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Original Article

Comparison of Cancer Survival Trends in the United States of Adolescents and Young Adults With Those in Children and Older Adults

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BACKGROUND: With prior reports indicating a lack of progress in survival improvement in older adolescents and young adults (AYAs) aged 15 to 39 years with cancer compared with both younger and older patients with cancer, the current analysis provides an update of survival trends of cancers among AYAs, children, and older adults. **METHODS:** Data from the National Cancer Institute Surveillance, Epidemiology, and End Results database for 13 regions were used to ascertain survival trends of the 34 most frequent cancers diagnosed in AYAs compared with children and older adults. **RESULTS:** As of 2002 through 2006, the 5-year relative survival rate for all invasive cancers in AYAs was 82.5% (standard error, 0.2%). In AYAs, 14 cancers demonstrated evidence of a statistically significant improvement in their 5-year relative survival since 1992. Survival improved less in AYAs than in children for acute myeloid leukemia and medulloblastoma. Fourteen cancers had survival improvements that were found to be less in AYAs compared with older adults, including hepatic carcinoma, acute myeloid leukemia, high-grade astrocytoma, acute lymphocytic leukemia, pancreatic carcinoma, low-grade astrocytoma, gastric carcinoma, renal carcinoma, cancer of the oral cavity and pharynx, Hodgkin lymphoma, ovarian cancer, fibromatous sarcoma, other soft tissue sarcoma, and thyroid carcinoma. **CONCLUSIONS:** Improvements in the survival of several cancer types that occur frequently in AYAs are encouraging. However, survival does not appear to be improving to the same extent in AYAs as in children or older adults for several cancers. Further investment in exploring the distinct biology of tumors in this age group, and of their hosts, must be a priority in AYA oncology. ***Cancer*** **2016;122:1009-16.** *© 2016 American Cancer Society.*

KEYWORDS: adolescent, adult, cancer, children, survival, trends, United States, young adult.

INTRODUCTION

Cancer in childhood became a focus of treatment and research in the 1950s[1] and the National Cancer Act of 1971 added adults with cancer as a priority in 1971,[2] but substantially less attention has been given to older adolescents and young adults (AYAs) who are diagnosed with cancer between the ages of 15 to 39 years. Between 1975 and 1980, AYAs diagnosed with cancer generally had a better prognosis than those diagnosed at a younger or older age; however, survival thereafter improved for both children and older adults without corresponding improvements in AYAs, such that their survival advantage diminished compared with younger and older individuals.[3-6] As a result, AYAs have become a national focus of investigation in the United States for nearly 10 years since the National Cancer Institute (NCI) and Livestrong Foundation's joint Adolescent and Young Adult OncologyProgress Review Group was convened in 2004 through 2005.[4] As part of a 2013 NCI-sponsored workshop with support from Livestrong, "Next Steps for Adolescent and Young Adult Oncology: A Scientific Update," this analysis attempts to assess subsequent improvements in survival after cancer among American AYAs. Using the NCI's Surveillance, Epidemiology, and End Results (SEER) program data, we provided an update of national survival trends among AYAs and compared trends in AYAs with those in children and older adults.

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See related Original article on pages 1000-8 and related review articles on pages 988-99, 1017-28 and 1029-37, this issue.

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MATERIALS AND METHODS

We obtained survival data for patients diagnosed with first primary, invasive cancer in the United States from the NCI's SEER 13 database using SEER*Stat software (version 8.1.2).[7] The SEER 13 database has averaged 15% of the US population since 1992,[7] and includes the original 9 SEER registries in existence since 1975 (Connecticut; Iowa; New Mexico; Utah; Hawaii; the metropolitan areas of Detroit, San Francisco-Oakland, and Atlanta; and 13 counties of the Seattle-Puget Sound region) and 4 more registries since 1992 (rural Georgia, Alaska natives, Los Angeles, and San Jose-Monterey).

