The Burden of Rare Cancers in the United States

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Abstract: There are limited published data on the burden of rare cancers in the United States. By using data from the North American Association of Central Cancer Registries and the Surveillance, Epidemiology, and End Results program, the authors provide information on incidence rates, stage at diagnosis, and survival for more than 100 rare cancers (defined as an incidence of fewer than 6 cases per 100,000 individuals per year) in the United States. Overall, approximately 20% of patients with cancer in the United States are diagnosed with a rare cancer. Rare cancers make up a larger proportion of cancers diagnosed in Hispanic (24%) and Asian/Pacific Islander (22%) patients compared with non-Hispanic blacks (20%) and non-Hispanic whites (19%). More than two-thirds (71%) of cancers occurring in children and adolescents are rare cancers compared with less than 20% of cancers diagnosed in patients aged 65 years and older. Among solid tumors, 59% of rare cancers are diagnosed at regional or distant stages compared with 45% of common cancers. In part because of this stage distribution, 5-year relative survival is poorer for patients with a rare cancer compared with those diagnosed with a common cancer among both males (55% vs 75%) and females (60% vs 74%). However, 5-year relative survival is substantially higher for children and adolescents diagnosed with a rare cancer (82%) than for adults (46% for ages 65-79 years). Continued efforts are needed to develop interventions for prevention, early detection, and treatment to reduce the burden of rare cancers. Such discoveries can often advance knowledge for all cancers. **CA Cancer J Clin 2017;67:261-272.** **© 2017 American Cancer Society.**

Keywords: epidemiology, incidence rates, rare cancers, survival

Introduction

Rare cancers present unique challenges for clinicians and their patients. For most rare cancers, research to identify causes or to develop strategies for prevention or early detection is limited or nonexistent. In addition, rare cancers can be challenging to diagnose, often resulting in numerous physician visits, misdiagnoses, and substantial delays in diagnosis. Treatment options for rare cancers are often more limited and less effective than for more common cancers. This is partly because there is less preclinical research and fewer clinical trials for rare cancers, which are often limited to select high-volume cancer centers.[1] Consequently, rare cancers have become an area of priority for some researchers and public health advocates.[2]

There is no universally adopted definition for rare cancers. The US Orphan Drug Act of 1983 defined rare diseases as those affecting less than 200,000 people in the United States.[3] In 2010, Greenlee et al described the US burden of rare cancers according to the National Cancer Institute's definition as those cancers with fewer than 15 cases per 100,000 people per year.[4] More recently, a consortium from the European Union, Surveillance of Rare Cancer in Europe (RARECARE), described the burden of rare cancers in Europe using a revised definition of rare cancers as those with fewer than 6 cases per 100,000 people per year.[5] As part of this effort, the RARECARE working group, consisting of pathologists, hematologists, other clinicians, and epidemiologists, produced a list of clinically relevant, histologically defined cancers. Herein, we describe the burden of rare cancers in the

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TABLE 1. List of Common Cancers, United States, 2009 Through 2013

Adenocarcinoma of colon*
Adenocarcinoma of rectum*
Adenocarcinoma of pancreas*
Hepatocellular carcinoma of liver and IBT
Squamous cell carcinoma of lung*
Adenocarcinoma of lung*
Poorly differentiated endocrine carcinoma of lung
Invasive ductal carcinoma of breast (females)
Invasive lobular carcinoma of breast (females)
Adenocarcinoma of corpus uteri*
Adenocarcinoma of ovary*
Adenocarcinoma of prostate*
Renal cell carcinoma*
Transitional cell carcinoma of bladder
Malignant skin melanoma
Carcinomas of thyroid gland
Diffuse B-cell lymphoma
Plasmacytoma/multiple myeloma (and heavy chain diseases)
Other non-Hodgkin mature B-cell lymphoma

IBT indicates intrahepatic bile tract.

*Includes variants.

United States, providing data on incidence, stage at diagnosis, and survival for 181 rare cancers according to the RARECARE definition and list of rare cancers.

Materials and Methods

Definition of Rare and Common Cancers

All cancers were defined using the list of cancers produced by the RARECARE study group.[6] The RARECARE cancer list classifies cancers using combinations of International Classification of Diseases for Oncology, third edition (ICD-O-3) morphology and topography codes and is hierarchically organized in to 3 layers.[7] The first layer consists of families of tumors according to a consensus-based clinical perspective. The second layer groups tumors into those perceived by clinicians as single diseases that are relevant for clinical management and research. The third layer consists of World Health Organization names of individual cancer entities and corresponding ICD-O-3 codes. We limited this analysis of rare cancers in the United States to those invasive cancers from the RARECARE list with an overall annual crude incidence rate of fewer than 6 cases per 100,000 people. For sex-specific cancers (eg, squamous cell carcinoma of the cervix uteri and seminoma of the testis), status as a rare cancer was based on the incidence rate in the appropriate population of males or females. In this report, we provide information for cancers in the second layer as well as for specific subtypes of adenocarcinoma of the breast, which are third-layer entities. The 19 cancers that were classified as common are listed in Table 1. In addition, we excluded 13 cancers for which there were fewer than 25 cases during 2009 through 2013 (Table 2).

Data Sources

Incidence rates and case distributions by sex, race/ethnicity, age, and stage at diagnosis were obtained using North American Association of Central Cancer Registries (NAACCR) data from 47 states and the District of Columbia, representing 96.7% of the US population.[8] Data from Minnesota, Nevada, and New Mexico were not included, because these states failed to meet NAACCR high-quality standards for a year or more during 2009 through 2013. Data for survival analyses were obtained from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (NCI) SEER 18 registries, which cover approximately 28% of the US population.[9] One-year and 5-year relative survival were based on patients who were diagnosed during 2008 through 2012 and 2006 through 2012, respectively, and were followed through 2013.

Statistical Analyses

Incidence rates and relative survival were calculated using the NCI's SEER*Stat software (version 8.3.2).[10] All incidence rates were age-standardized to the 2000 US standard population and expressed per 100,000 population. Stage distribution was analyzed using SEER Summary Stage. The percentage of cases diagnosed at regional or distant stage was based on patients who had known stage at diagnosis. Relative survival is the ratio of observed survival in a cohort of patients diagnosed with a specific cancer to the expected survival for a similar group of individuals without cancer in the general population and is an estimate of the percentage of patients expected to survive the effects of their cancer. Statistics are not shown when they are based on fewer than 10 cases.

Selected Findings

We identified 181 rare cancers with overall incidence rates of fewer than 6 cases per 100,000 per year during 2009 through 2013 (Table 3). Together, these rare cancers represent 20% of all cancers diagnosed in the United States

TABLE 2. Cancers With Fewer Than 25 Cases Diagnosed During 2009 Through 2013, United States

Lymphoepithelial carcinoma of nasal cavity and sinuses
Papillary adenocarcinoma of nasopharynx
Salivary gland-type tumors of esophagus
Serous cystadenocarcinoma of pancreas
Bile duct cystadenocarcinoma of IBT
Undifferentiated carcinoma of thymus
Lymphoepithelial carcinoma of thymus
Adenoid cystic carcinoma of corpus uteri
Undifferentiated carcinoma of vulva and vagina
Basal cell adenocarcinoma of prostate
Adenocarcinoma with variants of paratestis
Teratoma with malignant transformation
Pancreatoblastoma

IBT indicates intrahepatic bile tract.

