

Conclusions of evidence from the systematic literature search for breast cancer surveillance for female CAYA cancer survivors in 2013 versus 2020

	Quality of evidence 2013	Quality of evidence 2020
Breast cancer risk in CAYA cancer survivors		
Increased risk after ≥ 20 Gy chest radiation vs. no chest radiation	Level A	Level A ^{1,5,14-18}
Increased risk after 10-19 Gy chest radiation vs. no chest radiation	Level B	Level A ^{5,18-24}
No significant effect of 1-9 Gy chest radiation vs. no chest radiation	Level C	Level B ^{15,18-22,25,26}
Increased risk after TBI vs. no TBI	Level C	Level B ^{5,16,20,27}
Increased risk after upper abdominal radiation exposing breast tissue vs. none	Level C	Level B ^{5,20,23,24}
Decreased risk after radiation to volumes exposing the ovaries vs. no radiation to volumes exposing the ovaries	Level B	Level of evidence specified by age
Decreased risk after radiation to volumes exposing the ovaries vs. no radiation to volumes exposing the ovaries in survivors treated with chest radiation at younger ages (<21 yr)	Level of evidence not specified by age	Level A ^{3,5,14,18,21,22,33}
Decreased risk after radiation to volumes exposing the ovaries vs. no radiation to volumes exposing the ovaries in Hodgkin lymphoma survivors treated with chest radiation at older ages (21-49 yr)		Level C ^{15,26,28,30-32}
Decreased risk after alkylating agents vs. no alkylating agents in survivors treated with chest radiation	Level B	Level of evidence specified by age
Decreased risk after higher doses of alkylating agents vs. no alkylating agents in survivors treated with chest radiation at younger ages (<21 yr)	Level of evidence not specified by age	Level C ^{2,4,5,14,21,22,35}
Decreased risk after higher doses of alkylating agents vs. no alkylating agents in Hodgkin lymphoma survivors treated with chest radiation at older ages (21-49 yr)		Level A ^{15,17,26,28,30,32,34}
Decreased risk in survivors treated with chest radiation with a younger age at menopause vs. older age	No studies	Level A ^{14,15,28,32,38}
Decreased risk in survivors with a shorter duration of intact ovarian function after chest radiation vs. longer duration	No studies	Level A ^{14,15,28,32,38}
Increased risk in survivors treated with chest radiation close to menarche vs. longer time from menarche	No studies	Level B ^{14,15,38}
No significant effect of treatment of early menopause vs. no treatment	No studies	Level B ^{14,15,32}
Increased risk after anthracyclines vs. no anthracyclines in a dose-response relationship. However, the dose cut-off for survivors at low, moderate and high risk is difficult to determine.	No studies	Level A ^{16,18,21,39,40}
Increased risk after anthracyclines without chest	No studies	Level B ^{16,18,39}

radiation vs. no anthracyclines and no chest radiation in survivors of Li-Fraumeni syndrome-associated childhood cancer types (leukemia, CNS tumor and non-Ewing sarcoma)		
Increased risk after <i>high-dose alkylating agents without chest radiation</i> vs. no alkylating agents and no chest radiation	No studies	Level C ^{3,16,18,39,40}
Breast cancer latency time in CAYA cancer survivors		
Increased risk as early as 8 years after (high-dose) chest radiation or 25 years of age	Level A	Level A ^{1-5,17,20,28,30,78}
Breast cancer risk over time in CAYA cancer survivors		
Increased risk with increasing length of follow-up in survivors up to age 50 years	Level A	Level A ^{1-5,17,28,30,78}
Increased risk in survivors previously treated with (high-dose) chest radiation with an attained age 50-60 years	Level A	Level A ^{5,17,21,30,35}
Increased risk in survivors previously treated with (high-dose) chest radiation with an attained age ≥60 years	No studies	Level C ^{17,30}
Diagnostic value clinical breast exam, mammography and breast MRI in CAYA cancer survivors		
Diagnostic value of a breast MRI to detect breast cancer in Hodgkin lymphoma survivors is moderate (sensitivity ranged from 67% to 100%, specificity ranged from 80% to 94%)	No studies	Level B ^{21,41-45}
Diagnostic value of a mammogram to detect breast cancer in Hodgkin lymphoma survivors is moderate (sensitivity ranged from 54% to 73%, specificity ranged from 93% to 99%)	No studies	Level A ^{21,41-45}
Diagnostic value of breast MRI and mammogram is better than either test alone to detect breast cancer in Hodgkin lymphoma survivors (sensitivity ranged from 86% to 100%, specificity ranged from 89% to 99.7%)	No studies	Level B ^{21,41,42}
26.8% to 75.0% of breast cancers in Hodgkin lymphoma survivors treated with chest radiation are initially detected by mammogram screening	Level B	Level B ^{33, 45-49}

CAYA, childhood adolescent and young adult