

Screening for new primary cancers in cancer survivors compared to non-cancer controls: a systematic review and meta-analysis

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Received: 10 January 2013 / Accepted: 4 March 2013 / Published online: 5 May 2013
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Abstract

Purpose The goal of this study was to synthesize evidence comparing cancer screening receipt between cancer survivors and non-cancer controls by conducting a systematic review and meta-analysis.

Methods We searched PubMed, EMBASE, and CINAHL databases from inception through April 1, 2010 using search terms related to cancer, survivorship, and cancer screening. Studies were included if they reported a comparison of cancer screening receipt between cancer survivors and non-cancer controls. We performed a meta-analysis on the effect of cancer survivorship on breast, cervical, colorectal, and prostate cancer screening receipt.

Results Our search strategy identified 1,778 titles, of which 20 met our inclusion/exclusion criteria. In our meta-analyses, cancer survivors were more likely to be screened for breast, cervical, colorectal, and prostate cancer than non-cancer controls (pooled odds ratio, 1.27; 95 % CI, 1.19–1.36). We

observed significant heterogeneity between studies, most of which remained unexplained after subgroup and sensitivity analyses. Important contextual factors, such as how screening programs operate, were not reported in the primary literature. Many cancer survivors (along with non-cancer controls) still did not receive cancer screening.

Conclusion Compared with non-cancer controls, cancer survivors receive more frequent screening for new primary breast, cervical, colorectal, and prostate cancers. Future research should seek to determine whether increased uptake of cancer screening is associated with improved outcomes during cancer survivorship.

Implications for Cancer Survivors Our systematic review and meta-analysis demonstrated that cancer survivors received more frequent screening for second primary breast, cervical, colorectal, and prostate cancers than non-cancer controls. As many cancer survivors are at an increased risk of developing a second primary cancer, future research should seek to determine whether this increased uptake of cancer screening in cancer survivors leads to improved outcomes during cancer survivorship.

Research Support: Canadian Institutes of Health Research Knowledge Synthesis Grant, Nova Scotia Health Research Foundation Student Research Award.

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Keywords Early detection of cancer · Neoplasms ·
Second primary cancer · Survivors · Systematic review

Introduction

A current and future challenge for healthcare systems is to determine how to best provide long-term follow-up care to the growing prevalence of cancer survivors, estimated to number over 28 million worldwide [1]. An often overlooked, but nonetheless important, component of follow-up care for cancer survivors is screening for new primary cancers [2]. For

most malignancies, a cancer survivor's risk of developing a second primary cancer is at least as great as the general population. The epidemiology of second primary cancers is complex, and is a function of common risk factors, genetic links, and late carcinogenic effects from treatment of the primary cancer [3]. Among cancer survivors, often the risk of developing a second primary cancer at a different anatomical site can be much greater than the general population [4–9].

Conflicting theories suggest that cancer survivors, as individuals with a comorbid condition, may be either more or less likely to receive preventive care. One theory [10] and several researchers [11–13] have hypothesized that cancer survivors may receive more frequent screening due to increased contact with the healthcare system. Increased contact with the healthcare system and a recommendation from a primary care physician are both strongly associated with the uptake of cancer screening in the general population [14–17]. Conversely, the competing demands model [18] and other researchers [19, 20] have hypothesized that despite an increased amount of contact with the healthcare system, a cancer survivor's previous cancer diagnosis may shift healthcare workers' attention away from other preventive health services such as screening for new primary cancers.

While two prior systematic reviews have compared receipt of general preventive healthcare (including cancer screening) in cancer survivors and the general population [21, 22], the volume of available literature has substantially increased since these reviews were published. In addition, these two reviews reached conflicting conclusions, with Wilkins and Woodgate concluding “the prevalence of secondary prevention practices among cancer survivors is generally lower than recommended” [22], but Khan et al. concluding “cancer screening is generally well managed through normal channels and is adequate amongst survivors of adult cancer in the United States” [21]. An additional review by Treanor and Donnelly assessed health services utilization among cancer survivors, concluding “Overall, there is a need to improve access to care for all cancer survivors” [23]. However, this review did not compare health services utilization between cancer survivors and the general population. Given the conflicting results of these prior reviews, the objective of this review was to synthesize evidence comparing cancer screening receipt between cancer survivors and non-cancer controls.