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TABLE 3. Incidence Rates for Rare Cancers by Sex and Race/Ethnicity, United States, 2009 Through 2013*

	MALE					FEMALE				
	ALL RACES	NH WHITE	NH BLACK	HISPANIC	API	ALL RACES	NH WHITE	NH BLACK	HISPANIC	API
Digestive system										
SCC of nasal cavity and sinuses†	0.32	0.34	0.23	0.27	0.17	0.14	0.16	0.11	0.09	0.09
Undifferentiated carcinoma of nasal cavity and sinuses	0.03	0.03	0.03	0.02	0.03	0.02	0.02	0.01	0.01	‡
Intestinal-type adenocarcinoma of nasal cavity and sinuses	0.04	0.04	0.04	0.04	0.03	0.02	0.02	0.03	0.02	0.02
SCC of nasopharynx†	0.61	0.47	0.83	0.40	2.51	0.21	0.15	0.28	0.14	0.80
Epithelial tumors of major salivary glands	1.60	1.70	1.14	1.05	1.03	0.95	0.95	0.99	0.79	0.82
Salivary gland-type tumors of head and neck	1.11	0.85	2.01	1.78	2.77	0.75	0.60	1.31	1.00	1.25
SCC of hypopharynx†	1.10	1.05	1.87	0.90	0.65	0.23	0.24	0.29	0.11	0.12
SCC of larynx†	5.90	5.93	8.46	4.70	2.21	1.31	1.41	1.66	0.64	0.26
SCC oropharynx†	7.61	8.55	6.72	4.21	2.00	1.68	1.88	1.54	0.85	0.62
SCC of oral cavity†	3.89	4.21	2.75	2.55	3.10	2.24	2.49	1.20	1.45	1.81
SCC of lip†	0.90	1.06	0.09	0.43	0.07	0.25	0.30	0.03	0.14	0.08
SCC of esophagus†	1.96	1.53	5.52	1.87	2.27	0.88	0.77	1.88	0.52	0.75
Adenocarcinoma of esophagus†	5.37	6.37	1.28	2.52	1.03	0.72	0.84	0.28	0.39	0.14
Undifferentiated carcinoma of esophagus	0.01	0.01	‡	‡	<0.01	<0.01	<0.01	‡	‡	‡
Adenocarcinoma of stomach†	7.61	6.48	11.45	11.08	12.55	3.34	2.47	5.46	6.02	7.02
SCC of stomach†	0.11	0.10	0.21	0.10	0.10	0.04	0.03	0.08	0.04	0.03
Undifferentiated carcinoma of stomach	0.01	0.01	‡	‡	‡	<0.01	<0.01	0.01	‡	‡
Adenocarcinoma of small intestine†	0.87	0.83	1.52	0.66	0.51	0.60	0.54	1.15	0.52	0.38
SCC of small intestine†	<0.01	<0.01	‡	‡	‡	0.01	0.01	‡	‡	‡
SCC of colon†	0.02	0.02	0.02	‡	‡	0.02	0.02	0.03	0.02	‡
Fibromyxoma and low-grade mucinous adenocarcinoma of appendix	0.25	0.27	0.21	0.19	0.17	0.29	0.30	0.26	0.29	0.24
SCC of rectum†	0.16	0.16	0.21	0.12	0.05	0.28	0.31	0.22	0.27	0.06
SCC of anal canal†	1.14	1.18	1.55	0.70	0.23	1.85	2.09	1.41	1.40	0.36
Adenocarcinoma of anal canal†	0.24	0.23	0.34	0.21	0.19	0.15	0.15	0.22	0.12	0.14
Paget disease of anal canal	<0.01	<0.01	‡	‡	‡	0.01	0.01	‡	‡	‡
SCC of pancreas†	0.04	0.04	0.07	0.05	0.05	0.03	0.02	0.03	0.03	‡
Acinar cell carcinoma of pancreas	0.05	0.05	0.06	0.03	0.04	0.02	0.02	0.01	0.01	‡
Mucinous cystadenocarcinoma of pancreas	0.01	0.01	‡	‡	‡	0.02	0.02	0.02	0.02	‡
Intraductal papillary mucinous carcinoma (invasive) of pancreas	0.04	0.04	0.04	0.03	‡	0.03	0.03	0.03	0.02	0.03
Solid pseudopapillary carcinoma of pancreas	0.01	<0.01	0.02	‡	‡	0.03	0.02	0.05	0.06	0.03
Carcinoma with osetoclast-like giant cells of pancreas	0.01	0.01	‡	‡	‡	<0.01	<0.01	‡	‡	‡
Hepatocellular carcinoma, fibrolamellar	0.02	0.02	0.02	0.03	0.04	0.02	0.02	0.02	0.01	‡
Cholangiocarcinoma of IBT	0.97	0.94	0.88	1.08	1.42	0.80	0.78	0.68	1.08	0.97
Adenocarcinoma of liver and IBT†	0.37	0.35	0.35	0.50	0.42	0.25	0.24	0.21	0.35	0.31
Undifferentiated carcinoma of liver and IBT	<0.01	<0.01	‡	‡	‡	‡	‡	‡	‡	‡
SCC of liver and IBT†	0.01	0.01	‡	‡	‡	<0.01	<0.01	‡	‡	<0.01
Adenocarcinoma of gallbladder†	0.69	0.60	1.16	0.99	0.86	1.18	0.96	1.64	2.27	1.32
Adenocarcinoma of EBT†	1.96	1.88	1.72	2.40	2.73	1.31	1.21	1.37	1.91	1.74
SCC of gallbladder and EBT†	0.05	0.04	0.06	0.09	0.06	0.07	0.06	0.12	0.13	0.07
Gastrointestinal stromal sarcoma	0.99	0.88	1.92	0.80	1.14	0.80	0.70	1.61	0.70	0.96
Respiratory system										
SCC of trachea†	0.05	0.05	0.06	0.03	‡	0.02	0.02	0.03	‡	‡
Adenocarcinoma of trachea†	<0.01	<0.01	‡	‡	‡	<0.01	<0.01	‡	‡	<0.01
Salivary gland-type tumors of trachea	0.01	0.01	‡	‡	‡	0.01	0.01	0.01	0.01	‡
Adenosquamous carcinoma of lung	0.91	0.95	0.90	0.63	0.61	0.61	0.67	0.50	0.31	0.38
Large cell carcinoma of lung	2.16	2.23	3.01	1.15	0.95	1.10	1.19	1.28	0.46	0.32
Salivary gland-type tumors of lung	0.05	0.05	0.06	0.04	‡	0.04	0.04	0.05	0.03	0.04
Sarcomatoid carcinoma of lung	0.50	0.52	0.59	0.31	0.26	0.28	0.30	0.29	0.15	0.09
Breast										
Mammary Paget disease of breast	-	-	-	-	-	0.40	0.41	0.40	0.31	0.34
Special types of adenocarcinoma of breast	-	-	-	-	-	4.12	4.12	4.82	3.15	3.47
Tubular adenocarcinoma	-	-	-	-	-	0.68	0.80	0.37	0.34	0.32
Mucinous carcinoma	-	-	-	-	-	2.28	2.27	2.57	1.80	2.17
Medullary carcinoma, NOS	-	-	-	-	-	0.29	0.23	0.63	0.33	0.15
Papillary adenocarcinoma, NOS	-	-	-	-	-	0.38	0.33	0.68	0.35	0.37
Cribriform carcinoma	-	-	-	-	-	0.23	0.24	0.22	0.18	0.18
Apocrine adenocarcinoma	-	-	-	-	-	0.24	0.23	0.33	0.14	0.26
Secretory carcinoma	-	-	-	-	-	0.01	0.01	0.01	‡	‡
Glycogen-rich clear cell carcinoma	-	-	-	-	-	<0.01	<0.01	‡	‡	<0.01
Metaplastic carcinoma of breast	-	-	-	-	-	0.60	0.59	0.90	0.42	0.40
Salivary gland-type tumors of breast	-	-	-	-	-	0.11	0.12	0.11	0.05	0.07
Soft tissue sarcoma of breast	0.01	<0.01	‡	‡	<0.01	0.39	0.36	0.43	0.40	0.49
Epithelial tumor of male breast	1.31	1.32	1.94	0.75	0.58	-	-	-	-	-
Female genital system										
SCC of corpus uteri†	-	-	-	-	-	0.08	0.07	0.14	0.10	0.06
Clear cell adenocarcinoma of corpus uteri, NOS	-	-	-	-	-	0.32	0.28	0.57	0.35	0.28
Serous (papillary) carcinoma of corpus uteri	-	-	-	-	-	0.80	0.67	1.77	0.73	0.65
Mullerian mixed tumor of corpus uteri	-	-	-	-	-	1.13	0.96	2.53	0.99	0.81
SCC of cervix uteri†	-	-	-	-	-	4.94	4.34	7.25	6.58	3.98
Adenocarcinoma of cervix uteri†	-	-	-	-	-	1.83	1.93	1.33	2.09	1.45
Undifferentiated carcinoma of cervix	-	-	-	-	-	0.01	0.01	0.01	‡	‡