SEER*Stat was used to obtain 5-year relative survival from the SEER 13 database and to perform joinpoint analyses.[8] Relative survival, a net survival measure representing cancer survival in the absence of other causes of death, is defined as the ratio (expressed as a percentage) of the proportion of observed survivors in a cohort of patients with cancer to the proportion of expected survivors.[9] The SEER AYA recode, based on the AYA classification suggested by Barr et al[10] and updated based on histology changes in the World Health Organization(WHO) hematopoietic/lymphoid tissue book,[11] was used primarily to evaluate histologic types of cancer; for those primary sites not individually designated in the AYA recode listing, we used the SEER site recode (*International Classification of Diseases for Oncology, 3rd Edition*/WHO2008). Pilocytic astrocytoma was included in the low-grade astrocytoma category, as specified in the AYA recode, and bladder cancer in situ was included with invasive bladder cancer due to the changing definition of in situ over time. The footnotes of Tables 1 to 3 specify sites for which the SEER site recode was used. For example, instead of the AYA category of germ cell and trophoblastic tumors or carcinomas of the gonads, the SEER site recode was used for ovary and testicular cancers, a recode that includes all histologies except for lymphomas. Although astrocytomas are classified by WHO histologic grade, there were a substantial number of AYAs (247; 9.4% of all cases) diagnosed with astrocytoma from 2002 to 2006 who did not have their grade specified (5-year relative survival rate, 72%; data not shown); these data highlight the need for better reporting of grade in the medical record.

The 5-year relative survival rate was obtained for invasive cancers and cancers with distant disease at the time of diagnosis. Distant disease was based on SEER historic stage A for all cancers/histologies, except Hodgkin and non-Hodgkin lymphoma, for which distant disease was defined as Ann Arbor stage IV disease. To obtain reliable relative survival estimates, a minimum of 100 cases of each invasive cancer (Table 1) or 50 cases of each cancer with distant disease at diagnosis (Table 2) during 2002 through 2006 had to be in the SEER database. To understand the relative impact of individual cancer type on survival in AYAs, the percentage of AYAs with each cancer type is presented in Table 1; however, it should be noted that this percentage does not equal 100% because rarer cancer types with <100 patients are not included and using 2 types of cancer site/histology recodes (AYA recode and SEER site recode) resulted in the overlap of some cancer groups. For example, only 20% of eye and orbit cancers are carcinomas, with the rest overlapping with other AYA categories, including melanoma and sarcoma. However, because eye and orbit cancers are rare, they comprise a small percentageof the melanoma and sarcoma groups. Similarly, for the majority of the other histology/site categories, only a small percentage of cases overlapped (eg, oral cavity [$<5\%$] and colorectum and anus [$<1\%$ each]).

We calculated the annual percent change (APC) and statistical tests for relative survival trends, using log values of the original data for regression and F-test analyses. Only those cancers with at least 100 cases in the SEER database for each age group (Table 1) were analyzed for survival APC. Consistent with prior studies,[4] analyses were conducted by age group at the time of diagnosis: children aged<15 years, AYAs aged 15 to 39 years, and older adults aged ≥ 40 years. To illustrate changes in 5-year relative survival over time (2002-2006 vs 1992-1996), we presented relative survival estimates by 5-year age intervals for most cancers (Fig. 1). For the 2002 to 2006 survival analyses, there were 6309 malignant cancers among children aged<15 years, 45,164 malignant cancers among AYAs, and 667,371 malignant cancers among older adults aged ≥ 40 years.

During the human immuno deficiency virus (HIV)/acquired immuno deficiency syndrome (AIDS) epidemic of the 1980s and early 1990s, particularly virulent types of Kaposi sarcoma and non-Hodgkin lymphoma (NHL) occurred in young adults, primarily in males, that affected the overall survival trends of these cancers. Therefore, for analysis of relative survival trends in all cancers, we excluded Kaposi sarcoma and NHL in males.

