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Prior cancer among persons newly diagnosed with cancer: An initial report from the Surveillance, Epidemiology, and End Results program

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Abstract

Importance: The U.S. cancer survivor population is rapidly growing. Cancer survivors are frequently excluded from cancer clinical trials and observational research.

Objective: To examine prevalence of prior cancer among individuals newly diagnosed with cancer.

Design and Setting: Linked observations across the population-based Surveillance, Epidemiology, and End Results (SEER) program of cancer registries (1975—2013) for 740,990 persons newly diagnosed with cancer from January 2009 through December 2013. Prevalence of prior cancer was estimated by age (+/− 65 years) and incident cancer type.

Main Outcome and Measure: Prevalence of prior cancer was derived from SEER sequence numbers, which represent the order of all primary reportable tumors diagnosed in a lifetime. Incident cancers were categorized as: 1) first or only primary; 2) second order or higher primary in the same cancer site; and 3) second order or higher primary in a different cancer site.

Results: Of 765,843 incident cancers diagnosed in 2009—2013, 141,021 (18.4%) represented a second order or higher primary cancer. Overall, one-fourth (25.2%) of older (age ≥65 years) and 11% of younger adults newly diagnosed with cancer had a history of prior cancer. Prevalence of prior cancer ranged from 3.5% to 36.9% according to incident cancer type and age, with most prior cancers diagnosed in a different cancer site.

Conclusion and Relevance: A substantial proportion of patients diagnosed with incident cancer in the United States have survived a prior cancer. These patients may be excluded from clinical trials and underrepresented in observational research, and little is known about their treatment and survivorship needs. Understanding the nature and impact of prior cancer history is

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critical to improving clinical trial accrual and generalizability, disease outcomes, and patient experience.

The number of U.S. cancer survivors is rapidly growing, largely driven by the aging population, expanding cancer screening efforts, and improvements in cancer treatment. Over the past 30 years, the cancer survivor population increased four-fold to 15.5 million in 2016 and is expected to reach 26.1 million by 2040.[1] Almost half of all survivors have lived 10 years after their initial diagnosis, and two-thirds have survived beyond five years.[2] Survivors have complex health needs,[3] including surveillance for recurrence, monitoring treatment-related toxicities, and managing emerging diagnoses, such as chronic conditions[4] or new primary cancers.[5]

Cancer survivors are frequently excluded from cancer clinical trials. More than 80% of National Cancer Institute-affiliated lung cancer trials exclude patients with a prior cancer.[6] Such restrictive eligibility criteria may exclude as many as 25% of patients newly diagnosed with lung cancer from participating trials.[7] Although considerable scientific progress[5] has been made understanding risk of developing a *future* primary cancer among specific groups of cancer survivors, this earlier work does not address how many patients diagnosed with incident cancer have survived a *prior* cancer. Understanding prevalence of prior cancer among patients with different types of incident cancer has important implications for both treatment and research.

Methods

We report prevalence of prior cancer among individuals newly diagnosed with cancer during 2009–2013 using the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program of cancer registries. We linked observations across SEER 9 registries (Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah, 1975—2013) to estimate prevalence of prior cancer by incident cancer type and age (+/− 65 years). Prevalence of prior cancer was derived from SEER sequence numbers, which represent the order of all primary reportable tumors (i.e., not metastatic or recurrent tumors) diagnosed in a lifetime. Sequence number "00" indicates an individual has only one primary cancer. For persons with multiple primaries, the sequence number for the first cancer is "01," "02" for the second, and so forth. With few exceptions, including ovarian and prostate cancers, tumors from different anatomic sites, of different histology, or from separate organs of a pair are considered independent primaries.[8]

We categorized incident cancers as a: 1) first or only primary; 2) second order or higher primary in the same cancer site (e.g., two melanomas diagnosed at least one year apart); or 3) second order or higher primary in a different cancer site. Appendix 1 lists tumors classified as belonging to the same or different site. SEER collects the number but not site of cancers diagnosed outside geographically defined registry areas; therefore, some (range 1.0—14.3%) cases are categorized as having a prior cancer of an unknown site [data not shown].

For persons with more than one cancer diagnosed in the same year (n=23,150, 3.1% of total), we were unable to determine the order of diagnoses within that year; therefore, we randomly selected one cancer for analysis. The majority of persons diagnosed with more than one cancer in the same year (n=17,420, 75.2% of those with ≥ 1 cancer in same year, 2.4% of total) were diagnosed with two cancers of the same site (e.g., right and left breast cancer).