TABLE 3. *Continued*

	MALE					FEMALE				
	ALL RACES	NH WHITE	NH BLACK	HISPANIC	API	ALL RACES	NH WHITE	NH BLACK	HISPANIC	API
Mullerian mixed tumor of cervix uteri	-	-	-	-	-	0.04	0.03	0.10	0.04	‡
Mucinous carcinoma of ovary	-	-	-	-	-	0.63	0.68	0.46	0.51	0.62
Clear cell adenocarcinoma of ovary	-	-	-	-	-	0.55	0.59	0.25	0.37	0.99
Primary peritoneal serous/papillary carcinoma	-	-	-	-	-	0.66	0.73	0.35	0.46	0.45
Mullerian mixed tumor of ovary	-	-	-	-	-	0.33	0.35	0.28	0.27	0.20
Adenocarcinoma of fallopian tube†	-	-	-	-	-	0.64	0.72	0.41	0.38	0.44
Sex cord tumors of ovary	-	-	-	-	-	0.25	0.22	0.46	0.22	0.14
Malignant/Immature teratomas of ovary	-	-	-	-	-	0.14	0.10	0.17	0.17	0.18
Germ cell tumor of ovary	-	-	-	-	-	0.20	0.18	0.19	0.25	0.20
SCC of vulva and vagina†	-	-	-	-	-	2.59	2.85	2.19	1.88	0.73
Adenocarcinoma of vulva and vagina†	-	-	-	-	-	0.16	0.15	0.21	0.12	0.13
Paget disease of vulva and vagina	-	-	-	-	-	0.11	0.13	0.01	0.08	0.18
Choriocarcinoma of placenta	-	-	-	-	-	0.07	0.05	0.10	0.08	0.09
Soft tissue sarcoma of uterus	-	-	-	-	-	0.84	0.70	1.59	0.87	0.76
Male genital system										
SCC of prostate†	0.01	0.01	0.02	0.02	‡	-	-	-	-	-
Infiltrating duct carcinoma of prostate	0.18	0.17	0.28	0.14	0.18	-	-	-	-	-
Transitional cell carcinoma of prostate	0.02	0.03	0.02	‡	‡	-	-	-	-	-
Nonseminomatous testicular cancer	2.22	2.75	0.45	2.05	0.79	-	-	-	-	-
Seminomatous testicular cancer	2.93	3.70	0.78	2.08	0.95	-	-	-	-	-
Spermatocytic seminoma	0.04	0.05	‡	0.03	‡	-	-	-	-	-
Testicular sex cord stromal tumor (cancer)	0.04	0.04	0.07	0.03	‡	-	-	-	-	-
SCC of penis†	0.79	0.72	0.91	1.27	0.37	-	-	-	-	-
Adenocarcinoma of penis†	0.01	0.01	‡	‡	0.04	-	-	-	-	-
Soft tissue sarcoma of paratestis	0.08	0.08	0.08	0.10	0.08	-	-	-	-	-
Urinary system										
SCC spindle cell type of kidney	0.01	0.01	0.01	‡	‡	0.01	0.01	‡	‡	‡
SCC of kidney†	0.02	0.02	0.03	0.02	‡	0.01	0.01	0.01	‡	‡
Transitional cell carcinoma of pelvis and ureter	1.88	2.06	0.85	1.25	1.24	0.97	1.07	0.52	0.62	0.80
SCC of pelvis and ureter†	0.03	0.03	0.02	0.02	0.05	0.02	0.02	0.01	0.02	0.03
Adenocarcinoma of pelvis and ureter†	0.03	0.03	0.04	0.03	‡	0.02	0.02	0.02	0.02	‡
Transitional cell carcinoma of urethra	0.15	0.16	0.13	0.07	0.06	0.02	0.02	0.05	0.01	‡
SCC of urethra†	0.05	0.05	0.11	0.04	‡	0.02	0.02	0.03	0.02	‡
Adenocarcinoma of urethra†	0.02	0.02	0.04	‡	‡	0.03	0.02	0.12	0.02	‡
SCC of bladder†	0.30	0.32	0.33	0.20	0.13	0.22	0.23	0.29	0.19	0.09
Adenocarcinoma of bladder†	0.29	0.29	0.40	0.26	0.15	0.12	0.11	0.21	0.11	0.08
Endocrine system										
Well-differentiated, nonfunctional endocrine carcinoma of pancreas and digestive tract	2.62	2.41	4.40	2.14	2.10	2.50	2.22	4.29	2.35	1.62
Well-differentiated, functional endocrine carcinoma of pancreas and digestive tract	0.02	0.02	0.02	0.01	‡	0.02	0.02	0.03	0.02	‡
Poorly differentiated endocrine carcinoma of pancreas and digestive tract	1.92	1.89	2.57	1.55	1.35	1.51	1.45	2.27	1.30	0.80
Mixed endocrine-exocrine carcinoma of pancreas and digestive tract	0.02	0.02	0.02	0.02	‡	0.01	0.01	0.02	‡	‡
Endocrine carcinoma of thyroid gland	0.22	0.23	0.17	0.20	0.13	0.28	0.29	0.25	0.31	0.17
Neuroendocrine carcinoma of skin	0.96	1.11	0.11	0.40	0.17	0.39	0.44	0.08	0.30	0.14
Typical and atypical carcinoid of the lung	0.50	0.57	0.38	0.29	0.17	1.04	1.18	0.67	0.75	0.23
Neuroendocrine carcinoma of other sites	1.55	1.63	1.52	1.11	0.72	1.16	1.16	1.47	0.90	0.68
Pheochromocytoma, malignant	0.03	0.03	0.05	0.03	‡	0.03	0.03	0.06	0.03	0.02
Paraganglioma	0.03	0.03	0.05	0.02	0.03	0.03	0.02	0.06	0.02	0.03
Carcinoma of pituitary gland	0.02	0.02	0.04	0.02	‡	0.02	0.01	0.03	0.01	‡
Carcinoma of parathyroid gland	0.03	0.03	0.06	0.03	0.02	0.03	0.02	0.05	0.03	‡
Carcinoma of adrenal cortex	0.13	0.15	0.10	0.10	0.09	0.16	0.18	0.14	0.13	0.10
Nervous system										
Astrocytic tumors of CNS	6.15	6.94	3.75	4.56	3.18	4.32	4.93	2.62	3.32	2.28
Oligodendroglial tumors of CNS	0.41	0.50	0.19	0.30	0.26	0.31	0.37	0.13	0.23	0.19
Ependymal tumors of CNS	0.27	0.30	0.19	0.23	0.18	0.24	0.26	0.18	0.23	0.14
Choroid plexus carcinoma of CNS	0.01	0.01	‡	0.01	‡	0.01	0.01	‡	0.01	‡
Malignant meningioma	0.08	0.08	0.10	0.07	0.08	0.10	0.09	0.15	0.10	0.10
Neuroblastoma and ganglioneuroblastoma	0.21	0.26	0.18	0.14	0.17	0.19	0.23	0.17	0.12	0.15
Germ cell tumors of the CNS	0.10	0.10	0.06	0.09	0.16	0.03	0.03	0.03	0.03	0.05
Embryonal tumors of CNS	0.33	0.36	0.25	0.31	0.23	0.24	0.25	0.19	0.24	0.16
Soft tissue sarcoma of brain and CNS	0.15	0.14	0.18	0.12	0.15	0.12	0.11	0.15	0.10	0.09
Hematopoietic system										
Hodgkin lymphoma, classical	2.91	3.12	2.90	2.71	1.40	2.31	2.59	2.07	1.99	1.02
Hodgkin lymphoma nodular lymphocyte predominance	0.23	0.24	0.34	0.15	0.09	0.11	0.08	0.31	0.06	0.02
Precursor B-cell/T-cell lymphoblastic leukemia/lymphoma and Burkitt leukemia/lymphoma	1.34	1.36	1.16	1.48	1.11	0.65	0.63	0.57	0.83	0.57
T-cell cutaneous lymphoma (Sezary syndrome, mycosis fungoides)	0.92	0.89	1.12	0.62	0.50	0.59	0.51	0.93	0.46	0.33
Other T-cell lymphomas and NK cell neoplasms	1.21	1.11	1.77	1.21	1.26	0.74	0.66	1.17	0.73	0.79
Follicular B-cell lymphoma	3.77	4.21	1.60	2.90	1.84	3.24	3.64	1.49	2.78	1.37
Hairy cell leukemia	0.47	0.54	0.18	0.31	0.15	0.11	0.13	0.04	0.08	0.06
Mantle cell lymphoma	1.29	1.43	0.58	1.10	0.47	0.43	0.48	0.18	0.35	0.17

