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ORIGINAL PAPER

The effect of multiple primary rules on population-based cancer survival

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Abstract
Purpose Different rules for registering multiple primary (MP) cancers are used by cancer registries throughout the world, making international data comparisons difficult. This study evaluates the effect of Surveillance, Epidemiology, and End Results (SEER) and International Association of Cancer Registries (IACR) MP rules on population-based cancer survival estimates.
Methods Data from five US states and six metropolitan area cancer registries participating in the SEER Program were used to estimate age-standardized relative survival (RS%) for first cancers-only and all first cancers matching the selection criteria according to SEER and IACR MP rules for all cancer sites combined and for the top 25 cancer site groups among men and women.
Results During 1995–2008, the percentage of MP cancers (all sites, both sexes) increased 25.4 % by using SEER rules (from 14.6 to 18.4 %) and 20.1 % by using IACR rules (from 13.2 to 15.8 %). More MP cancers were registered among females than among males, and SEER rules registered more MP cancers than IACR rules (15.8 vs. 14.4 % among males; 17.2 vs. 14.5 % among females). The top 3 cancer sites with the largest differences were melanoma (5.8 %), urinary bladder (3.5 %), and kidney and renal pelvis (2.9 %) among males, and breast (5.9 %), melanoma (3.9 %), and urinary bladder (3.4 %) among females. Five-year survival estimates (all sites combined) restricted to first primary cancers-only were higher than estimates by using first site-specific primaries (SEER or IACR rules), and for 11 of 21 sites among males and 11 of 23 sites among females. SEER estimates are comparable to IACR estimates for all site-specific cancers and marginally higher for all sites combined among females (RS 62.28 vs. 61.96 %).
Conclusion Survival after diagnosis has improved for many leading cancers. However, cancer patients remain at risk of subsequent cancers. Survival estimates based on first cancers-only exclude a large and increasing number of MP cancers. To produce clinically and epidemiologically relevant and less biased cancer survival estimates, data on all cancers should be included in the analysis. The multiple primary rules (SEER or IACR) used to identify primary cancers do not affect survival estimates if all first cancers matching the selection criteria are used to produce site-specific survival estimates.

Keywords Cancer survival · Multiple primary rules · SEER Program

Abbreviations

ICD	International Classification of Diseases
IACR	International Association of Cancer Registries
NAACCR	North American Association of Central Cancer Registries
NPCR	National Program of Cancer Registries
SEER	Surveillance, Epidemiology, and End Results

Disclaimers: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Introduction

Population-based cancer registries serve a vital role by providing useful information for directing and monitoring cancer control activities and health policy initiatives [1, 2]. Much time and effort has been spent on standardizing the collection, consolidation, analysis, and reporting of cancer surveillance data to ensure that the data are high quality, complete, and comparable, and therefore suitable to aggregate among cancer registries in the United States [3, 4], Canada [5], and within North America [6]. Increasingly, population-based cancer registry data are being used to compare cancer incidence and survival rates among countries worldwide [7–10].

In the mid-1970s, the Surveillance, Epidemiology, and End Results (SEER) Program [11] developed coding rules that helped differentiate a new primary cancer from a distant metastasis or a recurrent cancer. SEER standardized the coding of multiple primary cancers diagnosed in an individual cancer patient, including cancers that were diagnosed concurrent with or subsequent to the first primary cancer [12]. These rules have been revised over time [13–17] and are used throughout the United States and in the majority of Canadian provinces beginning in 2007 [18]. In addition, the International Association of Cancer Registries (IACR) has developed multiple primary coding rules that are used worldwide [19]. In general, SEER rules are more liberal than IACR rules in allowing the registration of multiple primary cancers, particularly cancers that occur in paired organs, at the same anatomic site and with the same histologic type.

To address issues of comparability, IACR has developed a computer software program that processes data about multiple primary cancers reported for the same cancer patient and produces a file consistent with IACR multiple primary rules [20]. This program has been used to process data from North American cancer registries for inclusion in *Cancer Incidence in Five Continents* [7] and by the CONCORD Programme, when reporting global cancer survival data [9].

Historically, usage of different multiple primary rules has not hindered comparative analyses of population-based cancer survival because estimates have been based on the first primary cancer (i.e., only primary cancer or first of two or more primary cancers) diagnosed in a patient [8–10, 21]. But recently, Brenner and Hakulinen [22] have cautioned against the exclusion of patients with a prior cancer for comparative analyses of population-based cancer survival. As the authors noted, the proportion of cancer patients with a known prior cancer may depend on the length of operation of the cancer registry: Cancer registries that have been in operation for many years will have more information (i.e., past cancer diagnoses) with which to correctly identify a prior cancer than a cancer registry that has been in operation for fewer years. Because the prognosis of a subsequent cancer often differs from that of a first cancer (i.e., the inclusion of all cancers tends to produce somewhat lower survival estimates than those based solely on first cancers) [23, 24], the exclusion of cancer patients with a known prior cancer may introduce a bias in comparative studies because some cancers will be erroneously designated as first cancers when, in fact, they are subsequent cancers. The potential effect of this bias—if estimates are restricted to first cancers-only—will increase as the number and proportion of multiple primary cancers increases because of improved survival for many leading cancers [3, 8, 21, 25]. Furthermore, the mobility and migration patterns of North American populations are variable [26, 27], and a cancer registry may not have knowledge of a previous cancer if that cancer was diagnosed in a different state, province, or country.

International comparisons of cancer incidence [7] and survival [8, 9] are possible, but differences in the coding rules for multiple primary cancers need to be considered when comparing data. Although several studies have compared survival estimates by using first versus multiple cancers using IACR multiple primary rules [22–24], this study is the first, to our knowledge, to compare survival estimates by using both IACR and SEER multiple primary cancer rules among the same patient population.

Materials and methods

Source of data

Data collected according to SEER multiple primary cancer rules were available from cancer registries in five states (Connecticut, Hawaii, Iowa, New Mexico, Utah) and six metropolitan areas (Atlanta, Detroit, San Francisco-Oakland, Seattle, Los Angeles, San Jose—Monterey) participating in the SEER Program [11] and covering approximately 14 % of the US population (SEER-11). Primary site and histology were coded according to the edition of the *International Classification of Diseases for Oncology* in use at the time of diagnosis, converted to the third edition [28], and categorized according to the SEER cancer site recodes [29]. Record-level data for patients diagnosed beginning 1 January 1973 (1974 for Seattle, 1975 for Atlanta, and 1992 for Los Angeles and San Jose—Monterey) through 31 December 2008 were extracted from the November 2010 data submission to the SEER Program by using the Case Listing Session feature in SEER*Stat software (Version 7.0.4, Information Management Services, Inc., Silver Spring, MD) and processed by using SAS (Version 9.2, Cary, NC). The IACR multiple primary program [20] was applied to the extracted data for the

purpose of designating cases consistent with IACR multiple primary rules. The data were then processed by using SEER*Prep (Version 2.4.2, Information Management Services, Inc., Silver Spring, MD) for analysis in SEER*Stat.

