Among 13,976 survivors of childhood cancer (excluding retinoblastoma and germ cell tumors), cancer history in first-degree relatives was obtained by questionnaire. Ambiguous conditions were clarified by phone interview. 2038 invasive cancers and 461 non-melanoma skin cancers were reported with 2,215,373 person-years of follow-up. Using US Surveillance, Epidemiology and End Results (SEER) data, overall there was no excess cancer among first-degree relatives (Standardized incidence ratio (SIR) = .89; 95% confidence interval (CI) .85 -.93). There was a modestly increased incidence of cancer among siblings (SIR=1.5; 95% CI 1.3-1.7) and offspring (SIR=1.6; 95% CI .8-3.5), contrasted with fathers (SIR=.72, 95% CI .67-.77) and mothers (SIR=.93, 95% CI .87-.99). SIR decreased monotonically with age from 1.07, 95% CI .92-1.25 for age less than 20 to .80, 95% CI .70-.91 for age 65+. There was no difference in family incidence of cancer in the 402 cases with secondary primary neoplasms (SPN) compared with those without SPN. However, siblings (SIR=2.4; 95% CI 1.5-3.7) and offspring (SIR=15.4; 95% CI 5.4-43.4) of those with SPN had an increased incidence of childhood or early onset cancers. The lower than expected incidence of parental cancers may be due to several factors including under-reporting, selection bias for healthier adults, anticipation (parents developing cancers at older ages than successive generations), or lifestyles that promote cancer prevention. This data can be consistent with small subsets of patients with heritable syndromes, with de novo germline mutations, increased cancer in offspring and siblings and probands with multiple primary neoplasms, as with heritable retinoblastoma. With longer follow-up, validation of site-specific cancers and inclusion of second-degree relatives, analysis by family may reveal patterns of specific subtypes of childhood and adult cancers, including multiple primary neoplasms.