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TABLE 3. *Continued*

	MALE					FEMALE				
	ALL RACES	NH WHITE	NH BLACK	HISPANIC	API	ALL RACES	NH WHITE	NH BLACK	HISPANIC	API
Prolymphocytic leukemia B cell	0.05	0.06	0.05	0.03	0.03	0.03	0.03	0.02	0.02	‡
Acute promyelocytic leukemia	0.37	0.36	0.33	0.41	0.29	0.34	0.33	0.35	0.40	0.25
Acute myeloid leukemia	5.01	5.23	4.06	4.00	3.88	3.31	3.41	2.88	2.90	2.69
Chronic myeloid leukemia	1.53	1.52	1.49	1.45	1.02	1.07	1.07	1.12	0.97	0.63
Other myeloproliferative neoplasms	0.05	0.05	0.07	0.05	0.04	0.03	0.03	0.04	0.03	‡
Mast cell tumor	0.05	0.06	0.01	0.03	‡	0.05	0.06	0.02	0.03	‡
Chronic myelomonocytic leukemia	0.65	0.69	0.42	0.49	0.40	0.29	0.30	0.22	0.21	0.19
Atypical chronic myeloid leukemia BCR/ABL negative	0.02	0.02	0.03	0.03	‡	0.01	0.01	‡	‡	‡
Histiocytic malignancies	0.01	0.02	‡	0.02	‡	0.01	0.01	0.01	‡	‡
Lymph node accessory cell tumors	0.04	0.04	0.03	0.03	‡	0.02	0.02	0.03	0.03	‡
Others										
Malignant thymoma	0.25	0.21	0.45	0.20	0.42	0.22	0.18	0.38	0.18	0.39
SCC of thymus†	0.02	0.02	0.04	0.02	0.05	0.02	0.01	0.02	0.02	0.04
Adenocarcinoma of thymus†	<0.01	<0.01	‡	‡	‡	<0.01	<0.01	‡	‡	‡
SCC of eye and adnexa†	0.08	0.08	0.06	0.15	0.04	0.03	0.02	0.02	0.06	‡
Adenocarcinoma of eye and adnexa†	0.02	0.02	0.01	0.02	0.04	0.01	0.01	0.01	0.01	0.02
SCC of middle ear†	0.01	0.01	‡	0.03	‡	0.01	0.01	‡	‡	‡
Adenocarcinoma of middle ear†	<0.01	<0.01	‡	‡	‡	<0.01	<0.01	‡	‡	‡
Mesothelioma of pleura and pericardium	1.49	1.64	0.74	1.05	0.45	0.30	0.33	0.14	0.24	0.13
Mesothelioma of peritoneum and tunica vaginalis	0.12	0.14	0.06	0.10	0.04	0.08	0.08	0.06	0.08	0.03
Malignant melanoma of mucosa	0.08	0.09	0.04	0.06	‡	0.11	0.11	0.08	0.11	0.14
Malignant melanoma of uvea	0.59	0.74	0.05	0.19	0.06	0.46	0.58	0.04	0.22	0.06
Adnexal carcinoma of skin	0.65	0.66	0.36	0.37	0.58	0.36	0.36	0.25	0.27	0.23
Nephroblastoma	0.16	0.17	0.19	0.13	0.07	0.19	0.20	0.25	0.15	0.09
Retinoblastoma	0.08	0.08	0.08	0.10	0.07	0.09	0.09	0.11	0.10	0.10
Hepatoblastoma	0.07	0.06	0.05	0.08	0.09	0.04	0.04	0.03	0.04	0.05
Pleuropulmonary blastoma	<0.01	0.01	‡	‡	‡	<0.01	<0.01	‡	‡	‡
Olfactory neuroblastoma	0.06	0.06	0.04	0.04	0.07	0.04	0.04	0.02	0.04	0.03
Odontogenic malignant tumors	0.01	0.01	‡	‡	‡	0.01	<0.01	0.01	‡	<0.01
Extragonadal nonseminomatous germ cell tumors	0.08	0.09	0.04	0.10	0.08	0.09	0.07	0.14	0.09	0.11
Extragonadal seminomatous germ cell tumors	0.04	0.04	0.03	0.05	0.02	<0.01	<0.01	‡	‡	<0.01
Soft tissue sarcoma of head and neck	0.43	0.46	0.26	0.26	0.26	0.17	0.17	0.17	0.15	0.12
Soft tissue sarcoma of limbs	1.69	1.70	1.68	1.52	1.19	1.21	1.19	1.38	1.12	0.94
Soft tissue sarcoma of superficial trunk	0.80	0.81	0.75	0.80	0.60	0.60	0.59	0.71	0.52	0.44
Soft tissue sarcoma of mediastinum	0.03	0.03	0.04	0.02	0.03	0.02	0.02	0.02	0.02	‡
Soft tissue sarcoma of heart	0.02	0.02	0.03	0.01	‡	0.02	0.02	0.02	0.03	‡
Soft tissue sarcoma of other genitourinary tract	0.14	0.14	0.16	0.16	0.07	0.18	0.16	0.25	0.18	0.11
Soft tissue sarcoma of viscera	0.28	0.29	0.29	0.26	0.20	0.20	0.20	0.23	0.21	0.16
Soft tissue sarcoma of retroperitoneum and peritoneum	0.34	0.35	0.28	0.36	0.24	0.32	0.31	0.37	0.31	0.28
Soft tissue sarcoma of pelvis	0.37	0.38	0.33	0.33	0.21	0.28	0.27	0.40	0.24	0.17
Soft tissue sarcoma of skin	0.69	0.70	0.56	0.32	0.28	0.41	0.40	0.51	0.26	0.20
Soft tissue sarcoma of paraorbit	0.01	0.01	0.01	0.01	‡	0.01	0.01	‡	0.01	‡
Embryonal rhabdomyosarcoma of soft tissue	0.10	0.11	0.12	0.07	0.06	0.07	0.08	0.08	0.05	0.04
Alveolar rhabdomyosarcoma of soft tissue	0.05	0.05	0.07	0.05	0.04	0.06	0.06	0.07	0.05	0.07
Ewing sarcoma of soft tissue	0.09	0.10	0.06	0.09	0.06	0.08	0.09	0.05	0.09	0.06
Osteogenic sarcoma	0.31	0.29	0.35	0.33	0.22	0.25	0.24	0.32	0.24	0.19
Chondrogenic sarcomas	0.25	0.28	0.15	0.21	0.14	0.21	0.23	0.14	0.18	0.09
Notochordal sarcomas, chordoma	0.09	0.10	0.04	0.09	0.08	0.06	0.07	0.03	0.06	0.07
Vascular sarcomas	0.02	0.02	0.02	0.01	‡	0.01	0.01	‡	‡	‡
Ewing sarcoma	0.16	0.20	0.03	0.13	0.12	0.11	0.14	0.03	0.09	0.07
Epithelial tumors, adamantinoma	0.02	0.01	0.03	0.01	‡	0.01	0.01	0.02	‡	‡
Other high-grade sarcomas (fibrosarcoma, malignant fibrous histiocytoma)	0.01	0.01	0.02	‡	‡	0.01	0.01	‡	0.01	‡
Kaposi sarcoma	0.71	0.45	1.64	1.13	0.33	0.07	0.04	0.16	0.21	‡