The following cases were excluded: (a) in situ cancer (with the exception of in situ urinary bladder, which is considered invasive for incidence reporting) ($n = 397{,}637$) and (b) unknown age ($n = 724$). After these exclusions, 2,353,889 cases were diagnosed among cancer patients aged 15 years or older from 1 January 1995 to 31 December 2008. More cases were excluded from the survival analysis because they did not contribute survival time: (a) vital status of alive with zero survival times ($n = 20{,}416$) and (b) cases reported solely on the basis of a death certificate or autopsy report ($n = 29{,}537$).

Analysis

Observed survival is the proportion of patients alive at some specified time after diagnosis following the identification of deaths from any and all causes, including cancer, and adjustment for the number of patients at risk of dying. Relative survival is the ratio of the observed to expected survival [30] where expected survival, for this analysis, was derived from life tables available in SEER*Stat titled "US 1970–2006 by individual year (White, Black, Other (AI/API) All races for Other Unspec 1991+ and Unknown)."

Relative survival estimates were calculated using SEER*Stat software (Version 8.0.2, Information Management Services, Inc., Silver Spring, MD) for all races combined by using the actuarial method on monthly follow-up, and the cumulative summary survival rates at 12 months (1 year), 36 months (3 years), 60 months (5 years), and 120 months (10 years) are presented. All cancers and cancer-specific survival estimates were age-standardized to the International Cancer Survival Standards (ICSS) [31] by using five age-groups (15–44, 45–54, 55–64, 65–74, and 75+). Confidence intervals for the estimates were calculated on the basis of a log (−[log]) transformation.

In this analysis, we looked at the total number of first primary cancers according to SEER multiple primary rules and the additional number (if any) of primary cancers according to SEER and IACR rules, respectively. Case counts and survival estimates were generated according to SEER primary site recodes [29]. Parallel analyses were conducted on three data sets (first primary cancers-only [First]; first and IACR multiple primary cancers [IACR MP]; first and SEER multiple primary cancers [SEER MP]) in order to compare all cancer sites combined and site-specific case counts and survival rates by using different multiple primary cancer coding rules. The percentage of multiple primary cancer cases was calculated for both the SEER and IACR data sets, and sites with the largest absolute differences were ranked. For the SEER MP and IACR MP survival analyses, only the first primary cancer that matched to the selection criteria was used, such that an individual could contribute no more than one case per site category. For example, if a person had two oral cavity cancers and one esophagus cancer, they would contribute the earlier of the two oral cavity cases to the survival statistics for the oral cavity site category, the esophagus case to the esophagus category, and only the earliest of the three tumors to the "All sites" grouping.

There is no formal statistical test to compare survival estimates on (nearly) the same population by using different analytic methods. Therefore, we noted differences where 5-year point estimates from the first data set were not contained within the corresponding 95 % CIs from the SEER and IACR data sets, respectively. Differences were noted where 5-year point estimates from the IACR MP data set were not contained within the corresponding 95 % CIs from the SEER MP data set.

Results

Figure 1 shows the percentage of multiple primary cancers (all sites and both sexes combined) by year of diagnosis according to SEER and IACR multiple primary cancer coding rules. In 1995, 14.6 and 13.2 %, respectively, of all cancers were reported as multiple primary according to SEER and IACR rules. Between 2005 and 2006, the percentage of multiple primaries declined slightly before continuing to increase. By 2008, the percentage of multiple primary cancers increased to 18.4 % (+25.4 %) according to SEER rules and to 15.8 % (+20.1 %) according to IACR rules.

Table 1 shows the number of first primary cancer sites, by sex, according to SEER multiple primary cancer rules; the number and percentage of additional cancers by using IACR and SEER rules; and the percentage difference between SEER and IACR rules, for all cancer sites combined and the top 25 cancer sites for cancer patients aged 15 years or older at diagnosis and diagnosed between 1995 and 2008 in the SEER-11 area. During 1995–2008, there were 1,015,564 males and 951,022 females diagnosed with at least one primary cancer. According to SEER rules, 189,933 (15.8 %) and 197,370 (17.2 %) additional primary cancers were diagnosed among males and females, respectively. According to IACR rules, 171,363 (14.4 %) and 160,946 (14.5 %) additional primary cancers were diagnosed among males and females, respectively. For each of the top 25 cancer sites and all cancer sites combined, SEER rules identified more multiple primaries than IACR rules. The largest differences in the number of

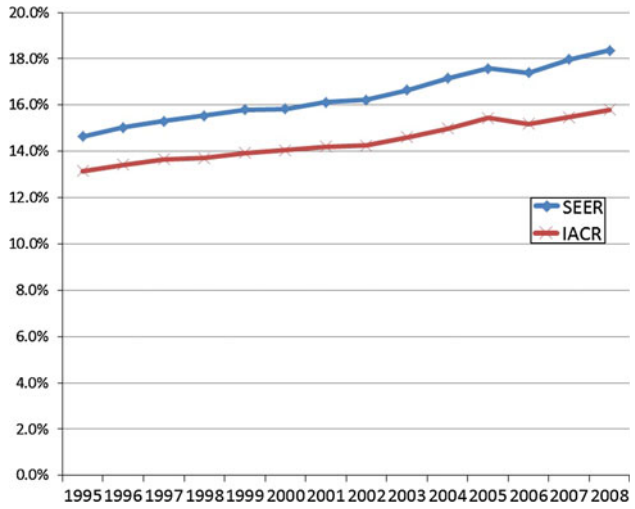

Fig. 1 Percentage of multiple primary cancers (all sites and both sexes combined) by IACR and SEER multiple primary rules (1995–2008): SEER 11 registries. *IACR* International Association of Cancer Registries. *SEER* Surveillance, Epidemiology, and End Results

multiple primary cancers between the two rule sets, in rank order, were as follows: melanoma of the skin (5.8 %), urinary bladder (3.5 %), kidney and renal pelvis (2.9 %), colon and rectum (2.7 %), and oral cavity and pharynx (1.6 %) among males; and breast (5.9 %), melanoma of the skin (3.9 %), urinary bladder (3.4 %), colon and rectum (2.9 %), and oral cavity and pharynx (2.2 %) among females.