Methods

To evaluate the above objective, we conducted a systematic review using methods similar to those advocated by the Cochrane Collaboration [24]. We systematically identified

and included observational studies that compared the receipt of any cancer screening test between cancer survivor and non-cancer control group populations. Our research question was developed and refined in consultation with healthcare professionals, program managers/administrators, and other decision makers and stakeholders from the cancer care community during interactive workshops.

Data sources and search strategy

We searched three electronic databases (PubMed, EMBASE, and CINAHL; all available years to April 1, 2010) using a combination of MeSH terms and keywords relating to cancer, cancer survivorship, and cancer screening. The PubMed search strategy is available in the [Appendix](#); the EMBASE and CINAHL search strategies used similar terms. No date or language restrictions were used in the search strategy. Reference lists of included studies and previous reviews were screened to identify additional articles. Previous reviews were identified through our search strategy.

Study selection and data abstraction

Studies that measured and compared the receipt of cancer screening in both cancer survivor and a non-cancer control group were included in this review. We included all definitions of a cancer survivor in this study, regardless of time since diagnosis or initial cancer site. We included studies of both adult and childhood cancer survivors. Secondary survivors, e.g., family members of the cancer survivor, were not eligible for inclusion in this review. All cancer screening sites and tests were eligible for inclusion, regardless of whether the screening was opportunistic or programmatic in nature. Studies that measured screening receipt outside of commonly recommended age ranges were included and explored with subgroup analysis. Unpublished literature was sought through contact with content experts.

A standardized study selection and data abstraction form was used. The initial literature screen of titles and abstracts was done by one author (MC) in order to remove citations that were clearly not relevant to the study objectives. Application of the study inclusion criteria to the full-text articles and abstraction of included articles was conducted independently by two reviewers (MC, CS) with formal systematic review training. If necessary, disagreements were resolved through consensus and consultation with a third reviewer (JH). If available, appropriately adjusted odds ratios were favoured over unadjusted estimates. If odds ratio estimates were not reported in the primary study, crude odds ratios were calculated from raw data. Data for individual screening tests [for example, fecal occult blood testing (FOBT) and endoscopy for colorectal cancer screening] were recorded

separately whenever possible. Study authors were contacted to retrieve missing data.

Risk of bias assessment

Study level risk of bias was assessed using four categories selected from quality assessment tools used to assess prognosis studies and randomized controlled trials of intervention effectiveness [25, 26], and modified to fit the review question and types of observational studies included in this review. These four risk of bias categories used were: (1) Selection bias; (2) Definition of cancer survivorship [low: long-term survivors (all ≥5 years); moderate: majority long-term survivors; high: time since diagnosis not measured or short-term survivors]; (3) Measurement of screening receipt (low: administrative data; moderate: self-report); and (4) Adjustment for confounding or use of a matched cohort. These risk of bias assessments were used to guide sensitivity analyses. Other categories explored in our subgroup and sensitivity analyses include the use of an exclusively elderly population (greater than age 65), the use of a childhood cancer survivor population, and the use of upper and/or lower age limits reflecting screening guidelines.

Analysis

We performed a meta-analysis on the effect of cancer survivorship on breast, cervical, colorectal, and prostate cancer screening receipt, supplemented with a thoughtful narrative discussion. Odds ratio effect estimates by cancer site and screening rate were pooled using a random effect generic inverse variance model with Review Manager 5.0 (Cochrane Collaboration, Oxford, UK) software. Meta-analyses were not conducted for skin and testicular cancer screening due to

the small number of studies reporting these outcomes ($n=1$ and $n=2$, respectively).

An overall summary estimate of the association between cancer survivorship and cancer screening was calculated using data from all included studies and any screening site. We selected and pooled the single odds ratio estimate from each included study that represented the screening site with the lowest standard error. This decision rule was determined a priori, and selected to minimize possible selection bias. Heterogeneity was measured using the I^2 statistic [24]. The narrative synthesis included studies which could not be quantitatively combined and analyzed, results from the risk of bias assessment, and other potential sources of heterogeneity from the meta-analysis, such as study-level demographic and cancer survivor information.

