The Occurrence of Rare Cancers in U.S. Adults, 1995–2004

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SYNOPSIS

Objective. Rare cancers have been traditionally understudied, reducing the progress of research and hindering decisions for patients, physicians, and policy makers. We evaluated the descriptive epidemiology of rare cancers using a large, representative, population-based dataset from cancer registries in the United States.

Methods. We analyzed more than 9 million adult cancers diagnosed from 1995 to 2004 in 39 states and two metropolitan areas using the Cancer in North America (CINA) dataset, which covers approximately 80% of the U.S. population. We applied an accepted cancer classification scheme and a published definition of rare (i.e., fewer than 15 cases per 100,000 per year). We calculated age-adjusted incidence rates and rare/non-rare incidence rate ratios using SEER*Stat software, with analyses stratified by gender, age, race/ethnicity, and histology.

Results. Sixty of 71 cancer types were rare, accounting for 25% of all adult tumors. Rare cancers occurred with greater relative frequency among those who were younger, nonwhite, and of Hispanic ethnicity than among their older, white, or non-Hispanic counterparts.

Conclusions. Collectively, rare tumors account for a sizable portion of adult cancers, and disproportionately affect some demographic groups. Maturing population-based cancer surveillance data can be an important source for research on rare cancers, potentially leading to a greater understanding of these cancers and eventually to improved treatment, control, and prevention.

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Rare health conditions typically receive far less scientific attention and fiscal support than their more common counterparts. This utilitarian approach has impeded the understanding of even the basic descriptive epidemiology of rare cancers.[1,2] Knowledge of rare cancers is often derived from case reports, single-institution case series, or, at best, smaller multicenter series.[3–5] Conclusions drawn from such selected studies may be misleading, as they do not necessarily reflect the characteristics of the underlying population of all similar cancers.[6] Many rare cancers can be highly fatal, and yet patients and caregivers have a limited evidence base to guide clinical deliberations. Enhanced research on rare cancers can facilitate improvements in diagnosis, treatment, and patient outcomes,[7] and can also lead to important discoveries about underlying mechanisms of tumor development.[8]

In an effort to promote and synergize epidemiologic research on rare and understudied cancers, the National Cancer Institute (NCI), in collaboration with the National Institutes of Health Office of Rare Diseases, hosted a series of three leadership workshops.[2,9,10] Advancing research on rare and understudied cancers within the context of consortia and transdisciplinary science was among the workshops' goals. To provide the foundation for such research, the group recognized the need for enhanced involvement of population-based cancer registries. With this in mind, our specific objectives were to (*1*) identify and describe the general occurrence of rare cancers in the U.S. using an accepted, conservative threshold and a well-established cancer classification system; (*2*) compare demographic and histologic characteristics between rare and common cancer sites; and (*3*) explore the occurrence of additional rare cancers typically overlooked in standard reports, including histologic types within anatomically defined rare cancers and distinct anatomic subsites that are otherwise collapsed within broader sites. This information can provide the basis for establishing collaborations, developing new initiatives, and influencing policy to prioritize funding and facilitate rare cancer research.

METHODS

For analysis, we used the Cancer in North America (CINA) Deluxe 1995–2004 research data file, based on the December 2006 data submission from members of the North American Association of Central Cancer Registries (NAACCR). NAACCR is a professional organization of state, provincial, territorial, regional, and metropolitan cancer registries in the U.S. and Canada (www.naaccr.org). Cancer registries in NAACCR are supported by multiple sources. In the U.S., they participate in NCI's Surveillance, Epidemiology, and End Results (SEER) Program or the Centers for Disease Control and Prevention's National Program of Cancer Registries. Among the objectives of NAACCR are to promote uniform data standards; evaluate data quality; certify registries; and compile, disseminate, and promote the use of population-based central cancer registry data. Each year, NAACCR compiles cancer incidence data from member registries that meet high-quality standards into the CINA analytic dataset.[11]

We limited analyses to U.S. registries that provided explicit permission for this project. To avoid case duplication, we excluded metropolitan-based registries if corresponding data from the entire state were available. As a result, we were able to analyze high-quality cancer incidence data from 41 population-based cancer registries (39 states, one metropolitan area, and Washington, D.C.) representing 80% of the U.S. population. For one registry, we excluded cancer counts and population denominators from one diagnosis year not meeting the highest certification standards because of unresolved data quality exceptions.

We included only invasive, microscopically confirmed cancers, with the exception of *in situ* urinary bladder cases, which are categorized with invasive disease. Basal cell and squamous cell cancers of the skin are not reportable and were not included in the analysis, whereas we could include basal and squamous cell histologies at all other anatomic sites. We limited cases and population denominators to adults aged 20 years and older. Anatomy and morphology of tumors were defined by the International Classification of Diseases for Oncology (ICD-O) using the standard version for the time and converted when necessary to the ICD-O Third Revision (ICD-O-3).[12] Unexpected anatomic site/histologic type combinations are only included in the CINA dataset after manual review and confirmation by the submitting registry. The term "cancer" refers to any invasive malignancy, regardless of site or histologic type.

The Institutional Review Boards at NAACCR and the Marshfield Clinic Research Foundation approved this study.

Statistical analysis

We used SEER*Stat analytic software version 6.3.6[13] in client-server mode to generate cancer counts, proportions, and rates for cancers classified by age, gender, and race/ethnicity. We directly age-adjusted all rates to the 2000 U.S. standard population, including age group-specific rates, which were age-adjusted in five-year intervals within each age group. We also generated

incidence rate ratios (IRRs) through SEER*Stat, including 95% confidence intervals (CIs) based on the method of Fay.[14]

We categorized cancers into the broad systems and specific "sites" employed by the SEER Site Recode scheme, which is predominantly anatomically based, but also includes exclusive categories for several histologically defined neoplasms.[15] Accordingly, most of the anatomic site-based rates exclude lymphoma, myeloma, leukemia, mesothelioma, and Kaposi sarcoma, as these are accumulated in their own histologically defined site categories regardless of anatomic location. We based primary histologic stratification on the 56 morphologic groups identified within ICD-O-3.[12] We also examined 32 distinct anatomic locations that are subsumed within broader site categories and so would not typically be identified separately in standard cancer surveillance reports.

We adopted the definition of "rare" from a recent NCI-sponsored cancer epidemiology workshop: an incidence of fewer than 150 per million per year (i.e., 15 per 100,000 per year), roughly corresponding in the U.S. to 40,000 new cases per year or fewer.[2,16] We also examined two lower thresholds—<10 cases and <1 case per million per year—to designate additional degrees of rareness.