RESULTS

For cases diagnosed from 2002 through 2006, the 5-year relative survival rate for all invasive cancers in AYAs was 82.5%. Sixteen of 34 different types of malignant disease in AYAs had an age-adjusted 5-year relative survival rate of $>80\%$, including 8 with a rate $>90\%$ and 7 with a rate $<50\%$ (Table 1). Melanoma; Hodgkin lymphoma; NHL;

TABLE 1. Five-Year Relative Survival of Cancers in Children, AYAs, and Older Adults Diagnosed in 2002 Through 2006 (SEER13) in Rank Order of AYA Survival

	Age, Years									
	<15			15-39				≥40		
Cancer (Invasive)	No.	Survival	SE	No.	Survival	SE	% of all[a] Cancer	No.	Survival	SE
All cancer	6322	82.0%	0.5%	45,235	82.5%	0.2%	-	667,789	65.9%	0.1%
>80% survival										
Thyroid carcinoma				5472	99.7%	0.1%	12.1%	11,752	96.3%	0.3%
Testicular cancer[b]				3721	96.1%	0.4%	8.2%	1580	95.1%	0.7%
Melanoma				5068	95.5%	0.3%	11.2%	25,319	90.5%	0.3%
Fibromatous sarcoma				534	95.1%	1.0%	1.2%	1719	81.4%	1.3%
Hodgkin lymphoma	234	96.2%	1.3%	2651	94.6%	0.5%	5.9%	2213	74.9%	1.1%
Bladder carcinoma				124	93.7%	1.3%	1.0%	235	79.7%	0.4%
Ependymoma	111	69.8%	4.4%	432	91.4%	2.6%	0.3%	27,425	85.6%	2.7%
Uterine corpus cancer[b]				913	91.0%	1.0%	2.0%	20,433	82.3%	0.3%
Eye and orbit cancer[b]	237	97.2%	1.2%	119	86.6%	3.3%	0.3%	1034	80.3%	1.7%
Chondrosarcoma				153	86.4%	2.9%	0.3%	443	76.1%	2.4%
Chronic myeloid leukemia				399	85.9%	1.8%	0.9%	2159	51.8%	1.2%
Breast carcinoma				6640	85.5%	0.5%	14.4%	101,906	90.6%	0.1%
Kidney cancer				883	85.1%	1.3%	1.9%	18,342	71.8%	0.4%
Low-grade astrocytoma	475	96.8%	0.8%	290	83.7%	2.2%	0.6%	237	45.6%	3.4%
Uterine cervix cancer[b]				2159	83.2%	0.8%	4.8%	5331	63.9%	0.7%
Oral cavity and pharynx cancer[b]				989	80.7%	1.3%	2.2%		62.0%	0.5%
50% to 80% survival										
Ovary cancer[b]				919	79.5%	1.4%	2.0%	10,552	41.4%	0.5%
Non-Hodgkin lymphoma	361	85.0%	1.9%	2857	77.6%	0.8%	6.3%	28,003	68.2%	0.3%
Myeloma[b]				171	74.4%	3.5%	0.4%	8955	42.1%	0.6%
Other softtissue sarcoma[b,c]				2121	71.3%	1.7%	1.6%	6973	60.8%	1.0%
Colorectal cancer[b]				2094	66.3%	0.7%	4.6%	70,296	64.2%	0.2%
Osteosarcoma	139	75.6%	3.7%	286	65.4%	2.9%	0.6%	159	39.1%	4.1%
Anus and anorectum cancer[b]				106	63.0%	4.8%	0.2%	2257	66.2%	1.2%
Medulloblastoma/PNET	258	65.1%	3.0%	152	62.2%	4.0%	0.3%			
Kaposi sarcoma				572	62.0%	2.1%	1.3%	828	72.5%	1.9%
Ewing sarcoma	112	77.4%	4.0%	188	53.5%	3.7%	0.4%			
Acute lymphoblastic leukemia	1673	89.8%	0.8%	676	51.8%	1.9%	1.5%	674	21.1%	1.6%
<50% survival										
Acute myeloid leukemia	286	65.9%	2.7%	713	49.9%	1.8%	1.7%	4289	16.7%	0.6%
Rhabdomyosarcoma	200	69.0%	3.5%	105	43.0%	5.0%	0.2%			
Lung carcinoma				709	36.8%	1.9%	1.6%	82,214	16.2%	0.1%
High-grade astrocytoma				478	34.0%	2.2%	1.1%	5077	5.1%	0.3%
Pancreatic carcinoma				259	33.0%	3.0%	0.6%	17,067	5.7%	0.2%
Gastric carcinoma				453	26.3%	2.2%	1.0%	11,501	25.9%	0.5%
Hepatic carcinoma				288	22.8%	2.6%	0.6%	10,685	15.1%	0.4%

Abbreviations: AYAs, adolescents and young adults; PNET, infratentorial primitive neuroectodermal tumor; SE, standard error; SEER 13, Surveillance, Epidemiology, and End Results data for 13 regions.