API indicates Asian/Pacific Islander; CNS, central nervous system; EBT, extrahepatic bile tract; IBT, intrahepatic bile tract; NH, non-Hispanic; NK, natural killer; NOS, not otherwise specified; SCC, squamous cell carcinoma.

*Rates are per 100,000 and age-adjusted to the 2000 US Standard Population.

†Includes variants.

‡Rates not shown when based on fewer than 10 cases.

Source: North American Association of Central Cancer Registries, 2016.

during 2009 through 2013. Of these 181 rare cancers, 119 cancers are considered very rare, that is, with an incidence rate $\leq$0.5 per 100,000. These very rare cancers represent only about 3% of all cancers diagnosed each year.

Variations in the percentages of rare cancers by sex, race/ethnicity, and age at diagnosis are shown in Figure 1. Some cancers cannot be classified as rare or common because of nonspecific morphology coding. Rare cancers make up a

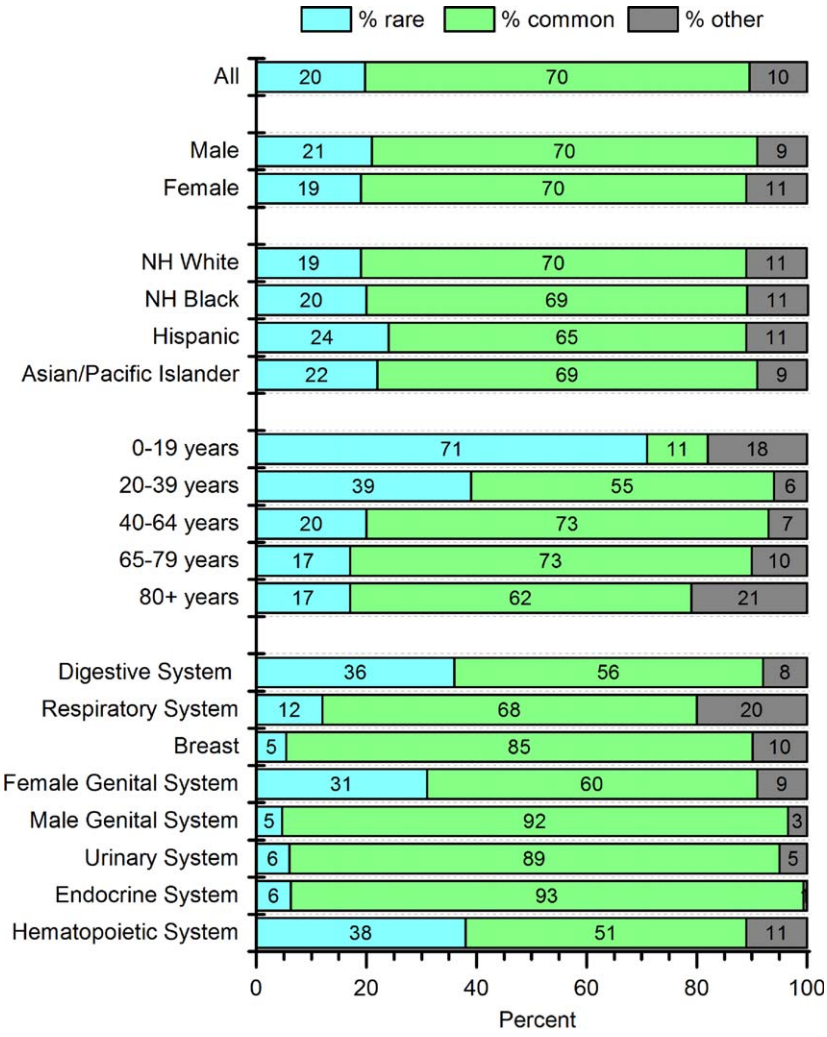

FIGURE 1. Distribution of Rare and Common Cancers, 2009 Through 2013, United States.
NH indicates non-Hispanic. Source: North American Association of Central Cancer Registries, 2016.

slightly larger proportion of cancers in males than females (21% vs 19%) and in Hispanics (24%) and Asians/Pacific Islanders (22%) compared with non-Hispanic (NH) blacks (20%) and NH whites (19%). The greater representation of rare cancers in racial/ethnic minorities may contribute to racial/ethnic disparities in overall cancer outcomes. The proportion of rare cancers is greater among children and adolescents and young adults; rare cancers accounted for the majority (71%) of diagnoses in those aged younger than 20 years and 39% of cancers in those ages 20 to 39 years. In contrast, rare cancers represented about 17% to 20% of cancers diagnosed in adults aged 40 years and older.

Figure 1 also describes the distribution of rare and common cancers by cancer site. Rare cancers account for only 5% of both breast and male genital system cancers but as much as 38% of hematopoietic and 36% of digestive system cancers, which include cancers that occur in the oral cavity and pharynx, all of which are rare. Rare cancers also make up nearly one-third of cancers of the female genital system (31%).

