

Risk and Impact of Pulmonary Complications in Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)

Andrew C. Dietz, MD, MS^{1,2}, Yan Chen, MMath³, Kirsten K. Ness⁴, PhD, James S. Hagoood, MD^{1,2}, Eric J. Chow, MD, MPH^{5,6}, Yutaka Yasui, PhD³, Marilyn Stovall, PhD⁷, Joseph P. Neglia, MD, MPH⁸, Kevin C. Oeffinger MD, MD⁹, Ann C. Mertens, PhD¹⁰, Leslie L. Robison, PhD⁴, Gregory T. Armstrong, M.D. MSCE⁴, Daniel A. Mulrooney, MD, MS^{4,11}; ¹University of California San Diego, ²Rady Children's Hospital, San Diego, CA, ³University of Alberta, Edmonton, AB, ⁴St. Jude Children's Research Hospital, Memphis, TN, ⁵Canada, Seattle Children's Hospital, ⁶University of Washington, Seattle, WA, ⁷MD Anderson Cancer Center, Houston, TX, ⁸University of Minnesota, Minneapolis, MN, ⁹Memorial Sloan Kettering Cancer Center, New York, NY, ¹⁰Emory University, Children's Hospital of Atlanta, Atlanta, GA, ¹¹University of Tennessee Health Science Center, Memphis, TN

Background: Pulmonary complications from exposure to radiation, bleomycin and the nitrosureas have been well-documented among adult survivors of childhood cancer. However, the magnitude of condition-specific risks, compared to a non-cancer population, and the long-term impact on physical activity have not been well described.

Methods: This analysis includes 13,208 five-yr survivors of childhood cancer (53% male, age 8 yrs [range: 0-21] at diagnosis, 33 yrs [6-59] at last follow-up), diagnosed \leq 21 yrs between 1970-1986. Self-reported pulmonary outcomes were compared to a sibling control group (N=4,023) using Poisson regression to estimate rate ratios (RR) and 95% confidence intervals (CI) adjusted for attained age, sex, race, body mass index, congestive heart failure, and smoking status. Logistic regression was used to estimate associations (odds ratios, OR) between pulmonary outcomes and daily physical activity (walk one block, carry groceries, climb stairs, etc).

Results: Compared to siblings, fewer survivors ever smoked (21.2% vs. 34.3%, $p < 0.001$) but were more likely to report asthma (RR 1.4, CI 1.2-1.6), bronchitis (RR 1.2, CI 1.1-1.3), chronic cough (RR 2.2, CI 1.9-2.5), emphysema (RR 2.5, CI 1.2-5.2), need for extra oxygen (RR 2.2, CI 1.8-2.6), pulmonary fibrosis (RR 3.9, CI 2.7-5.8), pleurisy (RR 1.3, CI 1.1-1.7), and recurrent pneumonia (RR 2.8, CI 1.9-4.0). Cumulative incidence of any pulmonary condition by age 40 was 78.7% (CI 78.3-79.2). Lung cancer was reported in 17 (0.1%) with a standardized incidence ratio of 3.9 (CI 2.3-6.2). The standardized mortality ratio for death due to a pulmonary condition was 9.1 (CI 7.4-11). Limited daily physical activities were more likely among survivors with a pulmonary condition vs. those without: asthma (OR 1.6, CI 1.4-1.8), bronchitis (OR 1.5, CI 1.4 - 1.7), chronic cough (OR 2.8, CI 2.5 - 3.1), emphysema (OR 2.6, CI 1.5 - 4.3), need for extra oxygen (OR 3.3, CI 2.9 - 3.7), lung fibrosis (OR 2.3, CI 1.9 - 2.8), pleurisy (OR 1.9, CI 1.6 - 2.3), and recurrent pneumonia (OR 3.6, CI 2.9 - 4.4).

Conclusion: Pulmonary complications are substantial among cancer survivors, significantly impacting daily activity and increasing risk of death.