When a study separately reported two different screening tests for a single cancer site, our decision rule was to choose the screening test we felt was more likely to be included in a programmatic, population-level screening intervention for that site. For example, in studies that separately reported the receipt of FOBT and endoscopy colorectal cancer screening, we included the FOBT screening test estimate in the colorectal cancer screening overall estimate. When multiple studies presented data from the same cohort, we avoided double counting participants by only including the single study with the largest sample size in the meta-analysis. Sensitivity analyses were conducted to determine whether changing these decision rules modified our results.

Results

The flow of study selection and reasons for full-text article exclusion are presented in Fig. 1. Table 1 summarizes the characteristics of the 20 studies which met our inclusion

Fig. 1 Flowchart showing selection of articles for inclusion in the systematic review

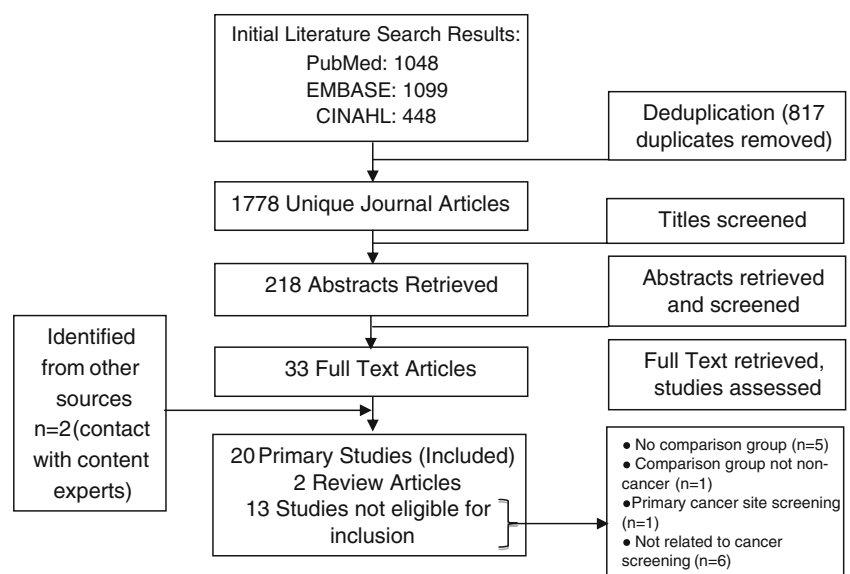


Table 1 Characteristics of included studies

Characteristics of Included Studies									Cancer Sites Screened For					
Study	Year	Country	Number of Participants (survivors/controls)	Survivor Characteristics	Initial Cancer Diagnosis Type	Study Design/Exposure Measurement/Outcome Measurement			Breast	Cervical	Colorectal	Prostate	Skin	Testicular
Aparicio-Ting [27]	2003	USA	112/ 2062	34% between age 50-64, 100% female, 100% Hispanic	Mixed	CS	SR	SR						
Bellizzi [28]	2005	USA	7,384/ 121,347	52.7% ≥ age 65, 60.6% female, 88.5% white ethnicity	Mixed	CS	SR	SR						
Bishop [11]	2010	North America	662/ 158	Median age: 49.1, 62% female, 92% Caucasian ethnicity	Mixed	CS	AD	SR						
Breslau [12]	2010	USA	1,502/ 31,911	Mean age: 66.8, 100% female, 76.3% white ethnicity	Breast Cancer	CS	SR	SR						
Duffy [19]	2006	USA	85/ 340	Mean age: 61.7, 100% female, 85.9% Caucasian /other ethnicity	Breast Cancer	CS	SR	SR						
Earle [29]	2003	USA	5,965/ 6,062	Mean age: 78.7, 100% female, 89% white ethnicity	Breast Cancer	RC	AD	AD						
Earle [20]	2004	USA	14,884/ 16,659	Mean age: 79.9, 57.6% female, 86.4% white ethnicity	Colorectal Cancer	RC	AD	AD						
Grunfeld [30]	n/a	Canada	21,111/ 105,340	Mean age: 58.6, 86% female, no ethnic information	Mixed	RC	AD	AD						
Hudson [41]	2009	USA	109/ 641	Mean age: 68.7, 59% female, 80% white ethnicity	Mixed	CS	SR	SR + CR						
Khan [31]	2010	United Kingdom	29,244/ 116,418	Mean age: 70.7, 73.4% female, no ethnic information	Mixed	RC	AD	AD						
Kwon [32]	2009	Canada	3,473/ n/a	Mean age: 63, 100% female, no ethnic information	Endometrial Cancer	RC	AD	AD						
Mayer [33]	2007	USA	619 / 2,141	Mean age: 58, 65.5% female, 81.5% white ethnicity	Mixed	CS	SR	SR						
McBean [35]	2008	USA	14,575/ 14,575	31.9% between ages 67-74, 100% female, 94.3% white ethnicity	Uterine Cancer	RC	AD	AD						
McBean [34]	2009	USA	7,666/ 36,433	Mean age: 73.6, 100% female, 85% white ethnicity	Colorectal Cancer	RC	AD	AD						
Ng [36]	2008	USA	511 / 224	Median age: 44, 51% female, no ethnic information available	Hodgkin's Lymphoma	CS	AD	SR						
Oeffinger† [37]	2009	North America	551/ 622	Chest RT: 46.3% between ages 40-50, 100% female, 92.4% white	Mixed	CS	AD	SR						
			561 / 622	No Chest RT: 45.8% between ages 40-50, 100% female, 93.2% white										
Snyder (a) [39]	2009	USA	1961/ 1961	Mean age: 75, 100% female, 90% white ethnicity	Breast Cancer	RC	AD	AD						
Snyder (b) [38]	2009	USA	23,731/ 47,127†	Mean age: 75.7, 100% female, 90% white ethnicity	Breast Cancer	RC	AD	AD						
Trask [13]	2005	USA	2,151/ 30,195	Mean age: 61.9, 59.7% female, 90% white ethnicity	Mixed	CS	SR	SR						
Yeazel [40]	2004	North America	9,434/ 2,667	No age information, 46.8% female, no ethnic information	Mixed	CS	AD	SR						