RESULTS

The 41 cancer registries recorded more than 9 million cases of incident, invasive adult cancers (4.7 million men and 4.4 million women) between 1995 and 2004. Based on an annual threshold of 150 cases per million, 60 of 71 cancer sites met the broad definition of rare, accounting for 25% of reported malignancies (Table 1). Only one site, pleura (non-mesothelial), had an incidence rate of fewer than one per million per year. Other cancers with incidence rates less than 10 per million per year accounted for almost half of the rare sites, ranging from 1.27 extranodal Hodgkin lymphomas per million (n=1,897) to 9.75 vaginal cancers per million women (n=8,058). Using this definition, cervix cancer was the most common of the rare sites, with a mean annual incidence of 131.8 per million women. With this definition, only 11 cancers were considered common, including cancers of the prostate, breast, lung, colon, uterine corpus, urinary bladder, rectum, ovary, kidney, melanoma of the skin, and nodal non-Hodgkin lymphoma.

The rates of most rare malignancies varied by gender, some with a male-to-female IRR of ≥3:1. Cancers of the oral cavity/pharynx, respiratory, and urinary system sites were considerably less common among women than among men, while peritoneal, gallbladder, and anal cancers were more common among women. Such differences in incidence notwithstanding, the designation of rare was consistent by gender across cancer sites with few exceptions. The most striking difference was for breast cancer, which meets the definition for rare among men but not among women.

In contrast to anatomic site, 14 of the 56 histologic groups occurred with an annual frequency of less than one per million, and the annual incidence of an additional 17 histologic types was less than 10 per million (Table 2). Only eight histologic categories had rates higher than 150 per million per year, although they accounted for 90% of all cancers. Many histologic types are more likely to be found at rare cancer sites than at common cancer sites, including various types of soft tissue sarcomas and basal cell carcinoma (non-skin).

The overall rare to non-rare IRR was 0.33 (Table 3). Rare cancers were proportionally (and absolutely) more common than non-rare cancers among young adults aged 20–29 years. The IRRs of rare relative to common cancers then decreased monotonically through adulthood until age 60 years, when the trend flattened and reversed, especially among women (Figure). Overall, men were more likely than women to have had a rare cancer diagnosis until age 70, after which the rare/non-rare ratios were fairly similar. Black, American Indian/Alaska Native, Asian/Pacific Islander, and Hispanic people with cancer were proportionally more likely to have been diagnosed with a rare cancer as defined in this study than were their white counterparts. This general relation held true for both genders and nearly all ages, except that black and white males older than 40 years of age had very similar rare/non-rare IRRs.

Examining race-specific incidence rates by cancer site provides detail into this general finding. For example, while the black/white IRR for all cancer sites combined was 1.02 (95% CI 1.018, 1.023), black people were less likely than white people to be diagnosed with eight of the 11 non-rare cancers: rectum/rectosigmoid junction (black/white IRR=0.91, 95% CI 0.89, 0.92), melanoma of the skin (IRR=0.06, 95% CI 0.05, 0.06), female breast (IRR=0.85, 95% CI 0.85, 0.86), corpus uteri (IRR=0.77, 95% CI 0.76, 0.78), ovary (IRR=0.66, 95% CI 0.64, 0.67), urinary bladder (IRR=0.49, 95% CI 0.48, 0.50), kidney/renal pelvis (IRR=0.96, 95% CI 0.95, 0.97), and nodal non-Hodgkin lymphoma (IRR=0.66, 95% CI 0.65, 0.67). On the other hand, black people were at least 50% more likely than their white counterparts to be diagnosed with cancer at many of the designated rare sites, especially along the aerodigestive tract: nasopharynx (black/white

Table 1. Cancer incidence by site,[a] adults, 41 U.S. registries combined, 1995–2004

	Overall		Male		Female	
System/site	*Rate[b]*	*Count*	*Rate[b]*	*Count*	*Rate[b]*	*Count*
Oral cavity and pharynx						
Other oral cavity and pharynx	4.20	6,208	6.69	4,471	2.14	1,737
Oropharynx	5.59	8,255	8.93	6,066	2.71	2,189
Nasopharynx	7.83	11,575	11.48	7,950	4.60	3,625
Floor of mouth	11.29	16,667	16.83	11,402	6.46	5,265
Hypopharynx	11.64	17,187	20.26	13,483	4.58	3,704
Lip	12.52	18,483	22.57	14,377	4.86	4,106
Salivary gland	16.09	23,803	21.79	13,852	12.26	9,951
Tonsil	19.48	28,685	32.00	22,135	8.26	6,550
Gum and other mouth	22.46	33,169	27.79	18,280	17.83	14,889
Tongue	36.68	54,143	54.27	36,757	21.43	17,386
Digestive system						
Other digestive organs	3.61	5,335	4.23	2,687	3.17	2,648
Retroperitoneum	4.82	7,133	5.23	3,477	4.57	3,656
Peritoneum, omentum, and mesentery	6.38	9,432	1.21	806	10.60	8,626
Intrahepatic bile duct	6.54	9,663	7.90	5,084	5.52	4,579
Gallbladder	15.61	23,044	10.90	6,727	19.34	16,317
Other biliary	17.61	26,004	22.11	13,884	14.34	12,120
Anus, anal canal, and anorectum	19.22	28,331	16.63	11,109	21.34	17,222
Small intestine	23.07	34,054	27.63	17,947	19.59	16,107
Liver	46.22	68,213	73.65	48,712	23.67	19,501
Esophagus	64.85	95,790	111.86	72,646	27.54	23,144
Stomach	104.37	154,138	150.57	94,947	69.77	59,191
Pancreas	116.18	171,556	135.67	87,894	100.62	83,662
Rectum/rectosigmoid junction	202.99[c]	299,760[c]	262.47	169,589	156.74	130,171
Colon excluding rectum	534.94[c]	789,944[c]	616.03	384,852	475.59	405,092
Respiratory system						
Pleura	0.38	565	0.58	360	0.25	205
Trachea, mediastinum, and other respiratory organs	2.20	3,282	3.25	2,281	1.24	1,001
Nose, nasal cavity, and middle ear	9.25	13,680	12.21	8,068	6.82	5,612
Larynx	60.78	89,801	107.96	71,389	22.97	18,412
Lung and bronchus	854.87[c]	1,263,090[c]	1,108.77	716,295	667.02	546,795
Bones and joints						
Bones and joints	8.91	13,310	10.34	7,254	7.70	6,056
Soft tissue, including heart						
Soft tissue, including heart	36.37	53,953	43.85	29,144	30.85	24,809
Skin, excluding basal and squamous						
Other non-epithelial skin	19.37	28,679	25.85	16,207	15.09	12,472
Melanoma of the skin	212.56[c]	314,683[c]	271.92	179,908	170.37	134,775
Breast						
Breast	961.75[c]	1,418,069[c]	18.67	11,995	1,759.92	1,406,074
Female genital system						
Uterus, NOS	NA[d]	NA[d]	NA[d]	NA[d]	8.34	6,722
Other female genital organs	NA[d]	NA[d]	NA[d]	NA[d]	8.55	6,843
Vagina	NA[d]	NA[d]	NA[d]	NA[d]	9.75	8,058
Vulva	NA[d]	NA[d]	NA[d]	NA[d]	31.39	26,040
Cervix uteri	NA[d]	NA[d]	NA[d]	NA[d]	131.84	101,804
Ovary	NA[d]	NA[d]	NA[d]	NA[d]	179.85[c]	144,313[c]
Corpus uteri	NA[d]	NA[d]	NA[d]	NA[d]	320.57[c]	257,620[c]
Male genital system						
Other male genital organs	NA[d]	NA[d]	3.23	2,066	NA[d]	NA[d]
Penis	NA[d]	NA[d]	12.02	7,627	NA[d]	NA[d]
Testis	NA[d]	NA[d]	68.43	51,779	NA[d]	NA[d]
Prostate	NA[d]	NA[d]	2,156.46[c]	1,401,006[c]	NA[d]	NA[d]