[a] Does not equal 100% because cancer sites with <100 patients in the AYA agegroup are not presented and 2 cancer site/histology recodes were used (AYA recode and SEER site recode), resulting in overlap of some cancer groups.

[b] Cancer type was based on SEER site recode.

[c] Other than rhabdomyosarcoma, fibromatous sarcoma, or Kaposi sarcoma, each of which was listed separately.

and thyroid, testicular, and breast tumors, all cancers with a relative survival rate of >80%, comprise 58% of all invasive cancers in AYAs. Those with a 5-year survival rate < 50% were acute myelogenous leukemia (AML); rhabdomyosarcoma (RMS); high-grade astrocytoma; and carcinomas of the lung, pancreas, stomach, and liver.

AYAs had a much lower 5-year survival than children for several cancers, including eye and orbit cancer, low-grade astrocytoma, Ewing sarcoma, acute lymphoblastic leukemia (ALL), AML, and RMS. Conversely, AYAs generally had better 5-year survival than older adults across the 34 cancers presented, with the exception of Kaposi sarcoma and carcinomas of the breast and anus.

Of 19 types of cancer that were staged at the time of diagnosis, 13 with distant disease at diagnosis had 5-year survival rates of <50%, including 6 cancers (colorectum, pancreas, kidney, lung, liver, and stomach) with survival rates of <20% (Table 2). Only 4 cancers with distant disease at diagnosis (thyroid carcinoma, testicular cancer, myeloma, and NHL) were found to have 5-year survival rates of >60%. AYAs had better survival than older adults across all cancers with distant disease at diagnosis.

TABLE 2. Five-Year Relative Survival of Cancers in Children, AYAs, and Older Adults Presenting With Distant Disease[a] During 2002 Through 2006 (SEER 13) in Rank Order of AYA Survival

	Age, Years								
	<15			15-39			≥40		
Cancer (Invasive)	No.	Survival	SE	No.	Survival	SE	No.	Survival	SE
All cancers	2550	80.8%	0.8%	6116	44.0%	0.7%	138,678	17.9%	0.1%
>80% survival									
Thyroid carcinoma				145	92.6%	2.2%	581	45.8%	2.3%
Hodgkin lymphoma				377	85.8%	1.9%	479	58.7%	2.5%
50% to 80% survival									
Testicular cancer[b]				422	77.5%	2.1%	156	65.0%	4.0%
Myeloma				174	74.4%	3.5%	8955	42.1%	0.6%
Non-Hodgkin lymphoma	141	79.4%	2.6%	842	60.1%	1.2%	9668	56.4%	0.4%
Ovary cancer[b]				346	57.4%	2.7%	7362	28.7%	0.6%
Oral cavity and pharynx cancer**				69	50.1%	6.1%	1832	32.4%	1.2%
20% to < 50% survival									
Breast carcinoma				482	36.6%	2.3%	6184	29.8%	0.6%
Uterine corpus cancer[b]				61	34.1%	6.2%	2052	22.8%	1.0%
Other softtissue sarcoma[b,c]				133	28.3%	5.1%	828	13.1%	1.5%
Uterine cervix cancer[a]				133	24.8%	3.8%	712	16.5%	1.5%
Ewing sarcoma				64	22.8%	5.4%			
Osteosarcoma				54	22.3%	5.7%			
Melanoma				99	21.8%	4.2%	1,046	15.9%	1.2%
<20% survival									
Colorectal cancer[b]				548	17.0%	1.2%	14,007	11.8%	0.2%
Pancreatic carcinoma				145	14.3%	3.0%	9248	1.9%	0.2%
Kidney cancer	75	70.1%	5.4%	84	13.6%	4.1%	3303	10.6%	0.6%
Lung carcinoma				386	8.2%	1.4%	45,845	3.3%	0.1%
Hepatic carcinoma				85	6.2%	2.9%	2038	1.8%	0.3%
Gastric carcinoma				275	4.4%	1.4%	4,333	3.3%	0.3%