CS Cross-Sectional Survey, RC Retrospective Cohort Study, SR Self-Reported exposure/outcome, AD Administratively determined exposure/outcome, CR Chart Review

^a Study contained two cancer survivor groups: one survivor cohort received chest radiotherapy, the other did not

^b Study contained two controls groups: 23,731 controls with mammogram in same year as survivor's dx., 23,396 controls with the same comorbidity score

criteria [11–13, 19, 20, 27–41]. Forty-eight cancer screening sites were reported in these studies: 14 breast, 11 cervical, 11 colorectal, 6 prostate, 1 skin, and 2 testicular. Only one study was conducted outside North America [32], which was conducted in the United Kingdom. Three overlapping study data sources were observed: the National Health Interview Survey [13, 28]; the Ontario Cancer Registry [30, 32]; and the Childhood Cancer Survivor Study [37, 40].

The demographics of the cancer survivors in the included studies varied greatly, and ranged from childhood cancer survivors to elderly populations. The predominant ethnicity, when reported, was white/Caucasian, with only one study focusing on an ethnic minority [27], which was Hispanic. Most studies contained survivor populations with mixed initial cancer diagnosis types ($n=10$); the most common single initial cancer diagnosis type reported upon was breast cancer ($n=5$).

Mammography was used for breast cancer screening in all studies except one which measured receipt of either a clinical breast examination or mammogram [11]. Cervical cancer screening consisted of the receipt of a Pap smear in all studies.

Colorectal cancer screening consisted of the receipt of FOBT, endoscopy procedures (colonoscopy, sigmoidoscopy, or proctoscopy), barium enema, or some combination of these three. Prostate cancer screening consisted of the receipt of a prostate specific antigen (PSA) test in all studies, except one that measured receipt of either a PSA or digital rectal examination.

The screening timeframes varied greatly between studies, and ranged from within the last 12 months to ever/never being screened. The most common screening timeframes were: breast cancer screening (2-year interval, 7/14 studies), cervical cancer screening (3-year interval, 7/14 studies), colorectal cancer screening (FOBT, 1-year interval, 4/9 studies; endoscopy, 5- or 10-year intervals, 4/11 studies), and prostate cancer screening (1-year interval, 4/6 studies). The proportion of cancer survivors and controls screened varied greatly between studies, and appeared to be influenced by the age of the participants in each study, the length of screening timeframe (longer screening timeframes resulted in a greater proportion of both cancer survivors and controls receiving screening),

and screening site (lower screening rates for colorectal cancer than breast or cervical cancer). Across all screening sites, a large proportion of both cancer survivors and non-cancer controls did not receive adequate screening for new primary cancers, as defined by the screening recommendations used in each primary study.