continued on p. 32

Table 1 (continued). Cancer incidence by site,[a] adults, 41 U.S. registries combined, 1995–2004

	Overall		Male		Female	
System/site	*Rate*[b]	*Count*	*Rate*[b]	*Count*	*Rate*[b]	*Count*
Urinary system						
Other urinary organs	3.57	5,270	5.80	3,527	2.09	1,743
Ureter	8.31	12,274	12.22	7,599	5.46	4,675
Kidney and renal pelvis	158.12[c]	233,444[c]	218.08	145,033	109.27	88,411
Urinary bladder	299.51[c]	442,354[c]	529.00	328,509	134.30	113,845
Eye and orbit						
Eye and orbit	6.61	9,773	8.45	5,543	5.20	4,230
Brain and other nervous system						
Cranial nerves other nervous system	4.41	6,539	4.53	3,146	4.33	3,393
Brain	65.67	97,423	80.21	55,178	53.30	42,245
Endocrine system						
Other endocrine, including thymus	6.74	9,993	7.43	5,124	6.18	4,869
Thyroid	101.70	151,352	53.39	37,344	148.41	114,008
Lymphoma						
Hodgkin—extranodal	1.27	1,897	1.45	1,017	1.12	880
Hodgkin—nodal	32.29	48,653	37.05	26,794	28.04	21,859
Non-Hodgkin lymphoma—extranodal	78.95	116,748	94.00	61,108	67.21	55,640
Non-Hodgkin lymphoma—nodal	173.61[c]	256,655[c]	208.40	136,152	146.07	120,503
Myeloma						
Myeloma	67.15	99,148	83.62	53,496	55.01	45,652
Leukemia						
Other myeloid/monocytic leukemia	2.09	3,086	2.71	1,710	1.64	1,376
Acute monocytic leukemia	2.71	4,016	3.47	2,229	2.19	1,787
Aleukemic, subleukemic and NOS	3.45	5,107	4.52	2,808	2.70	2,299
Other acute leukemia	3.94	5,830	5.29	3,213	3.04	2,617
Other lymphocytic leukemia	5.68	8,381	9.07	6,015	2.88	2,366
Acute lymphocytic leukemia	7.69	11,497	9.20	6,461	6.37	5,036
Chronic myeloid leukemia	19.13	28,333	25.20	16,417	14.53	11,916
Acute myeloid leukemia	44.66	66,140	55.83	35,954	36.79	30,186
Chronic lymphocytic leukemia	45.04	66,516	62.63	39,462	31.94	27,054
Mesothelioma						
Mesothelioma	14.75	21,786	27.54	17,126	5.61	4,660
Kaposi sarcoma						
Kaposi sarcoma	9.49	14,160	17.72	12,640	1.79	1,520
Miscellaneous						
Miscellaneous	122.40	180,735	142.41	90,782	107.09	89,953
Total	6,130.25	9,060,672	7,221.43	4,678,900	5,392.52	4,381,772

Source: North American Association of Central Cancer Registries file submission as of December 2006 from: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, Washington, D.C., Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Massachusetts, Detroit, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Texas, Utah, Washington, West Virginia, Wisconsin, and Wyoming

[a]Classification by SEER site recode: Ries LAG, Melbert D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, et al., editors. SEER Cancer Statistics Review, 1975–2004. Bethesda (MD): National Cancer Institute; 2007. Also available from: URL: http://seer.cancer.gov/csr/1975_2004 [cited 2008 Sep 25].

[b]Rates are invasive, microscopically confirmed cancers per 1 million per year and age-adjusted to the 2000 U.S. Standard Population (Census P25-1130).

[c]Non-rare cancers (incidence of at least 150 per million per year)

[d]Gender-specific site

NOS = not otherwise specified

NA = not applicable

Table 2. Cancer incidence by histologic grouping[a] among rare and non-rare cancer sites:[b] adults, 41 U.S. registries combined, 1995–2004

