

Multiple Primaries (MPs) in Survival Estimates: Should SEER include or exclude MPs?

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Introduction

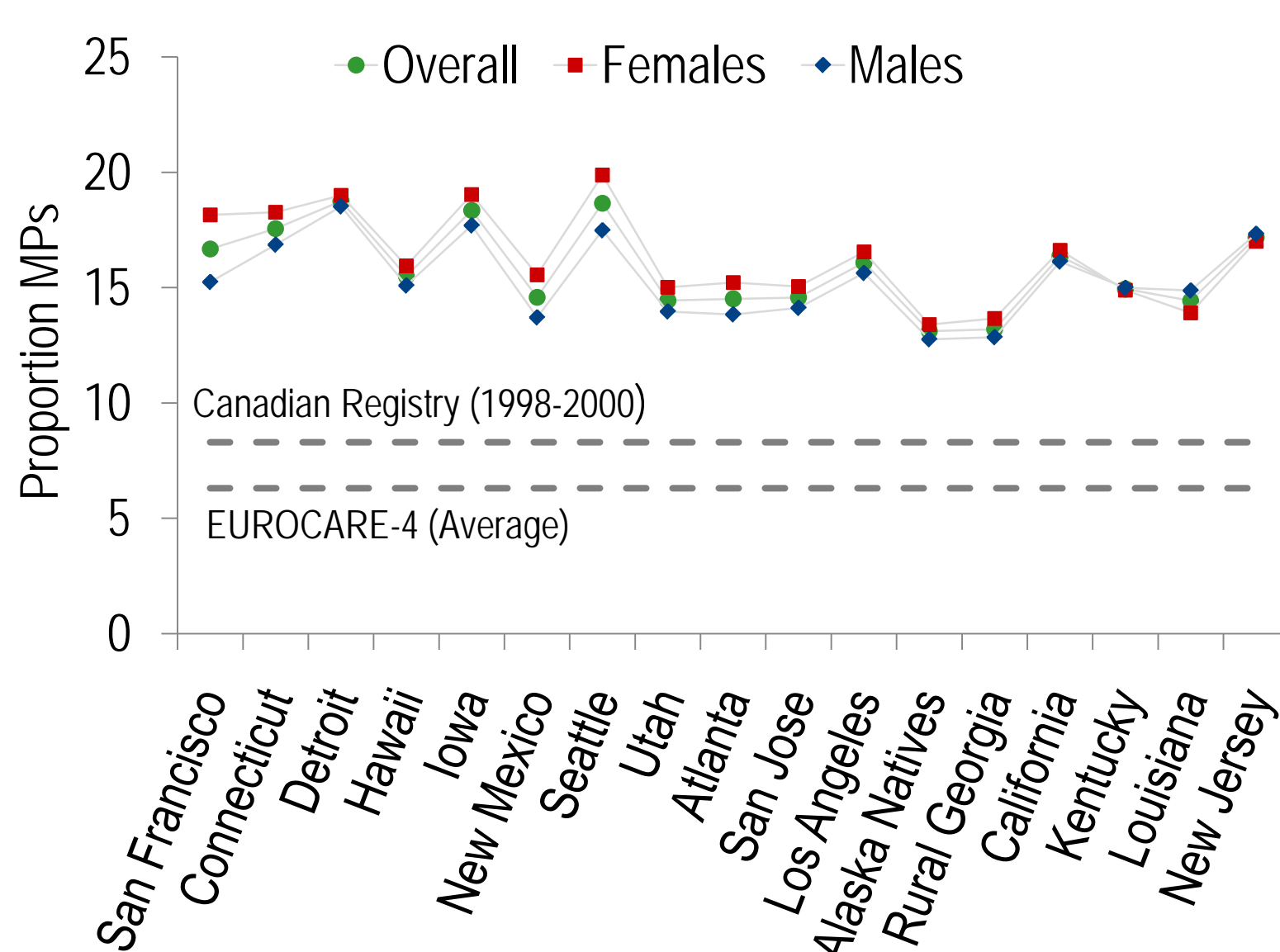
- The Surveillance, Epidemiology, and End Results (SEER) Program of NCI collects data on multiple primary cancers, although **second or higher tumors** are typically excluded from survival estimates
- Routine analysis of survival rates in SEER was restricted to create more homogenous groups of patients since later cancers may affect patient prognosis
- Rosso (2009) et al. evaluated the impact of including multiple primary tumors (second or higher) on relative survival estimates using data from 69 European cancer registries as part of the EUROCORE-4 study¹
 - Inclusion of multiple primaries reduced survival estimates
 - Advised that inclusion of multiple primaries reduces bias due to differences in registry running time, completeness, and quality
- Ellison (2010) evaluated the impact of including multiple primaries in the Canadian Cancer Registry²
 - Similar results to EUROCORE-4
- SEER registries have variable running times
 - Expect that longer running registries will contain more multiple primaries
- In this poster we:
 - Evaluate the impact of excluding multiple primaries using SEER data
 - Compare our results with EUROCORE-4 and Canadian results