Table 2 shows 1-, 3-, 5-, and 10-year age-standardized relative survival (RS%) estimates and 95 % CI for all cancer sites combined and for the top 25 cancer sites among males and females for each data set (First, SEER MP, and IACR MP) and differences for First versus SEER MP and IACR MP, respectively, and between SEER MP and IACR MP data sets. Differences where the point estimate from one data set was not contained within the confidence interval for the comparative data set were noted. Compared with estimates using first primary cancers-only, those that included all first primary cancers matching the selection criteria gave more conservative (i.e., lower) 5-year survival estimates for all sites combined (SEER: RS −1.30 %, IACR: RS −1.29 %) among males and (SEER: RS −0.23 %, IACR: RS −0.55 %) among females, respectively; and for 11 of the top cancers: oral cavity and pharynx (RS −2.26 %, RS −2.20 %), colon and rectum (RS −1.31 %, RS −1.30 %), larynx (RS −1.62 %, RS −1.59 %), melanoma of the skin (RS −1.05 %, RS −1.12 %), prostate (RS −1.06 %, RS −1.07 %), urinary bladder (RS −2.37 %, RS −2.06 %), kidney and renal pelvis (RS −0.78 % SEER only), thyroid (RS −1.90 %, RS −1.92 %), Hodgkin's lymphoma (RS −1.28 %, RS −1.22 %), non-Hodgkin's lymphoma (RS −0.76 %, RS −0.68 %), and leukemia (RS −0.91 %, RS −0.86 %) among males and oral cavity and pharynx (RS −1.73 %, RS −1.74 %), colon and rectum (RS −0.69 %, RS −0.69 %), larynx (RS −2.72 %, RS −2.72 %), melanoma of the skin (RS −0.89 %, RS −0.88 %), breast (RS −0.76 %, RS −0.67 %), corpus and uterus, NOS (RS −1.40 %, RS −1.40 %), urinary bladder (RS −2.54 %, RS −2.28 %), kidney and renal pelvis (RS −0.89 % SEER only), thyroid (RS −0.78 %, RS −0.77 %), non-Hodgkin's lymphoma (RS −0.77 %, RS −0.68 %), and leukemia (RS −1.99 %, RS −1.95 %) among females. Five-year cancer survival estimates differed between SEER MP and IACR MP for all sites combined (RS 0.32 %) among females.

Discussion

This study provided a unique opportunity to evaluate the effect of two widely used multiple primary cancer coding rules, SEER and IACR, on population-based survival estimates using SEER-11 cancer survival data, covering approximately 14 % of the US population.

Until recently, the presence of multiple primary cancers and the rules used to collect and report these cases were generally not considered in survival analyses because population-based survival estimates were based on first primary cancers—either the only cancer diagnosed in a patient or the first of multiple primary cancers diagnosed [8, 9, 21]. However, this practice is no longer advocated because it can result in the exclusion of a relatively large and growing number of cancer patients and can lead to the introduction of biases into survival analyses [22].

In the United States, the percentage of multiple primary cancers by using SEER rules is relatively large and increasing. The percentage was higher in females compared to males (17.2 vs. 15.8 %) reflecting, in large part, the influence of these rules on female breast cancer counts. Between 1995 and 2008, the percentage of multiple primary cancers increased 25.4 % among SEER-11 registries. This increase reflects improved survival for many adult cancers and the fact that cancer patients remain at risk, and in some cases increased risk, of developing subsequent primary cancers [32]. The SEER rules have changed over time and field studies to test the most recent rules began in late 2005 and may account for the slight reduction in the percentage of multiple primary cancers observed between 2005 and 2006. The rules were modified to include longer time requirements between same site primaries for certain sites [17].

This study confirmed the finding from previous studies [23, 24] that survival estimates based on first cancers-only exclude a large, varied, and increasing number of subsequent primary cancers and generally produce less

Table 1 Case counts by primary cancer type (first or only), cancers using SEER multiple primary (MP) rules, and cancers using IACR MP rules for the leading cancers among males and females, all races combined, aged 15 years or older (SEER-11: 1995–2008)

Site	First	SEER MP		IACR MP		Difference	
	(*a*) #	(*b*) #	(*c*) % ($b/a + b$)	(*d*) #	(*e*) % ($d/a + d$)	% ($c - e$)	Rank
Male							
All sites	1,015,564	189,933	15.8	171,363	14.4	1.3	
Oral cavity and pharynx	29,786	6,567	18.1	5,858	16.4	1.6	5
Esophagus	13,635	3,078	18.4	3,050	18.3	0.1	
Stomach	21,501	4,427	17.1	4,369	16.9	0.2	
Colon and rectum	102,158	25,179	19.8	20,977	17.0	2.7	4
Liver and intrahepatic bile duct	20,797	2,584	11.1	2,568	11.0	0.1	
Pancreas	23,187	4,933	17.5	4,928	17.5	0.0	
Larynx	11,648	2,536	17.9	2,434	17.3	0.6	
Lung and bronchus	129,085	33,367	20.5	31,067	19.4	1.1	
Melanoma of the skin	42,019	11,652	21.7	7,923	15.9	5.8	1
Prostate	335,565	31,951	8.7	31,939	8.7	0.0	
Testis	14,394	589	3.9	317	2.2	1.8	
Urinary bladder	57,628	18,240	24.0	14,904	20.5	3.5	2
Kidney and renal pelvis	30,518	8,395	21.6	7,010	18.7	2.9	3
Brain and other nervous system	14,680	1,883	11.4	1,782	10.8	0.5	
Thyroid	9,848	1,552	13.6	1,492	13.2	0.5	
Hodgkin's lymphoma	7,193	581	7.5	569	7.3	0.1	
Non-Hodgkin's lymphoma	45,204	9,051	16.7	8,342	15.6	1.1	
Myeloma	13,003	2,597	16.6	2,474	16.0	0.7	
Leukemia	28,504	5,760	16.8	5,524	16.2	0.6	
Mesothelioma	3,083	777	20.1	776	20.1	0.0	
Kaposi sarcoma	5,592	357	6.0	357	6.0	0.0	
Female							
All sites	951,022	197,370	17.2	160,946	14.5	2.7	
Oral cavity and pharynx	13,912	3,897	21.9	3,410	19.7	2.2	5
Esophagus	4,379	1,276	22.6	1,263	22.4	0.2	
Stomach	14,291	2,823	16.5	2,766	16.2	0.3	
Colon and rectum	100,719	24,785	19.7	20,375	16.8	2.9	4
Liver and intrahepatic bile duct	9,062	1,373	13.2	1,370	13.1	0.0	
Pancreas	24,631	4,740	16.1	4,738	16.1	0.0	
Larynx	2,847	742	20.7	713	20.0	0.6	
Lung and bronchus	107,755	29,548	21.5	27,388	20.3	1.3	
Melanoma of the skin	34,423	6,890	16.7	5,027	12.7	3.9	2
Breast	301,963	59,106	16.4	35,191	10.4	5.9	1
Cervix uteri	22,133	1,840	7.7	1,805	7.5	0.1	
Corpus and uterus, NOS	58,834	9,277	13.6	9,224	13.6	0.1	
Ovary	32,236	5,688	15.0	5,635	14.9	0.1	
Urinary bladder	19,543	6,268	24.3	5,161	20.9	3.4	3
Kidney and renal pelvis	19,042	4,742	19.9	4,165	17.9	2.0	
Brain and other nervous system	11,695	1,557	11.7	1,482	11.2	0.5	
Thyroid	32,382	3,459	9.7	3,301	9.3	0.4	
Hodgkin's lymphoma	6,005	484	7.5	473	7.3	0.2	
Non-Hodgkin's lymphoma	38,088	7,501	16.5	6,916	15.4	1.1	
Myeloma	11,426	1,920	14.4	1,826	13.8	0.6	
Leukemia	21,188	4,499	17.5	4,358	17.1	0.5	
Mesothelioma	911	226	19.9	226	19.9	0.0	
Kaposi sarcoma	295	55	15.7	55	15.7	0.0	