Morphology code range	Morphology type	Overall		Rare[c] sites		Non-rare sites	
		Rate[d]	Count	Rate[d]	Count	Rate[d]	Count
9170–9179	Lymphatic vessel tumors	0.03	40	0.03	38	0.00	2
9970–9979	Other hematologic disorders	0.03	47	0.03	47	0.00	0
9110–9119	Mesonephromas	0.05	78	0.04	52	0.02	26
9980–9989	Myelodysplastic syndromes	0.06	85	0.06	85	0.00	0
8840–8849	Myxomatous neoplasms	0.20	297	0.19	282	0.01	15
9950–9969	Chronic myeloproliferative disorders	0.21	307	0.21	307	0.00	0
9740–9749	Mast cell tumors	0.23	338	0.23	338	0.00	0
9580–9589	Granular cell tumors/alveolar soft part sarcomas	0.26	384	0.22	330	0.04	54
9270–9349	Ddontogenic tumors	0.26	389	0.26	389	0.00	0
9750–9759	Neoplasms of histiocytes/accessory lymphoid cells	0.29	425	0.29	425	0.00	0
9250–9259	Giant cell tumors	0.32	484	0.32	483	0.00	1
8680–8719	Paragangliomas and glomus tumors	0.72	1,073	0.70	1,035	0.03	38
9260–9269	Miscellaneous bone tumors	0.94	1,426	0.91	1,395	0.02	31
9490–9529	Neuroepithelialomatous neoplasms	0.94	1,393	0.93	1,382	0.01	11
9720–9729	Precursor cell lymphoblastic lymphoma	1.23	1,852	0.24	354	0.99	1,498
9350–9379	Miscellaneous tumors	1.47	2,189	1.44	2,136	0.04	53
9100–9109	Trophoblastic neoplasms	1.58	2,426	1.44	2,203	0.15	223
8590–8679	Specialized gonadal neoplasms	1.62	2,400	0.20	301	1.42	2,099
9530–9539	Meningiomas	1.92	2,830	1.91	2,828	0.00	2
9040–9049	Synovial-like neoplasms	1.98	2,971	1.89	2,847	0.08	124
9540–9579	Nerve sheath tumors	2.02	3,009	1.99	2,967	0.03	42
8090–8119	Basal cell neoplasms (other than skin)	2.10	3,101	2.08	3,070	0.02	31
9000–9039	Fibroepithelial neoplasms	2.47	3,651	0.01	10	2.46	3,641
8580–8589	Thymic epithelial neoplasms	2.62	3,874	2.62	3,868	0.00	6
9760–9769	Immunoproliferative diseases	3.89	5,744	3.89	5,744	0.00	0
9800–9809	Leukemia, NOS	5.85	8,652	5.85	8,652	0.00	0
8390–8429	Adnexal and skin appendage neoplasms	6.04	8,915	4.52	6,681	1.51	2,234
8430–8439	Mucoepidermoid neoplasms	6.40	9,489	6.02	8,921	0.38	568
9180–9249	Osseous and chondromatous neoplasms	6.76	10,067	6.66	9,929	0.09	138
9940–9949	Other leukemia	8.30	12,243	8.30	12,243	0.00	0
8850–8889	Lipomatous neoplasms	8.78	12,991	8.57	12,676	0.21	315
8800–8809	Soft tissue tumors and sarcomas, NOS	11.17	16,550	9.34	13,841	1.83	2,709
9120–9169	Blood vessel tumors	13.51	20,125	12.90	19,222	0.61	903
9050–9059	Mesothelial neoplasms	14.75	21,786	14.75	21,786	0.00	0
8890–8929	Myomatous neoplasms	16.58	24,504	12.54	18,541	4.05	5,963
9700–9719	Mature t- and nk-cell lymphoma	17.37	25,708	10.60	15,686	6.77	10,022
8810–8839	Fibromatous neoplasms	18.78	27,879	18.20	27,010	0.59	869
8550–8559	Acinar cell neoplasms	23.07	34,156	2.21	3,286	20.85	30,870
8930–8999	Complex mixed and stromal neoplasms	23.70	35,016	8.57	12,670	15.13	22,346
8560–8579	Complex epithelial neoplasms	24.68	36,461	6.45	9,547	18.22	26,914
9650–9669	Hodgkin lymphoma	33.56	50,550	33.56	50,550	0.00	0

continued on p. 34

Table 2 (continued). Cancer incidence by histologic grouping[a] among rare and non-rare cancer sites:[b] adults, 41 U.S. registries combined, 1995–2004

Morphology code range	Morphology type	Overall		Rare[c] sites		Non-rare sites	
		Rate[d]	Count	Rate[d]	Count	Rate[d]	Count
9060–9099	Germ cell neoplasms	35.27	53,522	33.95	51,491	1.33	2,031
8000–8009	Neoplasms, NOS	38.13	56,325	14.75	21,811	23.37	34,514
9590–9599	Malignant lymphomas, NOS or diffuse	42.88	63,393	12.96	19,174	29.91	44,219
9820–9839	Lymphoid leukemia	55.15	81,584	55.01	81,371	0.14	213
9840–9939	Myeloid leukemia	64.69	95,821	64.69	95,821	0.00	0
9380–9489	Gliomas	66.78	99,087	66.71	98,975	0.07	112
9730–9739	Plasma cell tumors	67.56	99,753	67.56	99,753	0.00	0
9670–9699	Mature b-cell lymphoma	190.91	282,190	55.12	81,487	135.79	200,703
8720–8799	Melanomas	220.88	326,984	7.97	11,771	212.92	315,213
8440–8499	Cystic, mucinous, and serous neoplasms	229.19	338,470	49.25	72,744	179.94	265,726
8120–8139	Transitional cell (papillary) carcinomas	311.51	460,059	13.50	19,929	298.01	440,130
8010–8049	Epithelial neoplasms, NOS	450.90	666,160	66.28	97,942	384.62	568,218
8050–8089	Squamous cell neoplasms (other than skin)	563.69	833,333	351.01	519,064	212.68	314,269
8500–8549	Ductal and lobular neoplasms	881.42	1,299,583	10.39	15,343	871.03	1,284,240
8140–8389	Adenocarcinomas	2,644.57	3,908,503	452.48	668,901	2,192.09	3,239,602
	Total	6,130.25	9,060,672	1,512.78	2,239,734	4,617.47	6,820,938

Source: North American Association of Central Cancer Registries file submission as of December 2006 from: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, Washington, D.C., Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Massachusetts, Detroit, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Texas, Utah, Washington, West Virginia, Wisconsin, and Wyoming

[a]Histology classification using groupings shown in: Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, et al., editors. International classification of diseases for oncology. 3rd ed. Geneva: World Health Organization; 2000.

[b]Classification by SEER site recode: Ries LAG, Melbert D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, et al., editors. SEER Cancer Statistics Review, 1975–2004. Bethesda (MD): National Cancer Institute; 2007. Also available from: URL: http://seer.cancer.gov/csr/1975_2004 [cited 2008 Sep 25].

[c]Cancers occurring at rare sites with an incidence rate of <150 per million per year

[d]Rates are invasive, microscopically confirmed cancers per million per year and age-adjusted to the 2000 U.S. Standard Population (Census P25-1130).

NOS = not otherwise specified

Table 3. Summary characteristics of rare and non-rare incident cancer sites: adults, 41 U.S. registries combined, 1995–2004