Abbreviations: AYAs, adolescents and young adults; SE, standard error; SEER 13, Surveillance, Epidemiology, and End Results data for 13 regions.
Leukemias are presented in Table 1.
[a] Distant disease was based on SEER historic stage for all cancers/histologies, except Hodgkin and non-Hodgkin lymphoma, for which distant was defined as Ann Arbor stage IV disease.
[b] Cancer type was based on SEER site recode.
[c] Other than rhabdomyosarcoma, fibromatous sarcoma, or Kaposi sarcoma, each of which was listed separately.

Of the 34 types of cancers reviewed in AYAs, 14 were found to have evidence of a statistically significant improvement in their 5-year relative survival since 1992, and 8 of these (ALL, AML, lung carcinoma, myeloma, chronic myeloid leukemia [CML], NHL, hepatic carcinoma, and Kaposi sarcoma) had statistically significant APC values >1.0 (Table 3). Six other cancers had statistically significant survival improvements at <1.0% since 1992: renal carcinoma, colorectal cancer, breast carcinoma, Hodgkin lymphoma, melanoma, and testicular cancer (Table 3) (most in Fig. 1). The remaining 20 common cancers in AYAs (59%), including bone sarcomas; astrocytomas; carcinomas of the cervix, head/neck, and thyroid; and cancer of the anus, did not have evidence of a statistically significant (Table 3) or visual (Fig. 1) survival improvement since 1992. NHL in females, which was less impacted by the HIV/AIDS epidemic, has shown a survival improvement (Fig. 1). However, with the exception of Kaposi sarcoma, AYAs with other soft tissue sarcomas have not experienced an improvement in survival.

When survival is considered for all cancers except Kaposi sarcoma and NHL in males, AYAs had an APC of 0.52 from 1992 to 2006; this APC was similar to the APC noted in older adults and somewhat lower than the APC observed in children (Table 3). When considering specific cancers among those in Table 3, survival improved less in AYAs than children for AML and medulloblastoma/infratentorial primitive neuroectodermal tumor (PNET). In addition, survival improved less in AYAs compared with older adults for 14 cancers, including hepatic carcinoma, AML, high-grade astrocytoma, ALL, pancreatic carcinoma, low-grade astrocytoma, gastric carcinoma, renal carcinoma, cancer of the oral cavity and pharynx, Hodgkin lymphoma, ovarian cancer, fibromatous sarcoma, other soft tissue sarcoma, and thyroid carcinoma. AYAs demonstrated less improvement in survival for AML than either younger or older patients.

DISCUSSION

During the past decade, the gap in survival improvement among AYAs with cancer in comparison with

TABLE 3. APC in 5-Year Relative Survival of Cancers in Children, AYAs, and Older Adults During 1992 Through 2006 (SEER13) in Rank Order of AYA APC