Cancer survivors were more likely to receive screening for new primary cancers than non-cancer controls across all four cancer sites where a meta-analysis was conducted, as well as for skin and testicular cancer screening. Across all studies, cancer survivors were 27 % more likely to receive screening for new primary cancers compared to non-cancer

controls [odds ratio (OR), 1.27; 95 % confidence interval (CI), 1.19–1.36]. Meta-analyses for breast, cervical, colorectal, and prostate cancer screening can be seen in Fig. 2. Cancer survivors were 19 % more likely to receive breast cancer screening (OR, 1.19; 95 % CI, 1.06–1.34), 22 % more likely to receive cervical cancer screening (OR, 1.22; 95 % CI, 1.12–1.33), 19 % more likely to receive colorectal cancer screening (OR, 1.19; 95 % CI, 1.10–1.30), and 22 % more likely to receive prostate cancer screening (OR, 1.22; 95 % CI, 1.10–1.36).

Two studies could not be incorporated into our meta-analyses. Duffy et al. [19] used different definitions of

Fig. 2 Meta analyses for breast, cervical, colorectal, and prostate cancer screening. Generic inverse variance random effects model

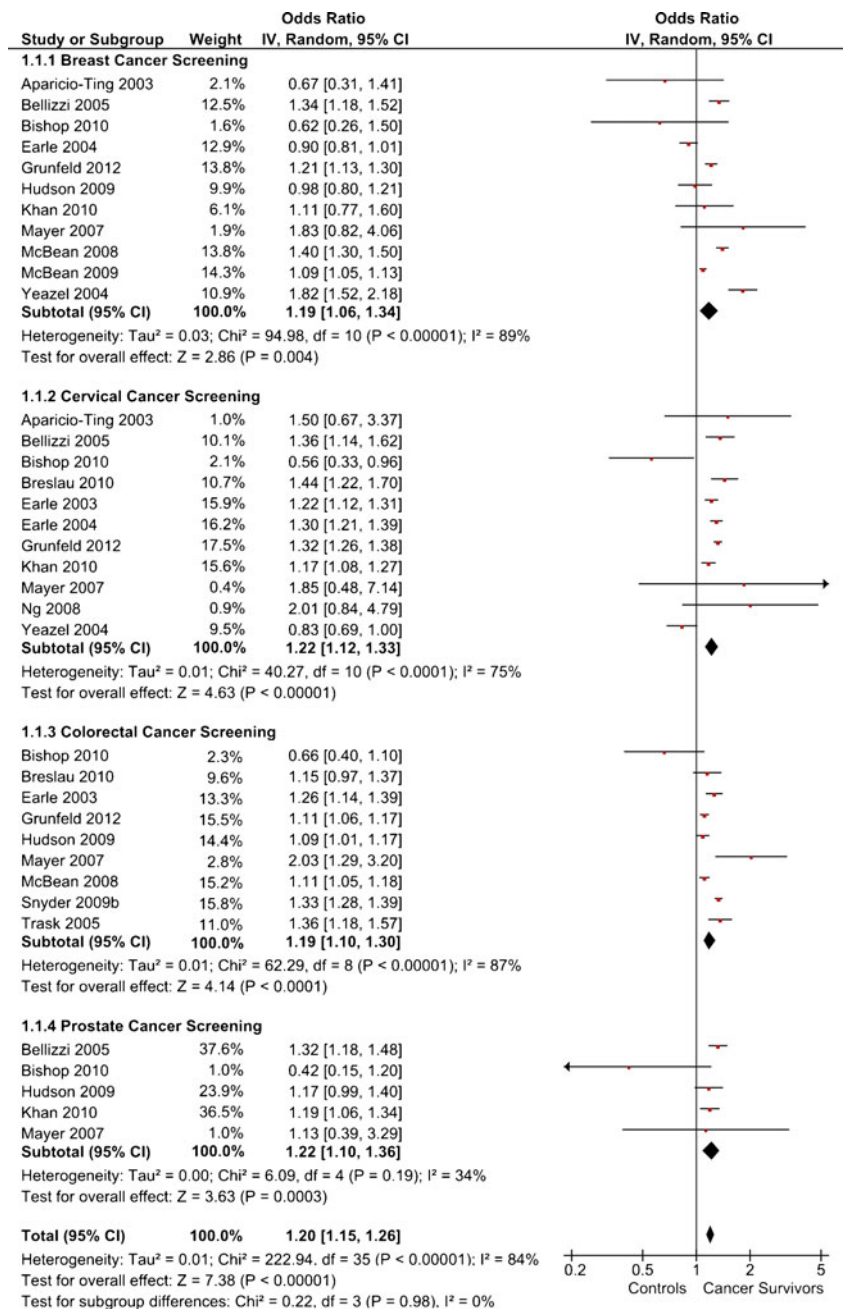


Table 2 Sensitivity and subgroup analyses for breast, cervical, and colorectal cancer screening

	Breast cancer screening Summary odds ratio estimate (95 % CI)	Cervical cancer screening Summary odds ratio estimate (95 % CI)	Colorectal cancer screening Summary odds ratio estimate (95 % CI)
All studies	1.19 (1.06–1.34) <i>n</i> =11	1.22 (1.12–1.33) <i>n</i> =11	1.19 (1.10–1.30) <i>n</i> =9
Study characteristics			
Elderly population (65+)	1.12 (0.91–1.37) <i>n</i> =3	1.26 (1.18–1.34) <i>n</i> =2	1.23 (1.08–1.40) <i>n</i> =3