Methods

- Data were from 17 areas of the SEER Program³
 - States of Connecticut, Hawaii, Iowa, New Mexico, Utah, Greater California, Kentucky, Louisiana, and New Jersey
 - Metropolitan areas of Atlanta, Detroit, Seattle-Puget Sound, San Francisco-Oakland, Los Angeles, San Jose-Monterey, and Rural Georgia
 - Alaska Native tumor registry
- Included malignant tumors diagnosed between 2000-2006 with follow-up through December 31, 2007
- Excluded autopsy or death certificate only cases, patients alive but without follow-up, tumors diagnosed at age less than 14
- Five-year relative survival was estimated using the actuarial method with monthly intervals
- First only group included tumors with sequence number 00 and 01; multiple group included sequence number 02+

Results

Figure 1: Proportion of multiple primaries by registry and sex. Reference lines are the percentage of MPs in EUROCORE-4 and Canadian registries.



Proportion of Multiple Primaries

- The overall proportion of multiple primaries (MPs) in SEER was 16.5% (range: 13.1-18.7) (Figure 1)
 - More MPs in women
 - Average proportion of MPs varied very little by SEER registries: SEER-9 17.2%, SEER-13 16.8%
 - Most registries in the SEER program have been in existence for many years, explaining the small difference in MPs by registries

Impact on Relative Survival Estimates

- 5-year relative survival estimates including MPs was lower than including first only for all cancers combined (Table 1)
 - Absolute difference in relative survival by registry ranged between -0.6 to -2.6

Table 1: 5-year relative survival estimates including only first tumors and MPs by registry and absolute difference between estimates

Registry	First Only			First & MPs			Registry	First Only			First & MPs		
	Only	MPs	Abs Diff.	Only	MPs	Abs Diff.		Only	MPs	Abs Diff.	Only	MPs	Abs Diff.
San Francisco	67.5	65.8	-1.7	Atlanta	68.5	66.7	-1.8						
Connecticut	68.4	66.8	-1.6	Los Angeles	65.5	63.8	-1.7						
Detroit	65.4	62.8	-2.6	Alaska	52.6	52.0	-0.6						
Hawaii	64.8	63.3	-1.5	Georgia	60.9	59.4	-1.5						
Iowa	66.2	63.9	-2.3	California	65.3	63.5	-1.8						
New Mexico	66.5	64.9	-1.6	Kentucky	59.0	57.1	-1.9						
Seattle	70.5	68.2	-2.3	Louisiana	59.5	57.7	-1.8						
Utah	73.6	71.8	-1.8	New Jersey	67.0	65.0	-2.0						
San Jose	70.3	68.5	-1.8										

- Difference in relative survival increased as the proportion of MPs increased for all cancers combined (Table 1)
 - Alaska Natives and Rural Georgia had the smallest proportion of MPs and small change in relative survival estimates
 - Detroit, Iowa, Seattle had largest proportion of MPs and largest change in relative survival estimates

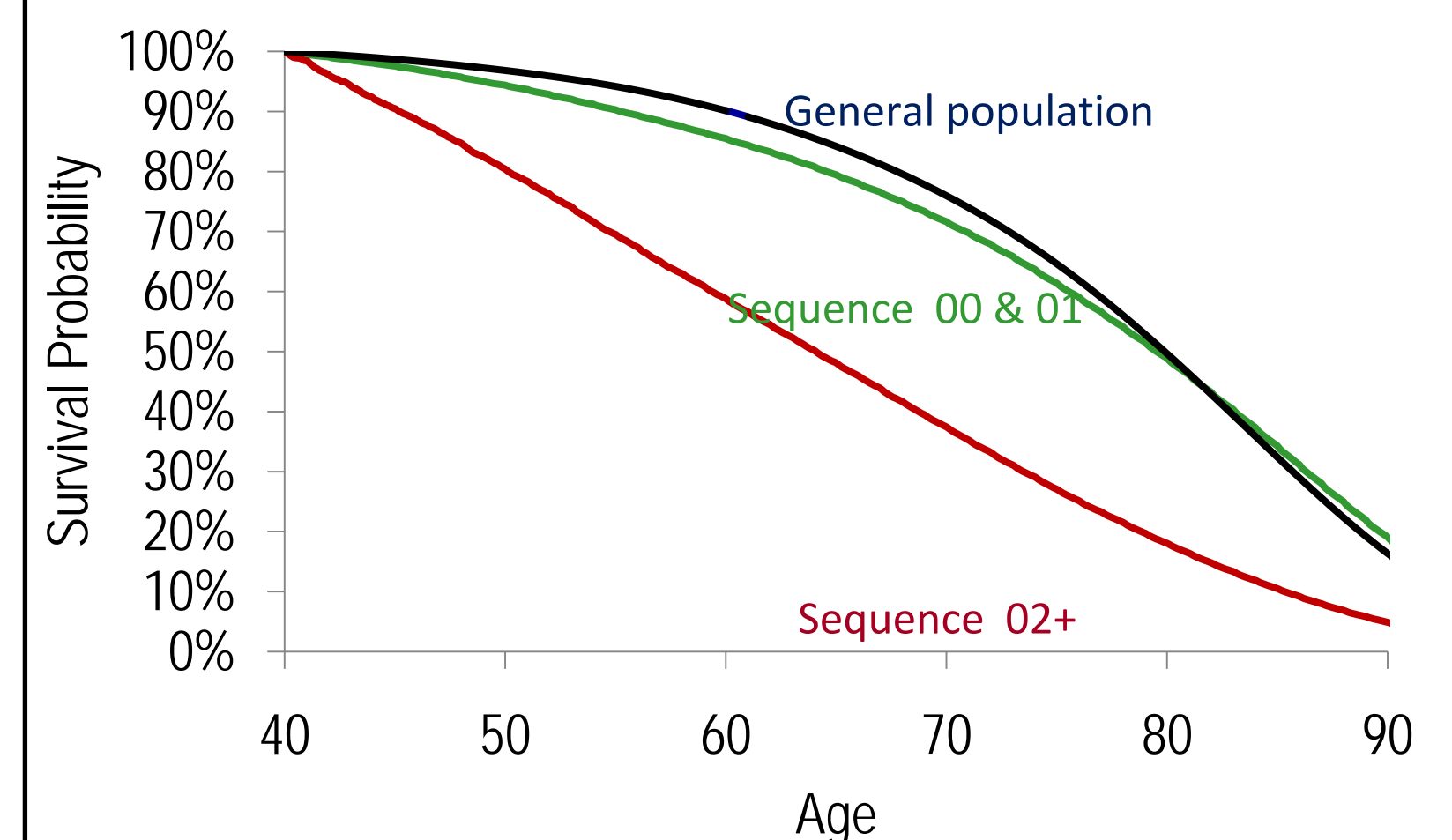
Table 2: 5-year relative survival estimates including only first tumors and MPs by tumor site, absolute difference between estimates, and proportion of tumors that were MPs