	Age, Years								
	<15			15-39			≥40		
Cancer (Invasive)	No.	APC	*P*	No.	APC	*P*	No.	APC	*P*
All cancer except AIDS malignancies[a]	17,306	0.58	[b]	121,374	0.52	[b]	1,815,294	0.51	[b]
Other softtissue sarcoma[c,d]	321			2636	−0.43		11,736	0.65	[e]
Eye and orbit cancer[d]	671	0.00		338	−0.43		2840	0.13	
Chondrosarcoma				457	−0.26		1125	−0.32	
Bladder carcinoma				1447	−0.11		78,391	0.07	
Fibromatous sarcoma				1756	−0.10		5237	0.88	[b]
Uterine corpus cancer[d]				2291	−0.03		56,500	−0.01	
Thyroid carcinoma				13,677	0.01		24,994	0.50	[b]
Osteosarcoma	414	0.72		767	0.05		440	−1.22	
Uterine cervix cancer[d]				7341	0.09		16,854	0.03	
Oral cavity, pharynx cancer[d]				2996	0.12		42,725	1.27	[b]
Testicular cancer[d]				10,665	0.12	[e]	4225	0.05	
Ovarian cancer[d]				2876	0.28		30,708	0.97	[f]
Melanoma				14,851	0.29	[b]	64,160	0.42	[b]
Ewing sarcoma	308	0.83		527	0.30		132	8.08	
Ependymoma	312	1.10		354	0.41		567	0.72	
Hodgkin lymphoma	673	0.47		7944	0.45	[b]	5809	0.97	[f]
Low-grade astrocytoma	1224	0.18		804	0.49		705	3.67	[e]
Medulloblastoma/PNET	905	1.77	[e]	465	0.61		177	−1.23	
Gastric carcinoma				1334	0.62		34,309	2.30	[b]
Breast carcinoma				19,855	0.76	[b]	291,240	0.43	[b]
Colorectal cancer[d]				5974	0.84	[f]	210,775	0.81	[b]
Renal carcinoma				2008	0.85	[f]	41,509	1.81	[b]
Rhabdomyosarcoma	595	−0.73		315	1.16		227	3.08	
Pancreatic carcinoma				670	1.35		42,473	3.86	[b]
Anus and anorectum cancer[d]				371	1.76		5433	0.57	
Acute lymphoblastic leukemia	4865	0.71	[b]	1726	1.78	[f]	1775	4.46	[f]
High-grade astrocytoma	241	−5.19		1428	1.92		13,814	5.05	[f]
Acute myeloid leukemia	921	3.83	[b]	2287	2.32	[f]	13,254	4.76	[b]
Lung carcinoma				2407	3.01	[f]	236,080	1.75	[b]
Myeloma[d]				483	3.89	[b]	24,499	3.28	[b]
Chronic myeloid leukemia				1257	4.75	[b]	6291	5.21	[b]
Non-Hodgkin lymphoma	1035	0.67		9543	4.92	[b]	75,154	2.53	[b]
Hepatic carcinoma				783	5.08	[e]	24,746	10.15	[b]
Kaposi sarcoma				5494	13.18	[b]	4479	10.66	[b]

Abbreviations: AIDS, acquired immunodeficiency syndrome; APC, annual percent change; AYAs, adolescents and young adults; PNET, infratentorial primitive neuroectodermal tumor; SEER 13, Surveillance, Epidemiology, and End Results data for 13 regions.

[a] Except Kaposi sarcoma and non-Hodgkin lymphoma in males.

[b] $P < 0.001$.

[c] Other than rhabdomyosarcoma, fibromatous sarcoma, and Kaposi sarcoma, each of which was listed separately.

[d] Cancer type was based on SEER site recode.

[e] $0.01 < P < 0.05$.

[f] $0.001 < P < 0.01$; others not significant.

children and older adults has been the focus of several national and international initiatives. Among AYAs in the current study, 14 cancers demonstrated evidence of a statistically significant improvement in 5-year relative survival since 1992. Despite this progress, survival improved less in AYAs than in children for AML and medulloblastoma/PNET and less in AYAs than in older adults for 14 cancers. We also observed a worse prognosis among AYAs than in younger or older patients for some cancers, suggesting that the biology of these cancers differs in AYAs compared with older or younger patients.

In the current study, it is encouraging to observe progress in the survival of AYAs with some cancers, particularly CML and AML and, to a lesser extent, NHL, breast cancer, and colorectal cancer (Fig. 1). The substantial improvements in survival after CML and AML are likely a result of major advances in therapy, including targeted therapy with tyrosine kinase inhibitors for patients with CML.[12-14] Similarly, improvements in NHL survival are likely related to the development of monoclonal antibody therapy as well as advances in the treatment of HIV-associated NHL that occurred primarily among males.[15,16] We also found survival improvements among

