

Deadline: February 17, 2020, at 11:59 PM (EST)

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## Efficacy and cost-effectiveness of breast cancer (BC) screening in chest-irradiated survivors of childhood Hodgkin lymphoma (HL)

**Background:** Female childhood HL survivors treated with  $\geq 10$  Gy of chest radiation are at high risk of developing BC. The Children’s Oncology Group (COG) guidelines recommend lifetime annual mammography (MAM) and breast Magnetic Resonance Imaging (MRI) starting 8y after chest radiation or age 25, whichever is later, and clinical breast examination (CBE) annually from puberty and semiannually from age 25. Initial model results suggest that CBE adds no survival benefit in this cohort. Digital breast tomosynthesis (DBT) is increasingly replacing digital MAM in clinical practice. Here, we present the efficacy and cost-effectiveness of COG’s imaging-based screening recommendations.

**Methods:** Life-years (LYs), quality-adjusted LYs (QALYs), BC mortality, and costs (2017 U.S.\$) were estimated from simulating the lifetimes of 5-million chest-irradiated 25y old HL survivors who underwent BC screening with each of the following strategies: annual digital MAM, MRI, MAM+MRI, annual DBT or DBT+MRI from age 25 onward. Treatment-related BC risk (in-situ and invasive) and non-BC mortality were estimated from female 5y HL survivors in the Childhood Cancer Survivor Study and from U.S. population rates. Test sensitivity was 70-74% for MAM (based on prior HL studies) and 89% for DBT and MRI (based on women at high risk of *de novo* BC). Costs and quality of life weights were obtained from medical literature.

**Results:** For HL survivors with no screening, lifetime BC risk was 42.7% and BC mortality was 18.1%. BC risk and non-BC mortality were, respectively, 7.4- and 5.2-fold higher at age 50 in HL survivors relative to the general population. Screening at ages 25-74 had similar LY gain and BC mortality reduction compared to lifetime screening; hence, we focused on screening for ages 25-74. For all strategies screening provided LY gain of 0.34-0.47 and reduced BC mortality by 6.7-9.8% compared with no screening; incremental cost-effectiveness ratio (ICER), or cost per QALY gained, for MAM alone was \$58,726 and for DBT alone was \$62,989. ICER of adding MRI to MAM (\$385,285) or to DBT (\$513,358) indicated lower cost-effectiveness of supplemental MRI (Table).

**Conclusion:** Annual screening at ages 25-74y in chest-irradiated HL survivors appears beneficial. Using \$100K per QALY gained as cost-effectiveness threshold, annual MAM or DBT are more cost-effective, whereas adding MRI to MAM is less cost-effective.

Strategy	LY gained	BC deaths reduced (%)	Cost	QALYs	ICER (vs. No screening)	ICER (vs. Comparator)
No screening	REF	REF	95,073	16.576	NA	NA
Annual imaging (ages 25-74)						
MAM	0.35	7.0	99,477	16.651	58,726	58,726!
MRI	0.34	6.7	107,035	16.652	157,625	Dominated¥
DBT	0.39	8.1	100,328	16.659	62,989	62,989!
MAM+MRI	0.46	9.7	109,726	16.678	144,222	385,285*
DBT+MRI	0.47	9.8	110,662	16.680	150,532	513,358#

!Compared with No screening

\*Compared with MAM

#Compared with DBT

¥ More expensive and less effective than DBT

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