	Rare		*Not rare*		*Rare/not rare*	
	Count	*Rate*[a]	*Count*	*Rate*[a]	*Incidence rate ratio*	*95% CI*
Age (in years)						
20–29	82,446	28.4	37,283	12.8	2.22	(2.19, 2.25)
30–39	160,999	49.8	171,407	53.5	0.93	(0.93, 0.94)
40–49	264,250	84.1	571,511	181.7	0.46	(0.46, 0.47)
50–59	375,508	164.6	1,181,249	517.3	0.32	(0.32, 0.32)
60–69	472,757	307.4	1,808,569	1,175.9	0.26	(0.26, 0.26)
70–79	548,717	456.7	2,024,502	1,684.2	0.27	(0.27, 0.27)
80+	335,057	481.0	1,026,417	1,472.6	0.33	(0.33, 0.33)
Gender						
Male	1,205,561	183.2	3,473,339	539.0	0.34	(0.34, 0.34)
Female	1,034,173	127.3	3,347,599	412.0	0.31	(0.31, 0.31)
Race						
White	1,913,211	149.5	5,981,468	464.6	0.32	(0.32, 0.32)
Black	220,878	166.9	584,880	459.7	0.36	(0.36, 0.36)
American Indian/Alaska Native	9,578	95.0	21,854	232.2	0.41	(0.40, 0.42)
Asian or Pacific Islander	70,556	126.1	142,399	266.0	0.47	(0.47, 0.48)
Other/unspecified	6,191	NA	14,689	NA	NA	NA
Unknown	19,320	NA	75,648	NA	NA	NA
Hispanic ethnicity						
Hispanic	192,314	148.2	378,045	325.5	0.46	(0.45, 0.46)
Non-Hispanic white	1,730,479	150.1	5,624,679	478.5	0.31	(0.31, 0.31)
Non-Hispanic black	216,364	169.6	575,276	467.8	0.36	(0.36, 0.36)
Non-Hispanic other	82,891	130.7	171,912	283.6	0.46	(0.46, 0.46)
Non-Hispanic unknown	17,686	NA	71,026	NA	NA	NA

Source: North American Association of Central Cancer Registries file submission as of December 2006 from: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, Washington, D.C., Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Massachusetts, Detroit, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Texas, Utah, Washington, West Virginia, Wisconsin, and Wyoming

[a]Rates are invasive, microscopically confirmed cancers per 100,000 per year and age-adjusted to the 2000 U.S. Standard Population (Census P25-1130)

CI = confidence interval

NA = not available

IRR=1.65, 95% CI 1.56, 1.75), oropharynx (IRR=1.85, 95% CI 1.74, 1.96), hypopharynx (IRR=1.80, 95% CI 1.73, 1.88), esophagus (IRR=1.57, 95% CI 1.54, 1.60), stomach (IRR=1.83, 95% CI 1.81, 1.86), small intestine (IRR=1.61, 95% CI 1.56, 1.66), liver (IRR=1.56, 95% CI 1.52, 1.60), larynx (IRR=1.50, 95% CI 1.47, 1.53), cervix (IRR=1.53, 95% CI 1.50, 1.56), vagina (IRR=1.67, 95% CI 1.57, 1.78), myeloma (IRR=2.12, 95% CI 2.08, 2.16), and Kaposi sarcoma (IRR=2.35, 95% CI 2.26, 2.45).

Incidence rates for distinct anatomic locations that are subsumed within broader rare cancer sites as defined by the standard SEER Site Recode scheme are shown for illustrative purposes in Table 4. All but one (parotid gland) have reported incidence rates below 10 per million per year, and most have a frequency of less than one case per million per year. Among the subsites that are not single-gender cancers, many demonstrate a higher incidence rate among men.

Each anatomically based rare cancer site comprised many histologic subtypes (range per site: 12–43 histologic groups, median = 25) (Table 5a). For most rare cancers, the most frequent histologic type generally accounted for a high proportion of the diagnoses, with other types usually representing less than 1% of the total. In contrast, histologic variability exists for some rare cancer sites (e.g., cancers of the salivary glands and retroperitoneum). Histologic variability was also more likely at cancer sites that are defined broadly, such as "other digestive organs" or "other urinary organs."

By contrast, several of the rare cancers defined histologically were prominent in multiple anatomic

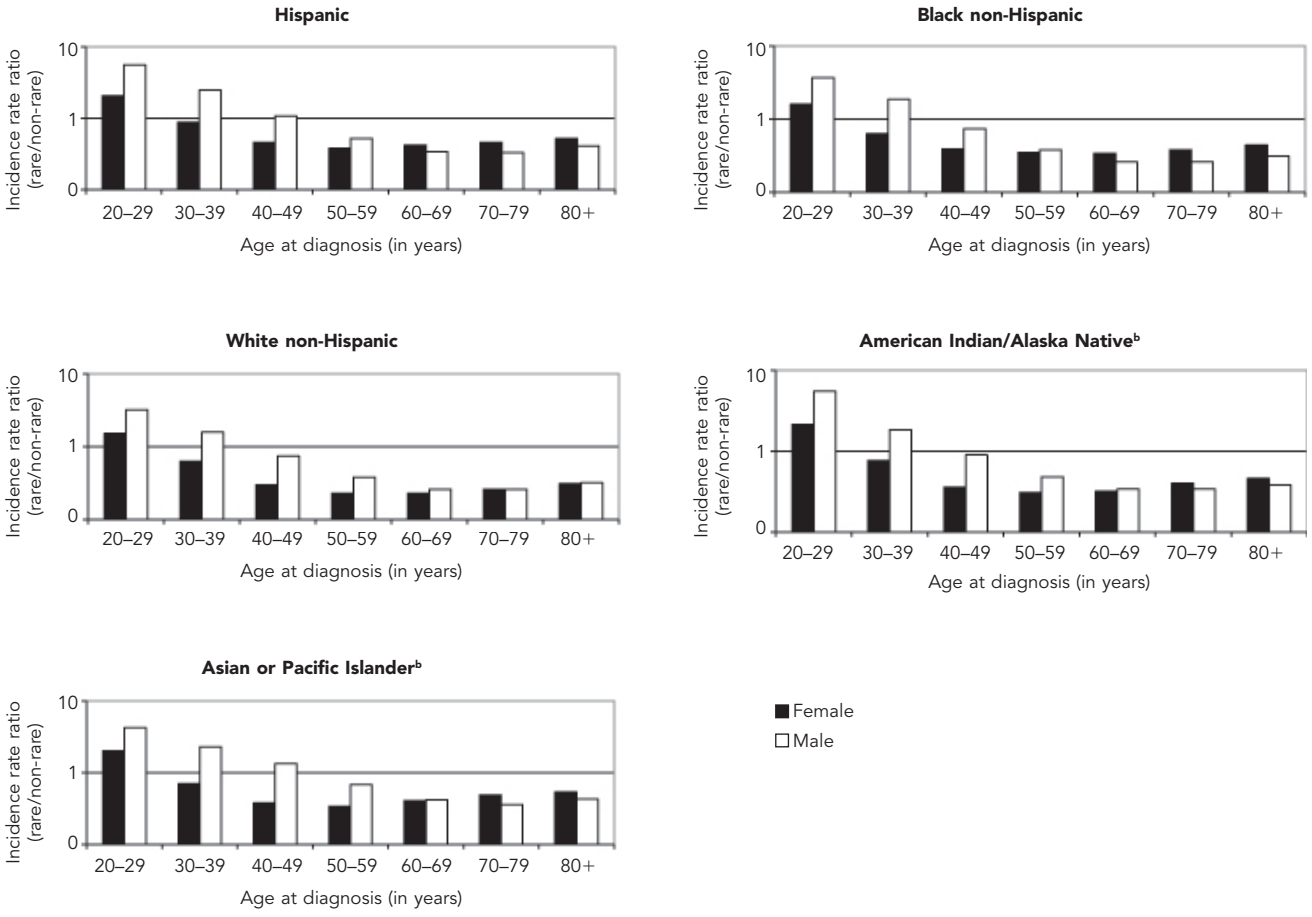
locations (Table 5b). For example, only 17% of extranodal non-Hodgkin lymphomas were diagnosed in the most common anatomic location—the skin—whereas 21 other anatomic sites each accounted for at least 1% of all extranodal non-Hodgkin lymphomas.