Table 2 The 1-, 3-, 5-, and 10-year age-standardized relative survival estimates and 95 % confidence limits by primary cancer type (first, SEER multiple primary [MP] rules, and IACR MP rules) for all cancer sites combined and the top 25 sites, by sex (1995–2008, SEER-11)

Site	Years	First	SEER MP	IACR MP	SEER MP−first	IACR MP−first	SEER MP–IACR MP
Males							
All sites	1	78.19 (78.10–78.28)	77.69 (77.61–77.78)	77.66 (77.57–77.74)	−0.50[a]	−0.53[a]	0.03
	3	68.57 (68.46–68.68)	67.56 (67.46–67.67)	67.55 (67.44–67.66)	−1.01[a]	−1.02[a]	0.01
	5	65.15 (65.02–65.29)	63.85 (63.72–63.98)	63.86 (63.73–63.99)	−1.30[a]	−1.29[a]	−0.01
	10	60.34 (60.10–60.57)	58.58 (58.37–58.8)	58.63 (58.42–58.85)	−1.76[a]	−1.71[a]	−0.05
Oral cavity and pharynx	1	81.25 (80.65–81.83)	80.44 (79.93–80.95)	80.39 (79.87–80.90)	−0.81[a]	−0.86[a]	0.05
	3	63.32 (62.52–64.10)	61.70 (61.01–62.37)	61.65 (60.96–62.33)	−1.62[a]	−1.67[a]	0.05
	5	56.31 (55.38–57.23)	54.05 (53.25–54.84)	54.11 (53.31–54.90)	−2.26[a]	−2.20[a]	−0.06
	10	45.25 (43.78–46.71)	42.98 (41.75–44.20)	43.08 (41.84–44.31)	−2.27[a]	−2.17[a]	−0.10
Esophagus	1	44.93 (44.03–45.83)	44.94 (44.12–45.75)	44.92 (44.1–45.74)	0.01	−0.01	0.02
	3	21.13 (20.33–21.94)	20.79 (20.07–21.52)	20.78 (20.06–21.51)	−0.34	−0.35	0.01
	5	15.99 (15.20–16.79)	15.47 (14.76–16.19)	15.46 (14.75–16.18)	−0.52	−0.53	0.01
	10	11.66 (10.53–12.85)	11.22 (10.27–12.22)	11.22 (10.27–12.21)	−0.44	−0.44	0.00
Stomach	1	49.94 (49.23–50.65)	49.78 (49.13–50.43)	49.77 (49.12–50.42)	−0.16	−0.17	0.01
	3	29.03 (28.33–29.73)	28.86 (28.22–29.51)	28.86 (28.22–29.51)	−0.17	−0.17	0.00
	5	24.00 (23.28–24.73)	23.60 (22.95–24.27)	23.59 (22.93–24.25)	−0.40	−0.41	0.01
	10	19.24 (18.28–20.22)	18.67 (17.81–19.55)	18.67 (17.81–19.55)	−0.57	−0.57	0.00
Colon and rectum	1	83.87 (83.61–84.12)	83.46 (83.23–83.69)	83.43 (83.2–83.67)	−0.41[a]	−0.44[a]	0.03
	3	70.98 (70.62–71.33)	70.04 (69.71–70.36)	70.01 (69.69–70.34)	−0.94[a]	−0.97[a]	0.03
	5	64.61 (64.19–65.03)	63.30 (62.91–63.68)	63.31 (62.92–63.69)	−1.31[a]	−1.30[a]	−0.01
	10	58.26 (57.56–58.96)	56.41 (55.79–57.03)	56.48 (55.86–57.10)	−1.85[a]	−1.78[a]	−0.07
Liver and intrahepatic bile duct	1	33.10 (32.37–33.82)	33.47 (32.79–34.14)	33.45 (32.78–34.13)	0.37	0.35	0.02
	3	15.95 (15.34–16.57)	16.16 (15.59–16.75)	16.16 (15.58–16.74)	0.21	0.21	0.00
	5	10.90 (10.31–11.50)	10.98 (10.43–11.54)	10.97 (10.43–11.53)	0.08	0.07	0.01
	10	6.74 (6.08–7.43)	6.77 (6.15–7.42)	6.77 (6.15–7.42)	0.03	0.03	0.00
Pancreas	1	24.63 (24.04–25.23)	24.91 (24.36–25.47)	24.91 (24.36–25.47)	0.28	0.28	0.00
	3	7.87 (7.46–8.29)	7.81 (7.43–8.21)	7.81 (7.43–8.21)	−0.06	−0.06	0.00
	5	5.32 (4.95–5.71)	5.32 (4.97–5.68)	5.32 (4.97–5.68)	0.00	0.00	0.00
	10	3.58 (3.16–4.03)	3.43 (3.04–3.86)	3.43 (3.04–3.86)	−0.15	−0.15	0.00
Larynx	1	85.99 (85.18–86.76)	85.51 (84.8–86.19)	85.52 (84.8–86.2)	−0.48	−0.47	−0.01
	3	70.67 (69.51–71.80)	69.12 (68.09–70.11)	69.12 (68.09–70.12)	−1.55[a]	−1.55[a]	0.00
	5	63.66 (62.26–65.01)	62.04 (60.82–63.23)	62.07 (60.85–63.27)	−1.62[a]	−1.59[a]	−0.03
	10	50.31 (48.01–52.55)	48.50 (46.51–50.46)	48.55 (46.56–50.52)	−1.81	−1.76	−0.05
Lung and bronchus	1	39.75 (39.45–40.04)	40.82 (40.55–41.09)	40.72 (40.45–40.99)	1.07	0.97	0.10
	3	18.36 (18.11–18.62)	18.96 (18.72–19.19)	18.90 (18.66–19.13)	0.60	0.54	0.06
	5	13.80 (13.55–14.04)	14.09 (13.87–14.32)	14.06 (13.83–14.29)	0.29	0.26	0.03
	10	9.05 (8.76–9.34)	9.07 (8.81–9.34)	9.07 (8.81–9.34)	0.02	0.02	0.00
Melanoma of the skin	1	97.13 (96.91–97.34)	96.90 (96.70–97.09)	96.90 (96.69–97.09)	−0.23[a]	−0.23[a]	0.00
	3	92.36 (91.97–92.74)	91.80 (91.45–92.14)	91.73 (91.38–92.07)	−0.56[a]	−0.63[a]	0.07
	5	90.03 (89.51–90.52)	88.98 (88.52–89.42)	88.91 (88.44–89.36)	−1.05[a]	−1.12[a]	0.07
	10	87.71 (86.73–88.62)	86.34 (85.52–87.12)	86.35 (85.51–87.14)	−1.37[a]	−1.36[a]	−0.01
Prostate	1	99.45 (99.37–99.52)	99.16 (99.08–99.24)	99.16 (99.08–99.24)	−0.29[a]	−0.29[a]	0.00
	3	98.67 (98.52–98.81)	97.88 (97.73–98.03)	97.88 (97.73–98.03)	−0.79[a]	−0.79[a]	0.00
	5	98.20 (97.98–98.39)	97.14 (96.92–97.33)	97.13 (96.92–97.33)	−1.06[a]	−1.07[a]	0.01
	10	96.39 (95.92–96.80)	94.77 (94.3–95.20)	94.76 (94.3–95.19)	−1.62[a]	−1.63[a]	0.01