Results

There were 765,843 incident cancers diagnosed among 740,990 persons during 2009–2013, of which 141,021 (18.4%) represented a second order or higher primary cancer. Table 1 shows the proportion of incident cancers diagnosed as the first or only primary or a second order or higher primary of the same or different site. Prevalence of prior cancer differed by age: 11.0% among ages 20–64 years and 25.2% among ages ≥ 65 years (Table 1). Prevalence also differed by incident cancer type. Among persons aged 20–64 years, prior cancer was most prevalent among incident myeloid and monocytic leukemia (24.8%); anus, anal canal and rectum (18.2%); cervix and other female genital organs (e.g., vagina, vulva; 15.0%); and lung and other respiratory (14.6%) cancers. Prior cancers in this younger age group generally occurred in a different cancer site, although second order breast, cervical and other female genital, male genital, and testicular cancers were more often in the same site. For persons aged ≥ 65 years, incident cancers with highest prevalence of prior cancer were melanoma (36.9%); myeloid and monocytic leukemia (36.9%); bone and joints (34.0%); and urinary bladder and other urinary organs (32.5%). With the exception of breast cancer melanoma, most prior cancers among the older age group occurred in a different site.

Discussion

Implications for Cancer Care Delivery

One quarter of older (age ≥65 years) and more than 10% of younger adults newly diagnosed with cancer have a history of prior cancer. Prevalence of prior cancer ranged from 3.5% to 36.9% according to incident cancer type and age, with most prior cancers diagnosed in a different cancer site.

Prior cancer history has important implications for cancer care delivery. Patients may have competing priorities concerning treatment decisions: a new diagnosis may interrupt management, treatment adherence, or outcomes related to a prior cancer. Differences in the prevalence of prior cancer by incident cancer type also highlight underlying or shared risk factors that may be amenable to targeted surveillance. For example, 30% or more of older persons diagnosed with cancers attributable to human papilloma virus (e.g., cervical and female genital, anal, oral cavity) or tobacco (e.g., lung, esophageal, oral cavity) had a prior cancer. An even larger proportion (36.9%) diagnosed with myeloid leukemia had a prior cancer, which may reflect leukemogenic effects of earlier cancer treatments.

Many cancer clinical trials exclude patients with a prior cancer, a practice that may exclude a substantial proportion of otherwise eligible patients. Excluding patients with a prior cancer likely arises from a long-held belief that a prior cancer diagnosis may interfere with study

conduct and/or outcomes. However, this restrictive criterion limits generalizability and trial-generated knowledge to patients with a first or only primary—a slight majority of patients with certain cancer types. This is particularly concerning for older adults with uncommon cancers, where trial accrual is critical, standard therapies may be suboptimal, and prior cancer history is prevalent.

Determining the impact of prior cancer exclusion criteria on trial accrual requires disease- and protocol-specific details, including stage and timing of prior cancer diagnoses.[9] In lung cancer, most trials use a 5-year exclusion window,[6] prior cancers generally occur within that window, and having a prior cancer does not adversely impact survival.[7,10,11] Consequently, including patients with a prior cancer in lung cancer trials could substantially *improve* accrual without affecting study outcomes. The sizable number of cancers newly diagnosed among cancer survivors highlights the importance of addressing similar questions for other cancer types.

Patients with prior cancer are also frequently excluded from observational research, including treatment and outcome studies using SEER-Medicare,[12] Patterns of Care,[13] Cancer Care Outcomes Research and Surveillance Consortium,[14] and Veterans Health Administration[15] data. Because observational studies often provide “real world” data to complement clinical trials, reconsidering the rationale of this eligibility criterion is important to advancing evidence-based practice.

Limitations

We could not determine order of multiple cancers diagnosed in the same year because only year of diagnosis is available in SEER data (i.e., not month or day). Prior cancers diagnosed outside of registry geographic areas are reflected in sequence number only, and there is no corresponding information on the prior cancer characteristics, including site. However, these limitations pertained to fewer than 5% of the total cancer cases diagnosed in the study period and are unlikely to impact our conclusions.

Conclusions

As the cancer survivor population continues to grow, understanding the nature and impact of a prior cancer is critical to improving trial accrual, generalizability of results from trials and observational studies, disease outcomes, and patient experience.