Non-elderly population	1.24 (1.05–1.46) <i>n</i> =8	1.19 (1.04–1.36) <i>n</i> =9	1.16 (1.05–1.29) <i>n</i> =6
Childhood cancer survivors	1.17 (0.41–3.28) <i>n</i> =2	0.87 (0.53–1.43) <i>n</i> =3	0.66 (0.40–1.10) <i>n</i> =1
Non-childhood cancer survivors	1.15 (1.02–1.28) <i>n</i> =9	1.28 (1.22–1.34) <i>n</i> =8	1.21 (1.11–1.31) <i>n</i> =8
Ages of cancer survivors/controls within screening guidelines			
Adequate lower and upper age limits	1.06 (0.95–1.19) <i>n</i> =5	1.14 (0.95–1.37) <i>n</i> =4	1.11 (1.06–1.17) <i>n</i> =1
No lower and upper age limits	1.34 (1.13–1.59) <i>n</i> =6	1.28 (1.16–1.41) <i>n</i> =7	1.21 (1.10–1.33) <i>n</i> =8
Risk of bias categories			
(1) Selection bias			
Low/moderate risk	1.16 (1.02–1.30) <i>n</i> =7	1.27 (1.21–1.33) <i>n</i> =6	1.22 (1.11–1.34) <i>n</i> =5
High risk	1.25 (0.78–2.02) <i>n</i> =4	1.08 (0.70–1.65) <i>n</i> =5	1.14 (0.92–1.42) <i>n</i> =4
(2) Adequate cancer survivor selection			
Low/moderate risk	1.23 (1.09–1.40) <i>n</i> =9	1.22 (1.12–1.33) <i>n</i> =10	1.18 (1.09–1.29) <i>n</i> =7
High risk	0.96 (0.78–1.17) <i>n</i> =2	1.50 (0.67–3.37) <i>n</i> =1	1.21 (0.99–1.47) <i>n</i> =2
(3) Screening measurement			
Administrative data	1.14 (0.99–1.30) <i>n</i> =5	1.26 (1.19–1.33) <i>n</i> =4	1.20 (1.08–1.33) <i>n</i> =4
Self-reported	1.22 (0.93–1.61) <i>n</i> =6	1.16 (0.87–1.54) <i>n</i> =7	1.19 (1.00–1.43) <i>n</i> =5
(4) Controlling for confounding/using a matched cohort			
Low/moderate risk	1.22 (1.02–1.38) <i>n</i> =9	1.24 (1.15–1.34) <i>n</i> =9	1.21 (1.11–1.31) <i>n</i> =8
Unadjusted studies (high risk)	0.65 (0.37–1.15) <i>n</i> =2	0.87 (0.33–2.29) <i>n</i> =2	0.66 (0.40–1.10) <i>n</i> =1

