7.1], significant excesses occurred following all primary diagnoses. Cumulative cancer incidence was 3.2% at 20 years of follow-up; bone tumors (SIR=19.1) and breast cancer (SIR=16.2) comprised the largest excess. Of 6,942 sexually active survivors, 3,162 reported 6,462 pregnancies. Compared to sibling controls, male survivors reported higher pregnancy loss while female survivors treated with pelvic radiation reported lower birth weights. Among 9,709 survivors over the age of 18 years, 28% initiated smoking and 17% were current smokers. Standardized to U.S. rates, the observed:expected ratio of cigarette smoking was 0.72 (95% CI=0.69-0.75). The CCSS, funded as a resource grant from the NCI, provides an opportunity to address important issues among this unique and ever-growing population.