Table 2 continued

Site	Years	First	SEER MP	IACR MP	SEER MP−first	IACR MP−first	SEER MP–IACR MP
Testis	1	95.38 (93.92–96.49)	95.20 (93.98–96.17)	95.15 (93.93–96.14)	−0.18	−0.23	0.05
	3	92.13 (90.13–93.73)	91.78 (90.07–93.21)	91.69 (89.96–93.13)	−0.35	−0.44	0.09
	5	90.90 (88.40–92.88)	91.10 (89.01–92.81)	90.96 (88.86–92.69)	0.20	0.06	0.14
	10	87.46 (83.90–90.28)	88.02 (84.47–90.80)	87.81 (84.32–90.57)	0.56	0.35	0.21
Urinary bladder	1	92.85 (92.59–93.10)	92.08 (91.84–92.31)	92.13 (91.89–92.36)	−0.77[a]	−0.72[a]	−0.05
	3	85.71 (85.30–86.11)	83.97 (83.6–84.34)	84.19 (83.81–84.55)	−1.74[a]	−1.52[a]	−0.22
	5	81.87 (81.34–82.39)	79.50 (79.03–79.97)	79.81 (79.34–80.28)	−2.37[a]	−2.06[a]	−0.31
	10	74.70 (73.69–75.67)	71.21 (70.34–72.05)	71.63 (70.76–72.49)	−3.49[a]	−3.07[a]	−0.42
Kidney and renal pelvis	1	79.34 (78.78–79.88)	79.72 (79.25–80.19)	79.63 (79.15–80.10)	0.38	0.29	0.09
	3	69.49 (68.77–70.20)	69.07 (68.45–69.67)	69.12 (68.49–69.73)	−0.42	−0.37	−0.05
	5	64.59 (63.72–65.44)	63.81 (63.06–64.54)	64.07 (63.32–64.81)	−0.78[a]	−0.52	−0.26
	10	54.99 (53.46–56.49)	53.97 (52.67–55.25)	54.21 (52.89–55.51)	−1.02	−0.78	−0.24
Brain and other nervous system	1	52.74 (52.01–53.46)	52.58 (51.89–53.27)	52.60 (51.91–53.29)	−0.16	−0.14	−0.02
	3	30.30 (29.60–31.00)	29.94 (29.27–30.61)	29.98 (29.31–30.66)	−0.36	−0.32	−0.04
	5	25.64 (24.93–26.37)	25.19 (24.50–25.89)	25.23 (24.54–25.93)	−0.45	−0.41	−0.04
	10	19.43 (18.60–20.27)	19.06 (18.27–19.87)	19.11 (18.32–19.92)	−0.37	−0.32	−0.05
Thyroid	1	94.06 (93.35–94.71)	93.92 (93.31–94.48)	93.91 (93.3–94.48)	−0.14	−0.15	0.01
	3	92.34 (91.41–93.17)	91.32 (90.48–92.08)	91.30 (90.46–92.07)	−1.02[a]	−1.04[a]	0.02
	5	90.92 (89.65–92.05)	89.02 (87.90–90.03)	89.00 (87.88–90.02)	−1.90[a]	−1.92[a]	0.02
	10	86.15 (83.59–88.33)	83.71 (81.51–85.68)	83.69 (81.49–85.66)	−2.44[a]	−2.46[a]	0.02
Hodgkin's lymphoma	1	89.03 (88.18–89.82)	88.68 (87.91–89.40)	88.69 (87.93–89.41)	−0.35	−0.34	−0.01
	3	83.70 (82.65–84.69)	82.82 (81.85–83.74)	82.86 (81.88–83.78)	−0.88	−0.84	−0.04
	5	80.03 (78.77–81.22)	78.75 (77.59–79.86)	78.81 (77.64–79.92)	−1.28[a]	−1.22[a]	−0.06
	10	72.39 (70.40–74.27)	71.40 (69.62–73.10)	71.44 (69.65–73.14)	−0.99	−0.95	−0.04
Non-Hodgkin's lymphoma	1	76.12 (75.66–76.58)	76.07 (75.66–76.48)	76.10 (75.69–76.51)	−0.05	−0.02	−0.03
	3	65.21 (64.62–65.78)	64.79 (64.27–65.30)	64.84 (64.32–65.36)	−0.42	−0.37	−0.05
	5	59.38 (58.68–60.06)	58.62 (58.01–59.23)	58.70 (58.09–59.31)	−0.76[a]	−0.68[a]	−0.08
	10	49.08 (47.91–50.25)	47.78 (46.75–48.81)	47.87 (46.83–48.91)	−1.30[a]	−1.21[a]	−0.09
Myeloma	1	75.09 (74.28–75.87)	74.92 (74.19–75.63)	74.95 (74.22–75.66)	−0.17	−0.14	−0.03
	3	52.84 (51.82–53.84)	52.41 (51.48–53.32)	52.47 (51.54–53.38)	−0.43	−0.37	−0.06
	5	37.86 (36.78–38.94)	37.65 (36.65–38.64)	37.71 (36.71–38.70)	−0.21	−0.15	−0.06
	10	19.09 (17.81–20.40)	19.24 (18.04–20.46)	19.26 (18.06–20.49)	0.15	0.17	−0.02
Leukemia	1	68.07 (67.47–68.67)	67.01 (66.46–67.55)	67.07 (66.53–67.61)	−1.06	−1.00	−0.06
	3	54.90 (54.19–55.61)	53.83 (53.19–54.47)	53.90 (53.26–54.54)	−1.07[a]	−1.00[a]	−0.07
	5	47.91 (47.12–48.70)	47.00 (46.28–47.71)	47.05 (46.33–47.76)	−0.91[a]	−0.86[a]	−0.05
	10	36.13 (34.95–37.30)	35.32 (34.26–36.38)	35.40 (34.34–36.47)	−0.81	−0.73	−0.08
Mesothelioma	1	42.09 (40.09–44.07)	41.81 (39.95–43.65)	41.81 (39.95–43.65)	−0.28	−0.28	0.00
	3	12.99 (11.49–14.59)	12.81 (11.41–14.29)	12.81 (11.41–14.29)	−0.18	−0.18	0.00
	5	8.01 (6.69–9.46)	7.73 (6.52–9.06)	7.73 (6.52–9.06)	−0.28	−0.28	0.00
	10	3.08 (2.02–4.50)	3.17 (2.15–4.49)	3.17 (2.15–4.49)	0.09	0.09	0.00
Kaposi sarcoma	1	83.20 (80.39–85.63)	83.19 (80.68–85.40)	83.19 (80.68–85.40)	−0.01	−0.01	0.00
	3	77.44 (73.70–80.72)	75.99 (72.48–79.13)	75.99 (72.48–79.13)	−1.45	−1.45	0.00
	5	73.66 (68.60–78.03)	71.91 (67.35–75.96)	71.91 (67.35–75.96)	−1.74	−1.74	0.00
	10	65.79 (56.20–73.77)	65.71 (57.74–72.54)	65.71 (57.74–72.54)	−0.08	−0.08	0.00
Females							