DISCUSSION

The historical focus of funded research, and corresponding attention in the medical literature, has been on the most common cancers.[10] The resources to identify and describe rare cancer occurrence; understand their causes; and determine the best approaches for prevention, detection, and treatment have been suboptimal, leaving patients, clinicians, and policy makers with limited information. Unfortunately, the deficit of attention has been even more considerable for very rare cancers.[17] Standard cancer surveillance summaries[15,18,19] also typically highlight more common cancers, often combining tumors from less frequent anatomic locations and overlooking many neoplasms defined histologically. In response to the recent interest in coordinating and enhancing epidemiologic research on rare cancers, the data presented in this article quantify the occurrence of rare cancers in the U.S. and describe their demographic, anatomic, and histologic features.

Based on the employed definition for "rare" of fewer

Figure. Incidence rate ratios (rare[a]/non-rare) by age at diagnosis, gender, and race/ethnicity, 41 U.S. registries combined, 1995–2004



Source: North American Association of Central Cancer Registries, Inc. file submission as of December 2006 from: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, Washington, D.C., Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Massachusetts, Detroit, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Texas, Utah, Washington, West Virginia, Wisconsin, and Wyoming

[a]Cancer site with incidence <150 per million per year

[b]Includes both Hispanic and non-Hispanic ethnicity

Table 4. Cancer incidence for subsites collapsed within rare sites: adults, 41 U.S. registries combined, 1995–2004

	Overall		Male		Female	
Site/code and subsite	*Rate*[a]	*Count*	*Rate*[a]	*Count*	*Rate*[a]	*Count*
Salivary gland						
C07.9—Parotid gland	12.82	18,962	17.78	11,236	9.52	7,726
C08.0—Submandibular gland	2.33	3,445	2.89	1,890	1.91	1,555
C08.1—Sublingual gland	0.16	235	0.14	94	0.18	141
Hypopharynx						
C12.9—Pyriform sinus	6.78	10,009	12.23	8,148	2.31	1,861
C13.0–13.9—Hypopharynx	4.86	7,178	8.03	5,335	2.27	1,843
Other oral cavity and pharynx						
C14.2—Waldeyers ring	0.02	27	0.03	19	0.01	8
C30.0—Nasal cavity	4.13	6,099	5.46	3,578	3.07	2,521
Nose, nasal cavity, and middle ear						
C30.1—Middle ear	0.26	389	0.34	215	0.22	174
C31.0—Maxillary sinus	3.03	4,475	4.06	2,687	2.15	1,788
C31.1—Ethmoid sinus	0.90	1,327	1.18	796	0.66	531
C31.2—Frontal sinus	0.09	133	0.13	87	0.06	46
C31.3—Sphenoid sinus	0.30	448	0.34	228	0.27	220
Trachea, mediastinum, and other respiratory						
C33.9—Trachea	0.91	1,347	1.19	790	0.69	557
C38.1–C38.3—Mediastinum	1.15	1,735	1.86	1,368	0.46	367
Soft tissue, including heart						
C38.0—Heart	0.29	437	0.32	227	0.27	210
Other female genital organs						
C57.0—Fallopian tube	NA[b]	NA[b]	NA[b]	NA[b]	5.63	4,503
C57.1—Broad ligament	NA[b]	NA[b]	NA[b]	NA[b]	0.14	108
C57.2—Round ligament	NA[b]	NA[b]	NA[b]	NA[b]	0.03	23
C57.3—Parametrium	NA[b]	NA[b]	NA[b]	NA[b]	0.03	22
Other male genital organs						
C63.0—Epididymis	NA[b]	NA[b]	0.09	60	NA[b]	NA[b]
C63.1—Spermatic cord	NA[b]	NA[b]	0.75	491	NA[b]	NA[b]
C63.2—Scrotum, NOS	NA[b]	NA[b]	2.13	1,352	NA[b]	NA[b]
Other urinary organs						
C68.0—Urethra	2.68	3,961	4.28	2,607	1.63	1,354
C68.1—Paraurethral gland	0.03	46	0.03	21	0.03	25
Other endocrine, including thymus						
C37.9—Thymus	3.14	4,635	3.72	2,546	2.63	2,089
C74.0–C74.9—Adrenal gland	2.42	3,583	2.35	1,603	2.53	1,980
C75.0—Parathyroid gland	0.49	719	0.53	365	0.45	354
C75.1—Pituitary gland	0.27	400	0.30	211	0.24	189
C75.2—Craniopharyngeal duct	0.01	10	0.01	7	0.00	3
C75.3—Pineal gland	0.27	415	0.38	289	0.17	126
C75.4—Carotid body	0.05	79	0.05	36	0.05	43
Miscellaneous						
C42.2—Spleen	0.08	121	0.08	57	0.08	64

Source: North American Association of Central Cancer Registries file submission as of December 2006 from: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, Washington, D.C., Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Massachusetts, Detroit, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Texas, Utah, Washington, West Virginia, Wisconsin, and Wyoming

[a]Rates are invasive, microscopically confirmed cancers per million per year and age-adjusted to the 2000 U.S. Standard Population (Census P25-1130), and exclude lymphomas, myeloma, leukemia, mesothelioma, and Kaposi's sarcoma.