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Appendix I.: Cancers considered to represent the same site

1. Anus, anal canal, anorectum
2. Bone and joints; soft tissue
3. Brain and other nervous system, including cranial nerves and other nervous system
4. Breast
5. Cervix; vagina; vulva; other female genital organs
6. Colon; rectum and rectosigmoid junction; small intestine
7. Corpus and uterus
8. Esophagus
9. Eye and orbit
10. Kaposi sarcoma
11. Kidney and renal pelvis
12. Liver and intrahepatic bile duct; gallbladder and other biliary; other digestive organs
13. Lung and bronchus; trachea, mediastinum, and other respiratory; pleura
14. Lymphocytic leukemia (including acute lymphocytic leukemia, chronic lymphocytic leukemia and other lymphocytic leukemia)
15. Lymphoma (including Hodgkin and non-Hodgkin lymphoma)
16. Melanoma of the skin; other non-epithelial skin
17. Mesothelioma
18. Myeloid and monocytic leukemia (including acute monocytic leukemia, acute myeloid leukemia, chronic monocytic leukemia, and other monocytic/myeloid leukemia)
19. Myeloma
20. Oral cavity and pharynx (lip, tongue, salivary gland, floor of mouth, gum and other mouth, nasopharynx, tonsil, oropharynx, hypopharynx, other oral cavity); nose, nasal cavity and middle ear; larynx
21. Ovary
22. Pancreas
23. Penis; other male genital organs
24. Prostate
25. Stomach; retroperitoneum; peritoneum, omentum, and mesentery

26. Testis

27. Thyroid; other endocrine including thymus

28. Urinary bladder; ureter; other urinary organs

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Key Points

Question: How many patients diagnosed with incident cancer are cancer survivors?

Findings: Approximately 25% of older adults (age ≥65 years) and more than 10% of younger adults newly diagnosed with cancer have a history of prior cancer. Prevalence of prior cancer ranged from 4% to 37% according to age and incident cancer type, with most prior cancers diagnosed in a different cancer site.

Meaning: As the cancer survivor population continues to grow, understanding the nature and impact of a prior cancer is critical to improving clinical trial accrual, generalizability of results from trials and observational studies, disease outcomes, and patient experience.

Table 1:

Proportion of incident cancer cases diagnosed as a first or only primary or second order or higher primary (same or different cancer site) by incident cancer type and age (+/− 65 years), SEER 9, 2009–2013

	Age <65 Years							Age ≥65 Years						
	Total	First or only primary		Second order or higher primary, same site		Second order or higher primary, different site		Total	First or only primary		Second order or higher primary, same site		Second order or higher primary, different site	
		N	%	n	%	n	%		n	%	n	%	n	%
All cancer types	364961	324992	89.0%	12034	3.3%	18353	5.0%	400882	299830	74.8%	20736	5.2%	60712	15.1%
Anus, anal canal, anorectum	3844	3145	81.8%	215	5.6%	321	8.4%	1306	905	69.3%	53	4.1%	262	20.1%
Bone and joints (including soft tissue)	3306	2867	86.7%	84	2.5%	234	7.1%	2329	1537	66.0%	79	3.4%	547	23.5%
Brain and other nervous system	5141	4694	91.3%	79	1.5%	237	4.6%	3559	2787	78.3%	8	0.2%	587	16.5%
Breast (female)[1]	78163	68273	87.3%	5318	6.8%	2921	3.7%	52940	39753	75.1%	7181	13.6%	3932	7.4%
Cervix and other female genital organs	9098	7734	85.0%	775	8.5%	312	3.4%	3906	2708	69.3%	452	11.6%	533	13.6%
Colon and rectum	28040	25536	91.1%	535	1.9%	1275	4.5%	37070	27954	75.4%	1759	4.7%	5684	15.3%
Corpus and uterus	13566	12440	91.7%	19	0.1%	782	5.8%	9642	7952	82.5%	24	0.2%	1315	13.6%
Esophagus	2839	2523	88.9%	12	0.4%	226	8.0%	4101	2945	71.8%	50	1.2%	850	20.7%
Eye and orbit	679	605	89.1%	15	2.2%	38	5.6%	680	495	72.8%	13	1.9%	128	18.8%
Kaposi sarcoma[2]	711	682	95.9%	__*	__*	13	1.8%	173	135	78.0%	__*	__*	27	15.6%
Kidney and renal pelvis	11633	10348	89.0%	197	1.7%	716	6.2%	11343	8242	72.7%	227	2.0%	2168	19.1%
Liver and intrahepatic bile duct	9107	8382	92.0%	39	0.4%	458	5.0%	9918	7720	77.8%	41	0.4%	1684	17.0%
Lung and other respiratory	25816	22056	85.4%	559	2.2%	2233	8.6%	58477	41862	71.6%	2346	4.0%	10928	18.7%
Lymphocytic leukemia	3675	3344	91.0%	10	0.3%	206	5.6%	5660	4257	75.2%	16	0.3%	1134	20.0%
Lymphoma	16124	14598	90.5%	408	2.5%	720	4.5%	17348	12546	72.3%	635	3.7%	3251	18.7%
Melanoma[3]	34033	29222	85.9%	2549	7.5%	1463	4.3%	32190	20317	63.1%	5330	16.6%	5065	15.7%
Mesothelioma	313	266	85.0%	__*	__*	34	10.9%	1064	758	71.2%	__*	__*	250	23.5%
Myeloid and monocytic leukemia	4583	3448	75.2%	39	0.9%	441	9.6%	5947	3754	63.1%	75	1.3%	1481	24.9%
Myeloma	3808	3425	89.9%	61	1.6%	210	5.5%	6437	4930	76.6%	58	0.9%	1117	17.4%