Table 2 continued

Site	Years	First	SEER MP	IACR MP	SEER MP−first	IACR MP−first	SEER MP–IACR MP
All sites	1	77.99 (77.90–78.09)	78.24 (78.15–78.32)	77.95 (77.86–78.03)	0.25	−0.04[a]	0.29[b]
	3	67.06 (66.95–67.18)	67.02 (66.91–67.13)	66.68 (66.57–66.79)	−0.04	−0.38[a]	0.34[b]
	5	62.51 (62.37–62.64)	62.28 (62.16–62.40)	61.96 (61.84–62.09)	−0.23[a]	−0.55[a]	0.32[b]
	10	56.60 (56.40–56.81)	55.92 (55.73–56.11)	55.68 (55.49–55.87)	−0.68[a]	−0.92[a]	0.24[b]
Oral cavity and pharynx	1	81.76 (81.01–82.48)	81.30 (80.64–81.94)	81.24 (80.58–81.89)	−0.46	−0.52	0.06
	3	66.40 (65.41–67.37)	64.78 (63.91–65.64)	64.76 (63.88–65.62)	−1.62[a]	−1.64[a]	0.03
	5	59.87 (58.75–60.98)	58.14 (57.15–59.11)	58.13 (57.14–59.11)	−1.73[a]	−1.74[a]	0.01
	10	49.17 (47.50–50.81)	47.15 (45.71–48.58)	47.25 (45.8–48.69)	−2.02[a]	−1.92[a]	−0.09
Esophagus	1	45.93 (44.27–47.57)	45.54 (44.05–47.01)	45.51 (44.02–46.99)	−0.39	−0.42	0.03
	3	22.31 (20.83–23.82)	21.87 (20.55–23.21)	21.84 (20.52–23.19)	−0.44	−0.47	0.03
	5	17.91 (16.46–19.41)	17.33 (16.04–18.66)	17.30 (16.01–18.64)	−0.58	−0.61	0.03
	10	12.00 (10.35–13.78)	11.18 (9.74–12.72)	11.18 (9.75–12.73)	−0.82	−0.82	−0.01
Stomach	1	52.61 (51.69–53.51)	52.50 (51.66–53.34)	52.45 (51.61–53.29)	−0.11	−0.16	0.05
	3	33.38 (32.45–34.31)	33.04 (32.19–33.89)	32.99 (32.14–33.84)	−0.34	−0.39	0.05
	5	28.68 (27.73–29.64)	28.20 (27.33–29.08)	28.15 (27.27–29.03)	−0.48	−0.53	0.06
	10	24.40 (23.20–25.62)	23.63 (22.53–24.74)	23.61 (22.51–24.73)	−0.77	−0.79	0.02
Colon and rectum	1	83.58 (83.33–83.83)	83.45 (83.22–83.68)	83.40 (83.17–83.63)	−0.13	−0.18	0.05
	3	70.85 (70.50–71.19)	70.34 (70.02–70.65)	70.32 (69.99–70.63)	−0.51[a]	−0.53[a]	0.03
	5	65.10 (64.69–65.50)	64.41 (64.03–64.78)	64.41 (64.03–64.78)	−0.69[a]	−0.69[a]	0.00
	10	59.58 (58.96–60.19)	58.26 (57.70–58.82)	58.32 (57.75–58.88)	−1.32[a]	−1.26[a]	−0.05
Liver and intrahepatic bile duct	1	36.09 (35.03–37.16)	36.96 (35.96–37.96)	36.95 (35.95–37.95)	0.87	0.86	0.01
	3	17.76 (16.84–18.71)	18.21 (17.33–19.11)	18.20 (17.32–19.10)	0.45	0.44	0.01
	5	12.62 (11.74–13.54)	12.94 (12.10–13.81)	12.94 (12.10–13.81)	0.32	0.32	0.00
	10	7.58 (6.58–8.67)	7.80 (6.83–8.84)	7.80 (6.83–8.84)	0.22	0.22	0.00
Pancreas	1	27.45 (26.80–28.10)	27.61 (27.00–28.22)	27.61 (27.00–28.22)	0.16	0.16	0.00
	3	9.50 (9.02–9.99)	9.55 (9.10–10.02)	9.55 (9.10–10.02)	0.05	0.05	0.00
	5	6.81 (6.36–7.27)	6.83 (6.41–7.26)	6.83 (6.41–7.26)	0.02	0.02	0.00
	10	4.73 (4.26–5.23)	4.77 (4.33–5.24)	4.77 (4.33–5.24)	0.04	0.04	0.00
Larynx	1	81.89 (80.18–83.47)	81.15 (79.66–82.54)	81.18 (79.69–82.58)	−0.74	−0.71	−0.03
	3	65.09 (62.90–67.19)	62.79 (60.87–64.65)	62.85 (60.92–64.71)	−2.30[a]	−2.24[a]	−0.05
	5	57.23 (54.74–59.64)	54.51 (52.35–56.63)	54.51 (52.34–56.63)	−2.72[a]	−2.72[a]	0.01
	10	41.36 (37.86–44.83)	38.68 (35.67–41.68)	38.65 (35.62–41.67)	−2.68	−2.71	0.05
Lung and bronchus	1	47.07 (46.74–47.39)	48.46 (48.16–48.75)	48.33 (48.03–48.62)	1.39	1.26	0.13
	3	24.49 (24.19–24.80)	25.51 (25.23–25.79)	25.41 (25.14–25.69)	1.02	0.92	0.09
	5	18.73 (18.43–19.02)	19.47 (19.20–19.75)	19.42 (19.15–19.69)	0.74	0.69	0.05
	10	12.92 (12.58–13.26)	13.11 (12.80–13.43)	13.10 (12.79–13.41)	0.19	0.18	0.01
Melanoma of the skin	1	97.95 (97.71–98.16)	97.76 (97.55–97.95)	97.78 (97.57–97.98)	−0.19	−0.17	−0.02
	3	95.01 (94.61–95.38)	94.45 (94.09–94.78)	94.45 (94.10–94.79)	−0.56[a]	−0.56[a]	−0.01
	5	93.33 (92.80–93.82)	92.44 (91.97–92.88)	92.45 (91.97–92.90)	−0.89[a]	−0.88[a]	0.00
	10	91.41 (90.57–92.17)	90.23 (89.49–90.93)	90.29 (89.51–91.02)	−1.18[a]	−1.12[a]	−0.02
Breast	1	97.39 (97.30–97.49)	97.29 (97.20–97.38)	97.25 (97.16–97.34)	−0.10[a]	−0.14[a]	0.04
	3	92.97 (92.80–93.14)	92.52 (92.36–92.67)	92.53 (92.36–92.69)	−0.45[a]	−0.44[a]	0.00
	5	89.55 (89.31–89.78)	88.79 (88.57–89.00)	88.88 (88.66–89.09)	−0.76[a]	−0.67[a]	−0.09
	10	83.63 (83.16–84.10)	82.29 (81.86–82.71)	82.56 (82.13–82.99)	−1.34[a]	−1.07[a]	−0.27
Cervix uteri	1	85.08 (84.48–85.66)	84.86 (84.30–85.40)	84.85 (84.28–85.39)	−0.22	−0.23	0.02
	3	70.68 (69.91–71.45)	70.31 (69.58–71.04)	70.31 (69.58–71.03)	−0.37	−0.37	0.00
	5	65.39 (64.52–66.24)	64.95 (64.13–65.75)	64.96 (64.14–65.76)	−0.44	−0.43	−0.01
	10	59.92 (58.74–61.08)	59.06 (57.96–60.14)	59.06 (57.96–60.15)	−0.86	−0.86	0.00