appropriate cervical cancer screening in their cancer survivor (annual screening) and non-cancer control (biennial screening) groups, and reported that cancer survivors were as likely to receive an annual Pap smear as non-cancer survivors were to receive a biennial Pap smear (OR, 0.98; 95 % CI, 0.60–1.60). Kwon et al. [32] compared receipt of breast and cervical cancer screening among cancer survivors to a general population screening rate, and found that cancer survivors were about twice as likely to receive breast cancer screening (cancer survivors, 64 %; general population, 31 %) and colorectal cancer screening (cancer survivors, 30 %; general population, 15 %) during their

study follow-up period. We did not include Kwon et al. [32] into our meta-analyses for two reasons: first, the study population overlapped with the study by Grunfeld et al. [30], which was larger; second, this was the only included study that used general population screening rates as a comparison group.

There was significant heterogeneity observed between studies for breast ($n=11$), cervical ($n=11$), and colorectal ($n=9$) screening sites ($I^2=89$ %, 75 %, and 87 % respectively). No single study accounted for the statistically significant heterogeneity for these sites. There was no significant heterogeneity observed between the five studies for prostate cancer screening

($I^2=34\%$, $p=0.19$), and therefore, we did not conduct subgroup or sensitivity analyses for prostate cancer screening.

Risk of bias varied considerably between studies, ranging from studies using linked administrative databases with low risk of selection and measurement bias, to higher risk of bias studies using responses from self-reported surveys. Most studies using self-reported surveys had low response rates, introducing a further potential source of bias. There was considerable variation between studies' lengths of cancer survivorship follow-up, with some studies exclusively focusing on long-term survivors, while others contained a wide range of cancer survivorship follow-up time. Risk of bias assessments for each individual study are available by contacting the authors.

To explore potential sources of heterogeneity in the breast, cervical, and colorectal cancer screening meta-analyses, we conducted several sensitivity and subgroup analyses, presented in Table 2. Two categories were found to be statistically significantly different in colorectal cancer screening: studies that did not control for confounding or use a matched cohort, and studies that used a cohort of childhood cancer survivors. These differences were localized to a single study, and are unlikely to be a clinically significant source of heterogeneity. No other statistically significant subgroup or sensitivity analyses were found. There was no significant effect on our overall meta-analysis results when we conducted a sensitivity analysis by changing our decision rule to exclude studies with overlapping study populations.

Discussion

Our meta-analyses indicate that cancer survivors were more likely to receive screening for new primary cancers across all screening sites included in this review (19 % more likely to receive breast and colorectal cancer screening, 22 % more likely to receive cervical and prostate cancer screening). Taking the effect estimate with the lowest standard error from all studies included in our meta-analysis, cancer survivors overall were 27 % more likely to receive screening for new primary cancers.

While cancer survivors were more likely to receive screening for new primary cancers at each of the screening sites reported in this review, this finding must be interpreted in light of the receipt of cancer screening as a whole. Studies in our review reported that many individuals from both the general population and cancer survivor subpopulation did not receive screening tests recommended for the detection of new primary cancers.

Our study has several strengths. We used a rigorous search strategy which identified a yet-to-be published primary study. We were able to use two authors to abstract data in an effort to minimize data abstraction errors. Our meta-analysis and sensitivity/subgroup analyses were planned a

priori. Finally, we tailored our review question and reporting of results to meet the needs of healthcare professionals, program managers/administrators, and other decision makers by holding interactive workshops with key stakeholders throughout the review process.

Our study limitations largely mirror the limitations of the included literature. As only 20 studies were identified, subgroup and sensitivity analyses were likely underpowered to detect potential differences. Important contextual factors were not available for analysis in our systematic review, such as how screening programs local to each study operate (e.g., whether screening programs actively target specific age groups, or depend on primary care- or self-referral), and the degree to which follow-up care is integrated with cancer screening programs. These contextual factors could be a potential source of hidden heterogeneity in our study. Many studies contained incomplete information, which we were mostly able to overcome through contact with study authors. Few studies reported results separately for short- or long-term cancer survivors. Some studies did not use upper or lower age limits to compare receipt of cancer screening between cancer survivors and non-cancer controls. There were inconsistencies between studies' use of screening timeframes, which often did not reflect national recommendations for population-based cancer screening. As the studies included in our systematic review are predominantly from the USA, it is unclear whether the summary estimates in this study are applicable to other healthcare systems.