	Age <65 Years							Age ≥65 Years					
	Total	First or only primary		Second order or higher primary, same site		Second order or higher primary, different site		Total	First or only primary		Second order or higher primary, same site		Second order or higher primary, different site	
		N	%	n	%	n	%		n	%	n	%	n	%
Oral cavity and pharynx	13197	11466	86.9%	617	4.7%	712	5.4%	10831	7503	69.3%	965	8.9%	1797	16.6%
Ovary[4]	5303	4820	90.9%	__*	__*	341	6.4%	4631	3795	81.9%	__*	__*	624	13.5%
Pancreas	6491	5818	89.6%	3	0.0%	453	7.0%	13223	10090	76.3%	11	0.1%	2469	18.7%
Penis and other male genital organs	587	503	85.7%	36	6.1%	21	3.6%	649	421	64.9%	42	6.5%	151	23.3%
Prostate[5]	43116	40940	95.0%	__*	__*	1532	3.6%	54480	48701	89.4%	__*	__*	4284	7.9%
Stomach	4797	4253	88.7%	55	1.1%	350	7.3%	7489	5644	75.4%	115	1.5%	1335	17.8%
Testis	3942	3802	96.4%	70	1.8%	31	0.8%	90	68	75.6%	0	0.0%	18	20.0%
Thyroid and other endocrine	17773	16276	91.6%	88	0.5%	885	5.0%	4431	3222	72.7%	26	0.6%	883	19.9%
Urinary bladder and other urinary organs	8835	7607	86.1%	196	2.2%	657	7.4%	23568	15911	67.5%	1086	4.6%	4920	20.9%
Miscellaneous	6456	5653	87.6%	42	0.7%	531	8.2%	16839	12528	74.4%	115	0.7%	3288	19.5%

SEER does not consider recurrences of tumors of the same histology reporting within 2 months as a new primary; both sides (left and right) of a paired organ site are generally considered independent primary cancers, with some exceptions: Kaposi sarcoma, mesothelioma, ovary, and prostate (described below)

Proportion of second order or higher primary cancers with unknown prior site ranges from 1.0% (testis, age≥65 years) to 14.3% (myeloid and monocytic leukemia, age <65 years), with median of 5.3% in ages <65 years and 2.9% in ages ≥65 years

[1]Among breast cancer cases with a prior breast cancer in ages <65 years (n=5318), 347 (6.5%, 0.4% of total) also had a prior cancer of a different site; in ages ≥65 years (n=7181), 897 (12.5%, 1.7% of total) also had a prior cancer of a different site

[2]Kaposi sarcoma (any site or sites) is always considered a single primary

[3]Among melanoma cases with a prior melanoma in ages <65 years (n=2549), 199 (7.8%, 0.6% of total) also had a prior cancer of a different site; in ages ≥65 years (n=5330), 1341 (25.2%, 4.2% of total) also had a prior cancer of a different site

[4]Bilateral epithelial tumors of the ovary within 60 days of diagnosis are a single primary

[5]Only the first invasive adenocarcinoma of the prostate is reported to SEER

*SEER coding rules specify that only the first of this cancer type is reportable (i.e., no subsequent primary tumors of the same site are reported to SEER)[8]