Table 3 shows variation in incidence rates for specific rare cancers by sex and race/ethnicity. Some cancers that are rare overall are more common in specific demographic groups. For example, although adenocarcinoma of the stomach is considered a rare cancer overall, it is a common cancer among males and Hispanic and Asian/Pacific Islander females. Conversely, NH white males and females have the highest rates of transitional cell carcinoma of the pelvis and ureter (2.06 and 1.07 per 100,000, respectively), and NH black males and females have the lowest (0.85 and 0.52 per 100,000, respectively). Similarly, NH whites have the highest rates of bladder cancer in the United States.[11] Malignant thymoma is a very rare cancer (<0.5 per 100,000) among all subgroups, but rates are twice as high in NH black and Asian/Pacific Islander men and women compared with NH white men and women. Racial differences in thymoma rates

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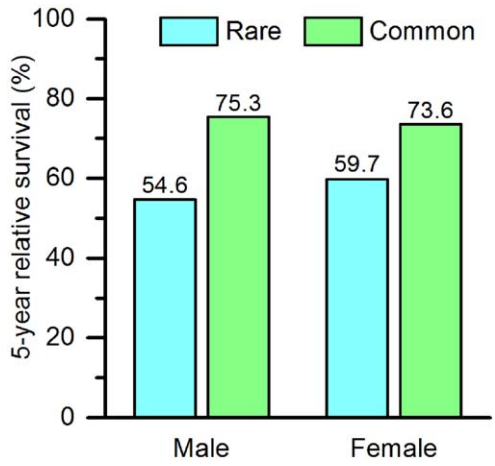

FIGURE 2. Five-Year Relative Survival for Rare and Common Cancers by Sex, 2006 Through 2012, United States.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, 18 SEER Registries, National Cancer Institute, 2016.

have been noted previously, but reasons for the disparities are not currently known.[12] Examining racial and ethnic differences in risk for some rare cancers may provide insights into their etiology.

Figure 2 compares 5-year survival for rare and common cancers by sex. Overall, 5-year relative survival for rare cancers is poorer than that for common cancers among both males (55% vs 75%) and females (60% vs 74%). The survival difference in part reflects differences in stage at diagnosis. Among solid tumors with information on stage at diagnosis, 59% of rare cancers are diagnosed at regional/distant stages compared with 45% of common cancers (Table 4). To some extent, delays in diagnosis are nearly inevitable, because, by definition, clinicians will not see rare cancers often and will initially seek to rule out more common causes of symptoms.[13-16]

Five-year relative survival for patients with rare and common cancers varies by age at diagnosis (Fig. 3). Five-year survival is substantially higher for children (ages birth-19 years) and young adults (ages 20-39 years) diagnosed with a rare cancer (about 80%) compared with older adults diagnosed with a rare cancer (60% or less). Nevertheless, patients with a rare cancer diagnosis have poorer survival than those with a common cancer diagnosis across all age groups. Notably, the difference in survival between rare and common cancers is much greater in older patients. For example, among patients diagnosed with cancer who are aged older than 80 years, the 5-year relative survival rate was 35% for those diagnosed with a rare cancer compared with 60% for those diagnosed with a common cancer (Fig. 3).

The proportion of late (regional/distant) stage diagnoses and the 1-year and 5-year relative survival rates for select rare cancers are provided in Table 4. The proportion of cancers diagnosed at late stage ranges from only 6% for soft tissue sarcoma of the skin and tubular adenocarcinoma of the breast to greater than 90% of mesothelioma of pleura and pericardium, squamous cell carcinoma (SCC) of gall bladder and extrahepatic bile duct, SCC of nasopharynx, undifferentiated carcinomas of the nasal cavities and sinuses, and Mullerian mixed tumors of the ovary. There are also wide variations in 1-year and 5-year relative survival for rare cancers. One-year relative survival ranges from 20% for SCC of the liver to 90% or greater for 72 rare cancers, including soft tissue sarcomas of the breast, limbs, paraorbit, paratestis, and skin, classical and nodular lymphocyte-predominant Hodgkin lymphoma, and uveal melanoma. Five-year relative survival ranges from less than 10% for 7 rare cancers, including undifferentiated carcinomas of the stomach (0%), mesothelioma of the pleura and pericardium (6%), SCC of pancreas (8%), and adenocarcinoma of the liver (8%), to nearly 100% for several rare subtypes of adenocarcinoma of the breast, including mucinous carcinoma, invasive cribriform carcinoma, and tubular carcinoma.

Discussion

In this report, we provide an overview of the burden of rare cancers in the United States. Overall, rare cancers represent 20% of cancers diagnosed in the United States. Previous studies using the RARECARE definition demonstrated that rare cancers represent 22% of cancer diagnoses in Europe (27 countries), 17% of cancers in the Netherlands, and 15% of diagnoses in Japan.[5,17,18] Similarly, Greenlee et al estimated that 25% of all cancers diagnosed in US adults during 1995 through 2004 were rare, considering rare cancers as those with rates less than 15 per 100,000 population.[4]

Overall, 5-year relative survival is poorer for patients with a rare cancer compared with those diagnosed with a more common cancer among both males (55% vs 75%) and females (60% vs 74%). Similarly, Gatta et al reported that the 5-year survival rate in Europe was 47% for patients with rare cancers compared with 67% for those with common cancers.[19] Reasons for poorer survival for rare cancers include lack of effective treatments and standard treatment guidelines as well as delays in diagnosis.[2] Poor survival for some rare cancers, such as those that are more prevalent among adolescents and young adults, may also in part reflect differences in tumor biology.[20,21]

Clinical trials to evaluate new treatments for rare cancers are inherently challenging. Billingham et al recently proposed methods that could increase the utility of clinical trials for rare cancers, including strategies that would maximize recruitment and minimize sample size in the conventional trial setting, as well as alternative study designs.[22] International collaboration in clinical trials is essential to improve outcomes for rare cancers. To this end, the International Rare Cancers Initiative was established in 2011 as a joint initiative between the NCI, Cancer Research UK, the

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TABLE 4. Stage Distribution and 1-Year and 5-Year Relative Survival for Select Rare Cancers, United States*

	% REGIONAL/ DISTANT STAGE*	1-YEAR RELATIVE SURVIVAL	5-YEAR RELATIVE SURVIVAL
All rare cancers	59%	76%	57%
All common cancers	45%	86%	75%
Digestive system			
SCC of nasal cavity and sinuses†	55%	87%	67%
Undifferentiated carcinoma of nasal cavity and sinuses	93%	72%	41%
Intestinal-type adenocarcinoma of nasal cavity and sinuses	70%	83%	55%
SCC of nasopharynx†	91%	84%	61%
Epithelial tumors of major salivary glands	52%	89%	73%
Salivary gland-type tumors of head and neck	57%	79%	58%
SCC of hypopharynx†	82%	66%	33%
SCC of larynx†	43%	85%	61%
SCC oropharynx†	85%	87%	66%
SCC of oral cavity†	48%	82%	59%
SCC of lip†	7%	98%	89%
SCC of esophagus†	79%	42%	16%
Adenocarcinoma of esophagus†	77%	52%	21%
Undifferentiated carcinoma of esophagus	90%	21%	14%
Adenocarcinoma of stomach†	75%	52%	25%
SCC of stomach†	74%	41%	18%
Undifferentiated carcinoma of stomach	81%	41%	0%
Adenocarcinoma of small intestine†	75%	55%	26%
SCC of colon†	76%	59%	42%
Fibromyxoma and low-grade mucinous adenocarcinoma of appendix	82%	92%	65%
SCC of rectum†	53%	81%	62%
SCC of anal canal†	46%	91%	70%
Adenocarcinoma of anal canal†	55%	84%	48%
Paget disease of anal canal	‡	94%	84%
SCC of pancreas†	90%	18%	8%
Acinar cell carcinoma of pancreas	82%	57%	26%
Mucinous cystadenocarcinoma of pancreas	58%	61%	44%
Intraductal papillary mucinous carcinoma invasive of pancreas	50%	79%	56%
Solid pseudopapillary carcinoma of pancreas	39%	94%	90%
Carcinoma with osetoclast-like giant cells of pancreas	75%	54%	38%
Hepatocellular carcinoma, fibrolamellar	61%	67%	38%
Cholangiocarcinoma of IBT	71%	35%	9%
Adenocarcinoma of liver and IBT†	68%	28%	8%
Undifferentiated carcinoma of liver and IBT	59%	‡	‡
SCC of liver and IBT†	60%	20%	9%
Adenocarcinoma of gallbladder†	90%	46%	19%
Adenocarcinoma of EBT†	84%	47%	17%
SCC of gallbladder and EBT†	92%	32%	13%
Gastrointestinal stromal sarcoma	30%	92%	79%
Respiratory system			
SCC of trachea†	59%	44%	19%
Adenocarcinoma of trachea†	41%	‡	‡
Salivary gland-type tumors of trachea	49%	99%	88%
Adenosquamous carcinoma of lung	75%	55%	28%
Large cell carcinoma of lung	79%	45%	18%
Salivary gland-type tumors of lung	49%	82%	71%
Sarcomatoid carcinoma of lung	84%	32%	19%
Breast			
Mammary Paget disease of breast (female)	30%	98%	87%
Special adenocarcinoma subtypes of breast (female)	14%	100%	99%
Tubular adenocarcinoma	6%	100%	100%
Mucinous carcinoma	12%	100%	100%
Medullary carcinoma, NOS	26%	100%	96%
Papillary adenocarcinoma, NOS	14%	99%	96%
Cribriform carcinoma	19%	100%	100%
Apocrine adenocarcinoma	38%	99%	91%
Secretory carcinoma	32%	94%	95%
Glycogen-rich clear cell carcinoma	27%	100%	89%
Metaplastic carcinoma of breast (female)	32%	90%	69%
Salivary gland-type tumors of breast (female)	7%	100%	97%
Soft tissue sarcoma of breast	19%	93%	83%
Epithelial tumor of male breast	51%	97%	84%
Female genital system			
SCC of corpus uteri†	57%	69%	47%
Clear cell adenocarcinoma of corpus uteri, NOS	55%	84%	60%
Serous (papillary) carcinoma of corpus uteri	58%	88%	50%
Mullerian mixed tumor of corpus uteri	59%	73%	41%