We conducted a subgroup analysis to examine whether cancer survivors might have higher uptake of cancer screening outside typical age restricted screening recommendations compared to non-cancer controls. This could have presented a source of bias in studies which did not use an upper age restriction. Healthcare providers or cancer survivors may recognize that cancer survivors are at a greater risk, and recommend starting or ending screening at earlier/later ages compared to the general population. However, our subgroup analysis found that studies without upper or lower age restrictions were not a significant source of heterogeneity. This finding is mirrored in studies that only contained an exclusively elderly population (\geq age 65), where we observed no significant difference in screening receipt. Future research should compare the receipt of screening within and outside guideline-based age recommendations to further explore whether the differences in screening uptake exclusively occur outside screening guideline age recommendations.

The two studies that were not included in our meta-analyses appeared to reach similar conclusions as the included literature. Despite using an annual screening timeframe for cancer survivors, and a biennial screening timeframe for non-cancer controls, Duffy et al. [19] found that cancer survivors were as likely to receive annual screening as non-cancer controls were to receive biennial screening. This suggests that if similar

screening timeframes were used for these two populations, cancer survivors would be screened more frequently than non-cancer controls. Kwon et al. [32] reported absolute screening differences that were much greater than any other study included in our review. This finding may be influenced by the researchers not restricting their analysis to guideline-based age recommendations, the inclusion of many survivors outside of screening age recommendations, and their comparison group being age-standardized general population screening rates.

In the absence of evidence which directly examines screening efficacy among cancer survivors, several studies have demonstrated that many cancer survivor populations are at an increased risk of developing second primary cancers [4–9]. Long-term cancer survivors, or short-term cancer survivors who are likely to survive long term based on the clinical characteristics of their disease, should be encouraged to meet population-based screening recommendations. Future research should directly measure the efficacy and cost-effectiveness of cancer screening among cancer survivors, and also seek to determine whether the optimal screening frequency for cancer survivors differs from the general population.

No studies in this review reported attempts to implement interventions to increase cancer screening receipt among cancer survivors. As cancer survivors represent a high-risk population, such interventions could have an impact on reducing the likelihood of cancer survivors being diagnosed with late-stage second primary cancers. Interventions that have been shown to increase screening uptake in the general population include: reminders, small media (e.g., videos and printed materials), one-on-one education, and reducing structural barriers (e.g., reducing travel distances and increasing hours of operation) [42]. Providing healthcare providers with assessment and feedback has also been shown to increase screening rates [42]. It is possible that these same interventions would increase the uptake of cancer screening among cancer survivors as well.

In conclusion, this study demonstrates that cancer survivors, a population that may be at a greater risk of developing a new primary cancer, are more likely to receive screening for new primary cancers than non-cancer controls. These results should be interpreted in light of suboptimal cancer screening rates in both cancer survivors and the general population. Whether increasing uptake of cancer screening is associated with improved outcomes during the cancer survivorship period should be a focus of future research.

Acknowledgments Funding for this research project was provided by the Canadian Institutes of Health Research through a Knowledge Synthesis Grant. The authors would like to thank those who participated in the workshops for contributing to the clinical context of this work.

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Appendix

Table 3 PubMed Search Strategy

#1	"Neoplasms by Histologic Type"[Mesh]	1153087
#2	"Neoplasms by Site"[Mesh]	1420041
#3	"Neoplasms, Second Primary"[Mesh]	8006
#4	"Neoplasms, Multiple Primary"[Mesh]	24727
#5	malign* [tiab]	322530
#6	tumour [tiab]	125997
#7	tumor [tiab]	573419
#8	cancer [tiab]	728755
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	2263065
#10	"Preventive Health Services"[Mesh]	339610
#11	"Early Detection of Cancer"[Mesh]	759
#12	"Mass Screening"[Mesh]	79128
#13	screen* [tiab]	327138
#14	#10 OR #11 OR #12 OR #13	611106
#15	"Survivors"[Mesh]	9554
#16	"previous malignancy"	103
#17	"previous cancer"	180
#18	"previous diagnosis"	1083
#19	survivor* [tiab]	46731
#20	#15 OR #16 OR #17 OR #18 OR #19	51822
#21	#9 AND #14 AND #20	1048

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