**Purpose:** To determine if survivors of acute lymphoblastic leukemia (ALL) are at increased risk for obesity, and to assess what patient and treatment variables modify risk. **Methods:** Adult survivors of childhood ALL (N=1949) who were participants of the Childhood Cancer Survivor Study, a large, retrospective cohort of 12,433 long-term survivors of childhood cancer who were diagnosed from 1970-1986, were compared with adult siblings (N=2565) of survivors from the full cohort (all cancer groups) and to participants, age 18-49, of the 1995 National Health Interview Survey (N=47,555). Mean age of leukemia survivors was 24.2 years (SD, 4.87; range 18-42 years) and of siblings was 29.0 years (SD 7.28; range 18-49 years; p<0.001). Body mass index (BMI; kg/m$^2$), calculated from self-reported heights and weights, was used to determine the prevalence of obesity (BMI $\geq$ 30). **Results:** After stratification by gender and age group at time of interview and adjusting for race, there were no significant differences in the prevalence of obesity between siblings and NHIS participants. The age- and race-adjusted odds ratio (OR) for obesity in ALL survivors treated with cranial irradiation (CRT) $\geq$ 20 Gy in comparison with siblings was 2.62 for females (95% CI; 1.95, 3.53; p<0.001) and 1.79 for males (95% CI; 1.29, 2.48; p=0.002). CRT effects were modified by age at diagnosis, with females treated at a younger age at highest risk. The age- and race-adjusted OR for obesity for females diagnosed 0-4 years of age and treated with CRT $\geq$ 20 Gy was 4.27 (95% CI; 2.57, 7.32; p<0.001). No association was found between obesity and ALL survivors, adjusted for age and race, who were treated with chemotherapy only (females, p=0.194; males, p=0.646) or with chemotherapy and CRT < 20 Gy (females, p=0.404; males, p=0.340). **Conclusions:** CRT $\geq$ 20 Gy is associated with an increased prevalence of obesity in ALL survivors, especially in females treated at a younger age. It is imperative that health care professionals recognize this risk and develop strategies to enhance weight control and encourage longitudinal follow up to screen for obesity-related diseases. (Supported by NIH Grant U24CA55727)