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TABLE 4. *Continued*

	% REGIONAL/ DISTANT STAGE*	1-YEAR RELATIVE SURVIVAL	5-YEAR RELATIVE SURVIVAL
SCC of cervix uteri†	58%	87%	67%
Adenocarcinoma of cervix uteri†	38%	91%	75%
Undifferentiated carcinoma of cervix	89%	47%	37%
Mullerian mixed tumor of cervix uteri	71%	60%	37%
Mucinous carcinoma of ovary	52%	82%	68%
Clear cell adenocarcinoma of ovary	67%	89%	67%
Primary peritoneal serous/papillary carcinoma	82%	86%	32%
Mullerian mixed tumor of ovary	95%	64%	24%
Adenocarcinoma of fallopian tube†	77%	94%	64%
Sex cord tumors of ovary	45%	95%	85%
Malignant/immature teratomas of ovary	39%	97%	93%
Germ cell tumor of ovary	61%	95%	93%
SCC of vulva and vagina†	41%	87%	69%
Adenocarcinoma of vulva and vagina†	‡	87%	60%
Paget disease of vulva and vagina	13%	100%	95%
Choriocarcinoma of placenta	70%	98%	89%
Soft tissue sarcoma of uterus	48%	74%	46%
Male genital system			
SCC of prostate†	66%	43%	‡
Infiltrating duct carcinoma of prostate	46%	96%	83%
Transitional cell carcinoma of prostate	27%	61%	52%
Nonseminomatous testicular cancer	41%	97%	93%
Seminomatous testicular cancer	23%	99%	99%
Spermatocytic seminoma	7%	95%	95%
Testicular sex cord cancer	10%	95%	86%
SCC of penis†	39%	87%	69%
Adenocarcinoma of penis†	22%	96%	97%
Soft tissue sarcoma of paratestis	27%	96%	87%
Urinary system			
SCC spindle cell type of kidney	54%	38%	27%
SCC of kidney†	82%	23%	9%
Transitional cell carcinoma of pelvis and ureter	60%	76%	49%
SCC of pelvis and ureter†	88%	43%	14%
Adenocarcinoma of pelvis and ureter†	56%	76%	63%
Transitional cell carcinoma of urethra	51%	80%	48%
SCC of urethra†	68%	82%	50%
Adenocarcinoma† of urethra	66%	85%	41%
SCC of bladder†	54%	41%	27%
Adenocarcinoma of bladder†	49%	72%	41%
Endocrine system			
Well-differentiated nonfunctional endocrine carcinoma of pancreas and digestive tract	35%	96%	91%
Well-differentiated functional endocrine carcinoma of pancreas and digestive tract	59%	87%	74%
Poorly differentiated endocrine carcinoma of pancreas and digestive tract	70%	74%	51%
Mixed endocrine-exocrine carcinoma of pancreas and digestive tract	80%	79%	51%
Endocrine carcinoma of thyroid gland	45%	96%	89%
Neuroendocrine carcinoma of skin	39%	84%	60%
Typical and atypical carcinoid of the lung	33%	95%	90%
Neuroendocrine carcinoma of other sites	‡	52%	30%
Pheochromocytoma, malignant	48%	84%	70%
Paraganglioma	73%	93%	68%
Carcinoma of pituitary gland	‡	83%	68%
Carcinoma of parathyroid gland	39%	97%	86%
Carcinoma of adrenal cortex	65%	57%	31%
Nervous system			
Astrocytic tumors of CNS	16%	57%	26%
Oligodendroglial tumors of CNS	12%	92%	76%
Ependymal tumors of CNS	12%	94%	86%
Choroid plexus carcinoma of CNS	27%	85%	65%
Malignant meningiomas	34%	80%	58%
Embryonal tumors of CNS	26%	83%	64%
Soft tissue sarcoma of brain and CNS	39%	79%	55%
Hematopoietic system			
Hodgkin lymphoma, classical	84%	92%	86%
Hodgkin lymphoma nodular lymphocyte predominance	61%	99%	95%
Precursor B-cell/T-cell lymphoblastic leukemia/lymphoma and Burkitt leukemia/lymphoma	-	79%	66%
T-cell cutaneous lymphoma (Sezary syndrome, mycosis fungoides)	-	96%	89%
Other T-cell lymphomas and NK cell neoplasms	-	63%	45%
Follicular B-cell lymphoma	71%	95%	88%
Hairy cell leukemia	-	96%	93%
Mantle cell lymphoma	90%	82%	56%
Prolymphocytic leukemia B-cell	-	74%	45%