[b]Gender-specific site

NA = not applicable

NOS = not otherwise specified

Table 5a. Occurrence and distribution of histologic groups[a] within rare cancer[b] sites: adults, 41 U.S. registries combined, 1995–2004

System/site	Total number of histologic groups represented[a] (maximum number = 38)	Most common histologic group	Percent of tumors accounted for by most common group	Percent of site's tumors accounted for by less common histologic groups		
				>10%	1% to 9.9%	<1%
				Number of groups	Number of groups	Number of groups
Oral cavity and pharynx						
Other oral cavity and pharynx	22	Squamous cell neoplasms	86.7	0	3	18
Oropharynx	21	Squamous cell neoplasms	94.3	0	1	19
Nasopharynx	27	Squamous cell neoplasms	69.1	1	1	24
Floor of mouth	20	Squamous cell neoplasms	95.8	0	2	17
Hypopharynx	24	Squamous cell neoplasms	96.1	0	1	22
Lip	23	Squamous cell neoplasms	94.4	0	1	21
Salivary gland	26	Adenocarcinomas	25.8	3	6	16
Tonsil	20	Squamous cell neoplasms	96.7	0	1	18
Gum and other mouth	27	Squamous cell neoplasms	82.0	0	4	22
Tongue	23	Squamous cell neoplasms	95.9	0	2	20
Digestive system, excluding colon and rectum						
Other digestive organs	21	Adenocarcinomas	55.1	1	4	15
Retroperitoneum	28	Lipomatous neoplasms	34.1	2	10	15
Peritoneum, omentum, and mesentery	30	Cystic, mucinous, and serous neoplasms	58.6	1	7	21
Intrahepatic bile duct	12	Adenocarcinomas	95.9	0	2	9
Gallbladder	17	Adenocarcinomas	81.9	0	4	12
Other biliary	18	Adenocarcinomas	86.8	0	4	13
Anus, anal canal, and anorectum	19	Squamous cell neoplasms	65.9	2	3	13
Small intestine	26	Adenocarcinomas	80.0	0	6	19
Liver	24	Adenocarcinomas	93.7	0	2	21
Esophagus	26	Adenocarcinomas	48.6	1	2	22
Stomach	27	Adenocarcinomas	70.9	1	2	23
Pancreas	28	Adenocarcinomas	75.0	0	4	23
Respiratory system, excluding lung and bronchus						
Pleura	17	Neoplasms, NOS	44.8	2	5	9
Trachea, mediastinum, and other respiratory organs	27	Squamous cell neoplasms	23.8	2	8	16
Nose, nasal cavity, and middle ear	30	Squamous cell neoplasms	54.3	1	5	23
Larynx	26	Squamous cell neoplasms	96.2	0	1	24
Bones and joints						
Bones and joints	22	Osseous and chondromatous neoplasms	63.8	0	9	12
Soft tissue, including heart						
Soft tissue, including heart	37	Fibromatous neoplasms	28.9	3	6	27
Skin, excluding basal and squamous (excluding melanoma)						
Other non-epithelial skin	28	Adenocarcinomas	33.8	2	5	20

continued on p. 39

Table 5a (continued). Occurrence and distribution of histologic groups[a] within rare cancer[b] sites: adults, 41 U.S. registries combined, 1995–2004

System/site	Total number of histologic groups represented[a] (maximum number = 38)	Most common histologic group	Percent of tumors accounted for by most common group	Percent of site's tumors accounted for by less common histologic groups		
				>10%	1% to 9.9%	<1%
				Number of groups	Number of groups	Number of groups
Female genital system, excluding ovary, corpus uteri						
Uterus, NOS	26	Adenocarcinomas	28.6	2	7	16
Other female genital organs	26	Adenocarcinomas	40.9	2	5	18
Vagina	26	Squamous cell neoplasms	67.2	1	6	18
Vulva	27	Squamous cell neoplasms	74.9	0	5	21
Cervix uteri	25	Squamous cell neoplasms	71.1	1	3	20
Male genital system, excluding prostate						
Other male genital organs	23	Squamous cell neoplasms	23.0	4	6	12
Penis	19	Squamous cell neoplasms	93.4	0	3	15
Testis	22	Germ cell neoplasms	95.5	0	1	20
Urinary system, excluding kidney/renal pelvis, urinary bladder						
Other urinary organs	16	Transitional cell (papillary) carcinomas	61.9	2	4	9
Ureter	15	Transitional cell (papillary) carcinomas	94.2	0	3	11
Eye and orbit						
Eye and orbit	27	Melanomas	75.9	1	2	23
Brain and other nervous system						
Cranial nerves and other nervous system	18	Gliomas	43.9	1	4	12
Brain	17	Gliomas	98.1	0	0	16
Endocrine system						
Other endocrine, including thymus	29	Thymic epithelial neoplasms	38.5	2	5	21
Thyroid	26	Adenocarcinomas	62.8	1	2	22

Source: North American Association of Central Cancer Registries file submission as of December 2006 from: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, Washington, D.C., Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Massachusetts, Detroit, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Texas, Utah, Washington, West Virginia, Wisconsin, and Wyoming

[a]Histology classification using groupings shown in: Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, et al., editors. International classification of diseases for oncology. 3rd ed. Geneva: World Health Organization; 2000. Classification excludes lymphomas, myeloma, leukemia, mesothelioma, and Kaposi sarcoma.

[b]Rare cancers (rate <15 per 100,000 per year) as classified by SEER Site Recode: Ries LAG, Melbert D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, et al., editors. SEER Cancer Statistics Review, 1975–2004. Bethesda (MD): National Cancer Institute; 2007. Also available from: URL: http://seer.cancer.gov/csr/1975_2004 [cited 2008 Sep 25].

NOS = not otherwise specified

Table 5b. Occurrence and distribution of anatomic sites within histologically based rare cancers:[b] adults, selected areas of the U.S., 1995–2004

System/site (type)	Total number of anatomic sites represented (maximum number = 71)	Most common anatomic site	Percent of malignancies accounted for by most common group	Percent of cancers accounted for by less common anatomic sites		
				>10%	1% to 9.9%	<1%
				Number of groups	Number of groups	Number of groups
Lymphoma, excluding Hodgkin—nodal						
Hodgkin—extranodal	44	Trachea, mediastinum, and other respiratory organs	27.0	2	15	26
Hodgkin—nodal	7	Lymph nodes	99.5	0	0	6
Non-Hodgkin—extranodal	55	Skin	16.9	1	20	33
Myeloma	47	Hematopoietic/reticuloendothelial systems	95.1	0	1	45
Leukemia						
Other myeloid/monocytic leukemia	38	Hematopoietic/reticuloendothelial systems	88.3	0	3	34
Acute monocytic leukemia	4	Hematopoietic/reticuloendothelial systems	100.0	0	0	3
Aleukemic, subleukemic, and NOS	5	Hematopoietic/reticuloendothelial systems	99.9	0	0	4
Other acute leukemia	1	Hematopoietic/reticuloendothelial systems	100.0	0	0	0
Other lymphocytic leukemia	1	Hematopoietic/reticuloendothelial systems	100.0	0	0	0
Acute lymphocytic leukemia	5	Hematopoietic/reticuloendothelial systems	99.9	0	0	4
Chronic myeloid leukemia	2	Hematopoietic/reticuloendothelial systems	100.0	0	0	1
Acute myeloid leukemia	3	Hematopoietic/reticuloendothelial systems	100.0	0	0	2
Chronic lymphocytic leukemia	1	Hematopoietic/reticuloendothelial systems	100.0	0	0	0
Mesothelioma	27	Pleura	84.2	0	2	24
Kaposi sarcoma	48	Skin	81.4	0	5	42

Source: North American Association of Central Cancer Registries file submission as of December 2006 from: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, Washington, D.C., Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Massachusetts, Detroit, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Texas, Utah, Washington, West Virginia, Wisconsin, and Wyoming

[b]Rare cancers (rate <15 per 100,000 per year) as classified by SEER Site Recode: Ries LAG, Melbert D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, et al., editors. SEER Cancer Statistics Review, 1975–2004. Bethesda (MD): National Cancer Institute; 2007. Also available from: URL: http://seer.cancer.gov/csr/1975_2004 [cited 2008 Sep 25].