	First Only	First & MPs	Abs Diff.	% MPs
All Sites	65.8	64.0	-1.8	16.5
Liver	14.0	13.7	-0.3	11.4
Pancreas	5.6	5.5	-0.1	17.2
Melanoma	91.2	89.9	-1.3	19.7
Breast	88.9	88.0	-0.9	15.9
Prostate	99.1	97.8	-1.3	8.8
Kidney & Renal Pelvis	68.8	67.4	-1.4	20.8
Lung & Bronchus	15.8	16.3	0.5	20.9
Colon & Rectum	64.9	63.5	-1.4	19.4
Oral Cavity & Pharynx	60.9	58.1	-2.8	19.0

- Difference varied by tumor site (Table 2)
- Small differences for both lethal and non-lethal cancers (e.g. Liver, Breast)
- Since breast and prostate tumors are commonly second primary cancers, they will be excluded for analyses using first tumors only⁴
 - Estimates did not appear very sensitive to exclusion of these tumors, possibly because survival rates for these cancers are very good

Other - Cause Survival by Sequence Number

Figure 2: Other-cause survival probability for all cancer patients by sequence number as compared with US general population.



- Other-cause survival from only tumor (seq 00) or first of multiple tumors (seq 01) is similar to the US general population for all cancers combined
- However, other cause-survival for patients with second or later tumors are considerably worse compared to those with only or first of multiple tumors

Conclusions

- Even though empirical estimates changed very little, current evidence does not warrant SEER to change their policy of excluding second or higher multiples in relative survival analyses unless appropriate expected rate tables could be developed for second or higher primaries
- Expected rates for cancer patients with 2 or more tumors are likely to be too high using general life table because it does not account for fact that these patients had prior cancers (see figure 2 comparing other cause survival curves)
 - Important to adjust the expected rates for 2nd or higher primaries by using a survival probability conditional on the initial or 1st primary
- Same patient is included more than once when all tumors are used in the relative survival calculation
 - While incidence and prevalence statistics are generated as "tumor-based", survival statistics are often thought of as "person-based" measures
- Patients diagnosed with two or more tumors (sequence 02+) are different than patients with only one tumor diagnosis (example: figure 2)
- Survival outcomes of patients with MPs may be best if reported separately

Future direction

- SEER has cause of death (COD) information. Could explore cause-specific survival for patients with more than one cancer
- Since older patients have more MPs, perhaps useful to calculate age-standardized survival rates

References

1. Rosso S, De Angelis R, Ciccolallo L, et al. (2009) Multiple Tumors in Survival Estimates. *European Journal of Cancer*; 45: 1080-1094.
2. Ellison, LF (2010) Measuring the Effect of Multiple Cancers in Survival Analysis Using Data from the Canadian Cancer Registry. *Cancer Epidemiology*.
3. Surveillance, Epidemiology, and End Results (SEER) Program SEER*Stat Database: Incidence - SEER 17 Regs Research database, released April 2010, November 2009 submission.
4. Mariotto A, Rowland JH, Ries LAG, et al. (2007) Multiple Cancer Prevalence: A Growing Challenge in Long-term Survivorship. *Cancer Epidemiology and Biomarkers*;16: 566-571.