Authors: Jenna R. Rogers, BS; Sarah Stein, PhD; Clyde B. Schechter, MD, MA; Kayla L. Stratton, MS; Wendy M. Leisenring, ScD; Chelsea Taylor, BA; Oguzhan Alagoz, PhD, MS; Gregory T. Armstrong, MD, MSCE; Melissa M. Hudson, MD; Allison W. Kurian, MD, MSc; Kathryn P. Lowry, MD; Jeanne S. Mandelblatt, MD, MPH; Lindsay M. Morton, PhD; Chaya S. Moskowitz, PhD; Kevin C. Oeffinger, MD; Lisa Diller, MD; Jennifer M. Yeh, PhD

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Missed Opportunity for Breast Cancer Prevention Among Pediatric Lymphoma Survivors Treated with Chest Radiation: Projected Gap in Breast Cancer Deaths with Real-world Uptake Rates

Background: For survivors of pediatric lymphoma previously treated with chest radiotherapy (RT), the Children's Oncology Group recommends initiation of breast cancer screening with mammography and MRI starting at age 25. The National Comprehensive Cancer Network also recommends risk-reducing medications (e.g., tamoxifen) for breast cancer prevention in high-risk women. While low uptake among survivors has been described, the missed opportunity in terms of avoidable breast cancer deaths remains unknown.

Methods: Using a Cancer Intervention and Surveillance Modeling Network model adapted to reflect the elevated breast cancer risk and competing mortality among 5-year lymphoma survivors previously treated with mediastinal RT, we estimated the number of breast cancer deaths by age 65 versus no screening or tamoxifen for a 20-year-old cohort under three scenarios: i) optimal uptake and adherence (100%) to early initiation of recommended screening (mammography with MRI) at age 25 and standard dose tamoxifen for 5 years at age 25; ii) real-world uptake of screening alone based on Childhood Cancer Survivor Study data (18% at age 25, increasing over time to 60% by age 35, with 50% reporting MRI within 1 year of mammogram); iii) real-world screening uptake as described in scenario 2, plus real-world tamoxifen use based on published estimates (16%). We assumed tamoxifen reduced breast cancer risk for a minimum of 20 years based on follow-up data from clinical trials. Breast cancer deaths averted were calculated as the difference in breast cancer deaths between each scenario and a baseline of no screening or tamoxifen.

Results: In the absence of screening or tamoxifen, 53.2 breast cancer deaths per 1000 female survivors were projected by age 65. Under optimal uptake, screening averted 28.5 deaths per 1000 women (54%); screening plus tamoxifen increased the number averted to 31.6 deaths per 1000 (59% total reduction). Under real-world uptake, the number of breast

cancer deaths averted was only 11.7 per 1000 women with screening alone and 12.6 for screening plus tamoxifen, suggesting only a 19-24% mortality reduction.

Conclusions: Low real-world uptake of screening and tamoxifen represents a substantial missed opportunity to prevent breast cancer deaths among survivors of pediatric lymphoma treated with chest RT. Strategies to increase uptake are needed to fully realize the mortality benefits of breast cancer control in this high-risk population.

Table. Modeled breast cancer mortality at age 65 under optimal and real-world uptake scenarios

	Breast Cancer Deaths per 1000	Breast Cancer Deaths Averted per 1000	% Breast Cancer Deaths Averted
No screening or tamoxifen	53.2	-	-
Optimal (100%)			
Mammo/MRI	24.8	28.5	54%
Mammo/MRI + tamoxifen	21.7	31.6	59%
Real world			
Mammo/MRI	41.5	11.7	19%
Mammo/MRI + tamoxifen	40.7	12.6	24%