Table 2 continued

Site	Years	First	SEER MP	IACR MP	SEER MP−first	IACR MP−first	SEER MP–IACR MP
Corpus and uterus, NOS	1	91.58 (91.29–91.87)	91.15 (90.88–91.41)	91.15 (90.88–91.42)	−0.43[a]	−0.43[a]	0.00
	3	83.83 (83.39–84.26)	82.67 (82.27–83.06)	82.67 (82.27–83.07)	−1.16[a]	−1.16[a]	0.00
	5	81.07 (80.53–81.60)	79.67 (79.18–80.15)	79.67 (79.18–80.15)	−1.40[a]	−1.40[a]	0.00
	10	78.25 (77.32–79.15)	76.19 (75.34–77.01)	76.20 (75.36–77.02)	−2.06[a]	−2.05[a]	−0.02
Ovary	1	72.20 (71.66–72.72)	72.60 (72.12–73.08)	72.60 (72.11–73.08)	0.40	0.40	0.01
	3	50.53 (49.89–51.16)	50.81 (50.23–51.39)	50.80 (50.22–51.38)	0.28	0.27	0.01
	5	38.86 (38.20–39.53)	39.17 (38.56–39.78)	39.16 (38.55–39.77)	0.31	0.30	0.01
	10	29.49 (28.66–30.32)	29.49 (28.73–30.26)	29.50 (28.74–30.27)	0.00	0.01	−0.01
Urinary bladder	1	87.84 (87.33–88.33)	87.09 (86.62–87.54)	87.06 (86.59–87.52)	−0.75[a]	−0.78[a]	0.03
	3	80.21 (79.51–80.90)	78.44 (77.8–79.07)	78.62 (77.97–79.25)	−1.77[a]	−1.59[a]	−0.17
	5	77.04 (76.19–77.86)	74.50 (73.74–75.25)	74.76 (73.99–75.51)	−2.54[a]	−2.28[a]	−0.25
	10	70.98 (69.58–72.33)	67.28 (66.06–68.47)	67.82 (66.59–69.02)	−3.70[a]	−3.16[a]	−0.53
Kidney and renal pelvis	1	79.69 (79.06–80.31)	79.92 (79.36–80.47)	79.88 (79.31–80.43)	0.23	0.19	0.05
	3	70.01 (69.21–70.79)	69.78 (69.07–70.48)	69.94 (69.22–70.64)	−0.23	−0.07	−0.15
	5	65.53 (64.60–66.45)	64.64 (63.80–65.46)	64.83 (63.99–65.66)	−0.89[a]	−0.70	−0.19
	10	57.57 (56.03–59.08)	56.14 (54.78–57.46)	56.35 (54.99–57.69)	−1.43[a]	−1.22	−0.21
Brain and other nervous system	1	54.73 (53.89–55.56)	54.53 (53.74–55.31)	54.54 (53.76–55.33)	−0.20	−0.19	−0.02
	3	34.28 (33.46–35.10)	33.87 (33.08–34.65)	33.86 (33.08–34.64)	−0.41	−0.42	0.00
	5	29.82 (28.97–30.67)	29.39 (28.59–30.20)	29.40 (28.59–30.21)	−0.43	−0.42	0.00
	10	24.31 (23.32–25.31)	23.83 (22.9–24.78)	23.85 (22.91–24.80)	−0.48	−0.46	−0.01
Thyroid	1	95.94 (95.55–96.29)	95.91 (95.57–96.22)	95.90 (95.56–96.22)	−0.03	−0.04	0.01
	3	95.37 (94.90–95.81)	94.98 (94.51–95.40)	94.98 (94.51–95.40)	−0.39	−0.39	0.00
	5	94.84 (94.14–95.46)	94.06 (93.43–94.64)	94.07 (93.44–94.64)	−0.78[a]	−0.77[a]	−0.01
Hodgkin's lymphoma	10	93.10 (91.72–94.25)	92.62 (91.40–93.68)	92.62 (91.39–93.68)	−0.48	−0.48	0.01
	1	91.44 (90.63–92.18)	91.51 (90.79–92.18)	91.48 (90.76–92.15)	0.07	0.04	0.03
	3	86.18 (85.15–87.15)	86.21 (85.27–87.10)	86.18 (85.24–87.07)	0.03	0.00	0.03
	5	83.08 (81.86–84.22)	82.83 (81.72–83.88)	82.83 (81.71–83.88)	−0.25	−0.25	0.01
	10	77.55 (75.84–79.15)	76.66 (75.11–78.12)	76.66 (75.12–78.13)	−0.89	−0.89	−0.01
Non-Hodgkin's lymphoma	1	80.04 (79.61–80.47)	80.04 (79.64–80.43)	80.05 (79.65–80.44)	0.00	0.01	−0.01
	3	71.04 (70.49–71.58)	70.65 (70.15–71.14)	70.7 (70.20–71.20)	−0.39	−0.34	−0.05
	5	66.42 (65.78–67.05)	65.65 (65.07–66.23)	65.74 (65.15–66.32)	−0.77[a]	−0.68[a]	−0.08
	10	55.69 (54.66–56.71)	54.48 (53.54–55.41)	54.56 (53.62–55.50)	−1.21[a]	−1.13[a]	−0.08
Myeloma	1	75.53 (74.69–76.36)	75.39 (74.6–76.16)	75.42 (74.63–76.19)	−0.14	−0.11	−0.03
	3	52.06 (50.99–53.12)	51.59 (50.59–52.58)	51.6 (50.60–52.59)	−0.47	−0.46	−0.01
	5	36.78 (35.65–37.92)	36.34 (35.28–37.40)	36.36 (35.30–37.43)	−0.44	−0.42	−0.02
	10	19.34 (18.01–20.71)	19.03 (17.80–20.30)	19.06 (17.83–20.33)	−0.31	−0.28	−0.03
Leukemia	1	66.41 (65.70–67.11)	64.70 (64.04–65.34)	64.75 (64.09–65.39)	−1.71[a]	−1.66[a]	−0.05
	3	53.78 (52.96–54.59)	51.80 (51.06–52.54)	51.85 (51.11–52.58)	−1.98[a]	−1.93[a]	−0.05
	5	48.36 (47.46–49.25)	46.37 (45.56–47.17)	46.41 (45.60–47.21)	−1.99[a]	−1.95[a]	−0.04
	10	38.42 (37.15–39.69)	36.72 (35.59–37.85)	36.75 (35.62–37.88)	−1.70[a]	−1.67[a]	−0.03
Mesothelioma	1	47.05 (43.59–50.44)	46.91 (43.79–49.96)	46.91 (43.79–49.96)	−0.14	−0.14	0.00
	3	22.81 (19.81–25.95)	23.01 (20.26–25.86)	23.01 (20.26–25.86)	0.20	0.20	0.00
	5	14.05 (11.47–16.89)	13.91 (11.57–16.46)	13.91 (11.57–16.46)	−0.14	−0.14	0.00
	10	9.70 (7.32–12.48)	9.32 (7.06–11.95)	9.32 (7.06–11.95)	−0.38	−0.38	0.00