NOS = not otherwise specified

than 150 incident cases per one million per year, only 11 cancer types are common in U.S. adults (prostate, breast, lung/bronchus, colon, uterus, bladder, melanoma, rectum, ovary, non-Hodgkin lymphoma, and kidney/renal pelvis neoplasms). Fully one-quarter of all adults with cancer were found to have a rare diagnosis.

For younger people, people of nonwhite race, and people of Hispanic ethnicity, the distribution of diagnosed cancers reflects a disproportionate occurrence at rare sites compared with their older, white, or non-Hispanic counterparts. The association with young adults is compatible with the recognition that rare cancers often have a larger genetic component to their etiology than more common cancers.[16,20] The greater likelihood of rare, understudied tumors occurring among nonwhite racial/ethnic groups creates added challenges to achieving our national goals for reducing health disparities in general,[21] and disparities in cancer mortality specifically.[22] This broad dichotomy of "rare" and "common" does mask site-specific heterogeneity in biology and epidemiology, and is partially an artifact of the cancer site distribution among older, white, and non-Hispanic people, in whom the majority of cancers occur. Nevertheless, the fact that cancer site distributions among younger, Hispanic, and nonwhite people are different and tend toward the less common, less studied cancer sites is a practical concern, regardless of the underlying reason.

Encouragingly, interest in rare cancers among scientists, funding agencies, and policy makers has grown in recent years. The U.S. Rare Diseases Act of 2002 focused attention on the benefits of education and research regarding rare conditions.[1] NCI and Office of Rare Diseases workshops on the epidemiology of rare and understudied cancers have brought together topical and methodologic experts to extend the dissemination of current knowledge, promote collaboration, and discuss research gaps along with novel approaches to enhancing rare cancer research capacity in the U.S.[2,9,10,16] Internationally, progress is evidenced by collaborative groups, such as the InterLymph Consortium[23] and Europe's Rare Cancer Network,[24] and scientific articles encouraging the use of population-based data to support rare cancer research.[25,26]

Well-established population-based resources, such as NCI's SEER program, have been supporting a growing number of rare cancer analyses[7,27–29] and new research efforts.[30] While an assessment of all CINA-based site-specific publications to date indicates a predominant focus on six common cancer sites,[31] recent studies of rare malignancies within the CINA dataset include analyses of biliary tumors, penile cancers, and leukemia subtypes.[32–34] Other CINA studies have included investigations into rare aspects of common cancer sites, such as primary extraovarian tumors,[35] inflammatory breast cancer,[36] non-carcinoma breast cancers,[37] and non-cutaneous melanomas.[38]

Future epidemiologic research with this national dataset can retain substantial case numbers while enhancing disease homogeneity through subsite or histologic stratification.[39] For example, although squamous cell carcinoma is the most common histology in the cervix, adenocarcinomas accounted for 17% of cervical tumors and more than 17,000 cases. This distinction can be important for monitoring the potential impact of the recently introduced prophylactic vaccine against oncogenic human papillomavirus types 16 and 18, as these two viruses are more predominant in cervical adenocarcinomas.[40]

For very rare cancers, proponents are calling for the publication of case series, and even single case reports to combat the lack of information.[8,17] Such cancers can be challenging to diagnose, have limited treatment options, and can be rapidly fatal.[10,17] Rates lower than one per million per year nevertheless result in hundreds of cases in the CINA file potentially available for further research. For example, while sarcomas comprise less than 1% of laryngeal tumors, published findings from a recent case series of 10 laryngeal sarcoma patients[41] could be augmented by investigation of the 352 cases of laryngeal sarcoma contained thus far in the CINA database. Furthermore, over time the numbers of rare cancers in the database will continue to increase.

The CINA analytic file is available to NAACCR members for research following approval of research proposals by NAACCR. Variables in the analytic file include reporting registry; year of diagnosis; type of reporting source; case demographics, such as age, gender, race, and Hispanic ethnicity; tumor characteristics, including site, morphology, behavior, stage and other extent of disease information, grade, diagnostic confirmation, laterality, and sequence number; and links to area-level census attributes and geocoded great-circle distances from care facilities. Select treatment data are also included. Survival data are not yet available in the dataset, but may be in the future as more registries institute systematic case follow-up procedures. With appropriate permissions, CINA data can also support data collection from patients or medical records, and rapid case ascertainment procedures are being piloted in some registries to facilitate such work.

Limitations

This study had several limitations. Analysis was restricted to adults aged 20 years and older. Thus, this article does not provide a complete picture for some cancers prevalent in both children and young adults, such as germ cell tumors or osteosarcomas. Rare cancers among younger age groups will be the subject of a separate analysis. This analysis overlooked some cancers that can be considered rare from other perspectives, including cancers rare in one gender (e.g., male breast cancer),[42] rare cancer subsites within common sites (e.g., appendiceal tumors),[43] and less common histologies of common cancer sites (e.g., rectal carcinoids).[44]

The study employed a fairly high threshold for rareness, and it is recognized that research approaches will necessarily differ for very rare cancers with only dozens or hundreds of new cases per year compared with rare cancers with tens of thousands of new cases per year. The designation of rare in this study was also dependent on the narrowness or broadness of the chosen site and histologic definitions. Optimal categorization for each cancer could be addressed during further topic-specific inquiry, such as the recent work developing lymphoma classifications for epidemiologic research by the Inter-Lymph Consortium[45] or a CINA-based investigation into ovarian tumors.[46] Finally, myeloproliferative disorders have only been reportable to cancer registries since 2001, leading to an artificially low case count relative to other cancer types.

CONCLUSIONS

The epidemiology of rare cancers is a challenging area of study, and tumors that are uncommon in the population are also somewhat scarcely documented in the medical and public health literature. The maturing of a nationally representative dataset provides new opportunities to explore the occurrence and characteristics of rare and very rare cancers that have historically been understudied. The use of surveillance data for case ascertainment with possible linkages back to additional data sources could provide opportunities to explore disease etiology, and could potentially lead to advances in treatment and prognosis. We hope that our descriptive analysis encourages such uses of this robust national cancer data resource.

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