

**Title:** Intestinal obstruction in survivors of childhood cancer: A report from the Childhood Cancer Survivor Study (CCSS)

**Background:** For adult survivors of childhood cancer, knowledge about the long-term risk of intestinal obstruction from surgery, chemotherapy, and radiotherapy is limited.

**Methods:** Intestinal obstruction requiring surgery (IOS) occurring 5 or more years after cancer diagnosis was evaluated in 12,316 five-year survivors from the CCSS cohort (2,002 with and 10,314 without abdominopelvic tumors) and 4,023 sibling participants. Cumulative incidence of IOS was calculated with second malignant neoplasm, late recurrence, and death as competing risks. Piecewise-exponential models assessed the associations of clinical and demographic factors with rate of IOS.

**Results:** IOS was reported by 165 survivors (median age at IOS=19 years, range=5-50 years; median time from diagnosis to IOS=13 years) and 14 siblings. Cumulative incidence of IOS at 35 years was 5.8% (95% confidence interval [CI]=4.4-7.3%) among survivors with primary abdominopelvic tumors, 1.0% (95% CI=0.7-1.4%) among those without abdominopelvic tumors, and 0.1% (95% CI=0.1-0.5%) among siblings. Survivors of abdominopelvic lymphoma had the highest 35 year cumulative incidence of IOS, 7.2% (95% CI=2.8-12.5%). Among all survivors, abdominopelvic tumor (adjusted rate ratio [ARR]=3.6, 95% CI=1.9-6.8,  $P<0.001$ ) and abdominal/pelvic radiotherapy within 5 years of diagnosis (ARR=2.4, 95% CI=1.6-3.7,  $P<0.001$ ) increased the rate of IOS, adjusting for year of diagnosis; sex; race/ethnicity; age at diagnosis; age during follow-up (as natural cubic spline); primary cancer type; and chemotherapy, radiotherapy, and surgery occurring within 5 years of diagnosis. Developing IOS increased the subsequent mortality among survivors (ARR=1.8, 95% CI=1.1-2.9,  $P=0.016$ ), adjusting for the same clinical and demographic factors.

**Conclusions:** In the decades following diagnosis and treatment, survivors of childhood cancer are at increased risk of developing late-onset IOS, with subsequent increased risk of mortality. These findings underscore the need to promote long-term awareness of these risks among patients and providers, especially for survivors with abdominal or pelvic tumors who have undergone treatment with surgery or radiotherapy.