Table 2 continued

Site	Years	First	SEER MP	IACR MP	SEER MP−first	IACR MP−first	SEER MP–IACR MP
Kaposi sarcoma	1	84.25 (76.76–89.49)	81.77 (74.45–87.17)	81.77 (74.45–87.17)	−2.48	−2.48	0.00
	3	74.82 (66.00–81.67)	72.07 (63.72–78.82)	72.07 (63.72–78.82)	−2.75	−2.75	0.00
	5	69.65 (59.18–77.93)	67.09 (57.44–75.02)	67.09 (57.44–75.02)	−2.56	−2.56	0.00
	10	53.01 (36.74–66.87)	54.22 (39.41–66.87)	54.22 (39.41–66.87)	1.21	1.21	0.00

[a] Point estimates from the first data set were not contained within the corresponding 95 % CIs from the SEER or IACR data sets

[b] Point estimates from the IACR data set were not contained within the corresponding 95 % CIs from the SEER data set

conservative (i.e., higher) 5-year survival estimates than estimates produced by using all primary cancers based on SEER or IACR multiple primary cancer coding rules. Therefore, attempting to exclude subsequent cancers could introduce a systematic bias into survival analyses if the rules for registering multiple primaries are not applied consistently among all registries, or over time within a registry, or if information on previous cancer diagnoses is missing.

Clinicians may intuitively recognize a new primary cancer from that of a distant metastasis, extension, or recurrent cancer. However, it can be difficult to codify the rules for reporting these cancers by using routinely collected surveillance data. The identification of multiple primary cancers may reflect the following: (1) the quality and completeness of the surveillance data being reported to the cancer registry by hospitals, physicians' offices, and laboratories and (2) the training of hospital and registry staff to code the data and interpret the rules. These coding rules may be particularly challenging for registries that use SEER rules because these rules are more complex and require more detailed information than IACR rules. Cancer registries may lack information on previous cancers if the patient was diagnosed in a different state, province, or country from their current residence. This lack of information could be problematic for cancer registries in the United States because registries operate independently in each of the 50 states, the District of Columbia, and six metropolitan areas [6] with support from one or both of the two federal cancer surveillance programs: the National Cancer Institute's SEER Program [11] or the Centers for Disease Control and Prevention's National Program of Cancer Registries (NPCR) [4]. NPCR-funded cancer registries could be particularly impacted because many of them have been fully operational since the mid-1990s or later, and SEER metropolitan area registries, with substate catchment areas.

Furthermore, survival estimates based on first cancers-only do not represent the clinical experience of the entire cancer patient population [23]. For example, the introduction of screening practices, such as the prostate-specific antigen (PSA) test, may advance the diagnosis date of prostate cancer by many years before the cancer would be, if at all, clinically detectable. Early-stage prostate cancers can have high survival rates [32], and a patient may die from a subsequent cancer (e.g., colorectal) rather than their prostate cancer. Including both prostate and colorectal primary cancers in survival analyses would be clinically and epidemiologically relevant.

Although it clearly makes sense to use all primary cancers in population-based survival studies, the question remains: Does the choice of SEER or IACR multiple primary cancer coding rules affect survival estimates? This study did not find any appreciable difference between site-specific survival estimates based on SEER or IACR multiple primary rules. SEER multiple primary coding rules are more liberal than IACR rules in allowing the registration of multiple primary cancers, particularly cancers that occur at the same site including paired organs (breast, kidney) and organs with relatively large surface areas (skin, urinary bladder, colon and rectum, oral cavity and pharynx). However, for both the SEER MP and the IACR MP analyses, cases were selected based on using the first cancer that matched to the selection criteria (first cancer in primary site category). This selection criterion appears to have mitigated the influence of SEER multiple primary rules. The one exception was for all sites combined among females where SEER rules produced marginally higher survival estimates than IACR rules (RS 62.28 vs. 61.96 %, respectively). In preparing the data sets, the IACR rules were applied to data from all diagnosis years, including those prior to the reference years for this study (1995–2008) that resulted in the exclusion of some cases that the SEER rules identified as multiple primary cancers. Hence, the case counts differed for the all sites combined category (Table 1) as did the survival estimates (Table 2).

In conclusion, our results showed that survival estimates based on SEER multiple primary rules, which are used by cancer registries in the United States and in the majority of provincial registries in Canada [18], are comparable to those based on IACR rules, which are used by cancer registries throughout the remaining world, when

site-specific analyses include all first primary cancers matching the selection criteria. Therefore, to produce clinically and epidemiologically relevant and less biased cancer survival estimates, researchers may consider including data on all cancers in their analysis. However, the multiple primary rules used to collect and record the cancer case data do not affect survival estimates if all first cancers matching the selection criteria are used to produce site-specific survival estimates.

Population-based cancer survival is an important outcome measure for assessing cancer control and health policy initiatives. Together with information on cancer incidence and death, survival data can be used to evaluate progress in preventing, screening, diagnosing, and treating cancer patients [33]. To facilitate the comparison and interpretation of international data and to align the incidence data more closely with the cases used in the survival analyses, cancer registries in North America may want to consider publishing population-based incidence and survival statistics that are based on IACR multiple primary cancer coding rules.

Limitation

Survival estimates from this study were calculated for the purpose of comparing SEER and IACR multiple primary cancer coding rules and were not intended to represent the survival experience of cancer patients in the study area. Life expectancy varied among geographic areas in the United States [9, 34], and estimates were not adjusted for state-specific life expectancy because these life tables are not currently available. Life tables were based on the life expectancy of the general population. As such, these tables may overestimate life expectancy for individuals with subsequent cancers.

Conflict of interest None.

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