TABLE 4. *Continued*

	% REGIONAL/ DISTANT STAGE*	1-YEAR RELATIVE SURVIVAL	5-YEAR RELATIVE SURVIVAL
Acute promyelocytic leukemia	-	76%	70%
Acute myeloid leukemia	-	43%	22%
Chronic myeloid leukemia	-	91%	77%
Other myeloproliferative neoplasms	-	88%	76%
Mast cell tumor	-	92%	75%
Chronic myelomonocytic leukemia	-	64%	23%
Atypical chronic myeloid leukemia BCR/ABL negative	-	53%	26%
Histiocytic malignancies	80%	98%	87%
Lymph node accessory cell tumors	37%	67%	46%
Others			
Malignant thymoma	65%	91%	76%
SCC of thymus†	81%	84%	53%
Adenocarcinoma of thymus†	71%	80%	53%
SCC of eye and adnexa†	21%	99%	86%
Adenocarcinoma of eye and adnexa†	58%	94%	72%
SCC of middle ear†	69%	76%	44%
Adenocarcinoma of middle ear†	63%	100%	59%
Mesothelioma of pleura and pericardium	91%	41%	6%
Mesothelioma of peritoneum and tunica vaginalis	79%	58%	33%
Malignant melanoma of mucosa	58%	66%	24%
Malignant melanoma of uvea	8%	99%	82%
Adnexal carcinoma of skin	‡	98%	94%
Neuroblastoma and ganglioneuroblastoma	76%	93%	78%
Nephroblastoma	60%	99%	92%
Retinoblastoma	18%	98%	95%
Hepatoblastoma	55%	89%	82%
Pleuropulmonary blastoma	50%	100%	89%
Olfactory neuroblastoma	76%	91%	78%
Odontogenic malignant tumors	69%	90%	80%
Extragonadal nonseminomatous germ cell tumors	60%	76%	63%
Extragonadal seminomatous germ cell tumors	54%	93%	89%
Germ cell tumors of the CNS	25%	94%	86%
Soft tissue sarcoma of head and neck	37%	88%	68%
Soft tissue sarcoma of limbs	26%	91%	75%
Soft tissue sarcoma of superficial trunk	41%	77%	56%
Soft tissue sarcoma of mediastinum	65%	62%	37%
Soft tissue sarcoma of heart	67%	54%	12%
Soft tissue sarcoma of other genitourinary tract	52%	74%	55%
Soft tissue sarcoma of viscera	64%	54%	32%
Soft tissue sarcoma of retroperitoneum and peritoneum	53%	78%	52%
Soft tissue sarcoma of pelvis	44%	81%	59%
Soft tissue sarcoma of skin	6%	98%	93%
Soft tissue sarcoma of paraorbit	37%	95%	87%
Embryonal rhabdomyosarcoma of soft tissue	56%	90%	71%
Alveolar rhabdomyosarcoma of soft tissue	85%	86%	37%
Ewing sarcoma of soft tissue	60%	80%	54%
Osteogenic sarcoma	61%	88%	61%
Chondrogenic sarcomas	41%	91%	81%
Notochordal sarcomas, chordoma	51%	95%	81%
Vascular sarcomas	74%	53%	34%
Ewing sarcoma	69%	92%	63%
Epithelial tumors, adamantinoma	29%	100%	96%
Other high-grade sarcomas (fibrosarcoma, malignant fibrous histiocytoma)	55%	85%	59%
Kaposi sarcoma	‡	81%	73%

CNS indicates central nervous system; EBT, extrahepatic bile tract; IBT, intrahepatic bile tract; NK, natural killer; NOS, not otherwise specified; SCC, squamous cell carcinoma.

*Stage distribution for solid tumors diagnosed with known stage.

†Includes variants.

‡Stage distribution not shown for cancers with 20% or more cases with unknown stage. Survival not shown when based on fewer than 10 cases.

Sources: Stage distribution - North American Association of Central Cancer Registries, 2016.

Survival - Surveillance, Epidemiology, and End Results (SEER) Program, 18 SEER Registries, National Cancer Institute, 2016.

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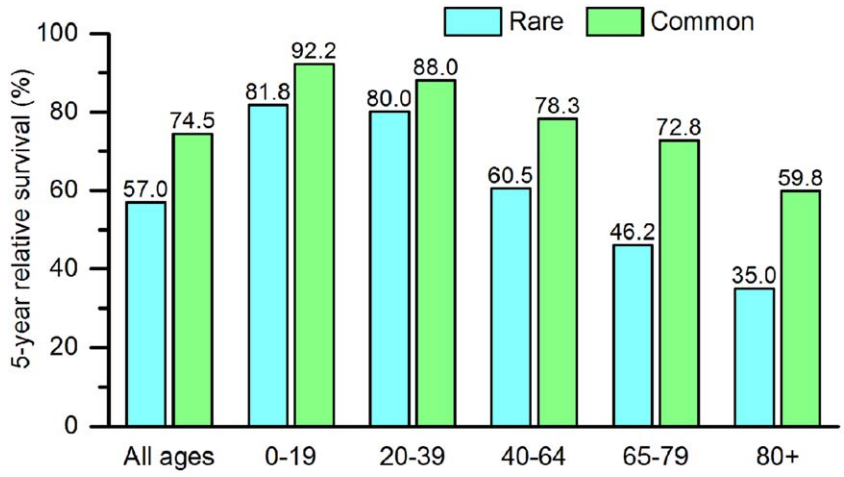

FIGURE 3. Five-Year Relative Survival for Rare and Common Cancers by Age at Diagnosis (Years), 2006 Through 2012, United States.

Source: Surveillance, Epidemiology, and End Results (SEER) Program, 18 SEER Registries, National Cancer Institute, 2016.

National Institute for Health Research Clinical Research Network: Cancer, the European Organization for Research and Treatment of Cancer, the French National Cancer Institute, and the National Cancer Institute of Canada Clinical Trials Group to facilitate the development of international trials and boost the progress of new treatments that initially focused on 9 specific rare cancers.[23] In addition, in 2014, the National Clinical Trials Network was launched in the United States with a focus on the study of rare cancers.[24] Notably, there has been tremendous success in the advancement of treatment for many childhood cancers, in large part because treatment for children's cancers has been concentrated in specialized centers and the joint research collaborations among these centers.[25–27]

Among solid tumors, 59% of rare cancers are diagnosed at regional/distant stages compared with 45% of all common cancers. Progress in screening and detection of cancer has generally been limited to more common cancer sites. Of course, some rare histologic subtypes of more common cancer sites, such as rare subtypes of adenocarcinoma of the breast, are detectable through current screening modalities. Screening of rare cancer sites is generally impractical because of the extremely large numbers of patients that would need to be screened to prevent one death.[28] As a result, most patients with a rare cancer present with symptoms, which are often nonspecific.[29] Efforts to increase awareness of rare cancer symptoms in patients and clinicians could lead to earlier detection and improvements in survival.[30]

There are several limitations in this analysis of rare cancers. It may be more difficult to diagnose and register rare cancers than common cancers. In this study, 775,645 of 7,465,548 cases (10%) could not be classified as rare or common cancers; 127,105 of these (16%) were unknown primary (C80.9), 285,600 (36%) were classified as neoplasms (C8000) without additional detail regarding morphology, and 134,839 (17%) were classified as carcinoma not otherwise specified (NOS) (C8010). Unspecified morphology (ie, NOS) may reflect difficulty making a precise diagnosis or inadequate documentation, which could result in an underestimate for some rare cancers. The RARECARE group conducted a sensitivity analysis and concluded that the vast majority of NOS cases in Europe were due to genuine difficulties in assigning more specific diagnoses.[5] It is also notable that some cancers that are defined herein as rare according to the RARECARE framework may in fact be well studied and/or not "clinically rare," in that they do not require unique treatments. Finally, the number of rare cancers will likely continue to increase as cancers are being further defined on the basis of molecular markers; however, these data are generally not currently available from cancer registries.

Collectively, rare cancers contribute to a substantial portion of the cancer burden in the United States. The proportion of rare cancers is likely to grow because of the increasing use of molecular markers in the classification of cancers. Research and resources have historically focused on the most common cancers and thus the development of novel therapeutics has lagged behind for rare cancers, except for childhood cancers, which have had remarkable progress in treatment and survival.[25,26] Continued efforts are needed to develop interventions for prevention, early detection, and treatment to reduce the burden of rare cancers. Notably, the study of rare cancers has led to the identification of numerous cancer genes and has increased understanding of cancer biology.[31,32] Discoveries for rare cancers can further knowledge for all cancers. ■

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