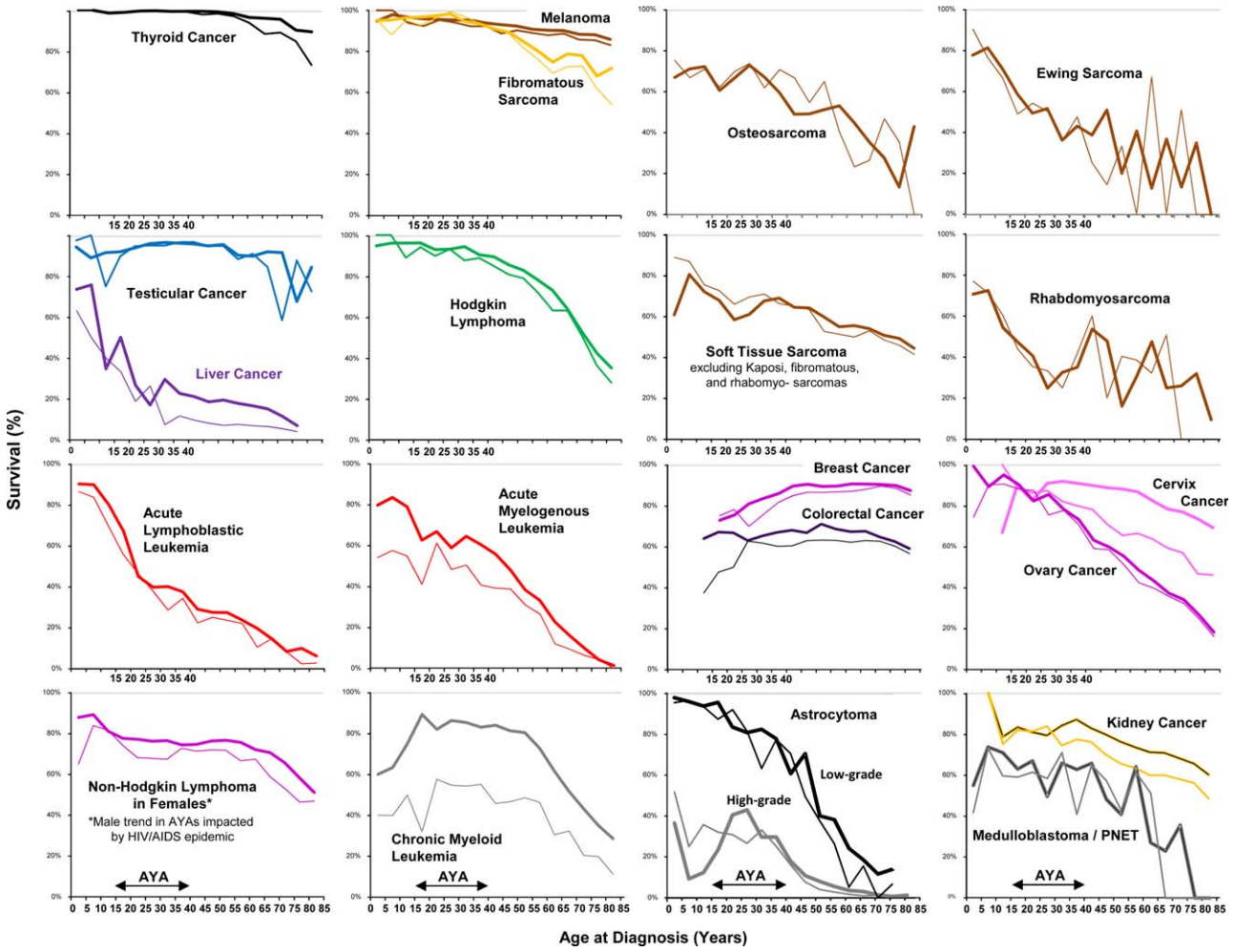

Figure 1. The 5-year relative survival rate of cancers diagnosed between 1992 and 1996 (thin curve) and 2002 and 2006 (thick curve) by 5-year intervals of age at diagnosis using the Surveillance, Epidemiology, and End Results 13 registry data. AIDS indicates acquired immunodeficiency syndrome; AYA, adolescents and young adults; HIV, human immunodeficiency virus; PNET, infratentorial primitive neuroectodermal tumor.

AYAs diagnosed with breast and colorectal cancer, which were reported previously to have worse outcomes in AYAs than older adults.[17,18] For colorectal cancer, survival in AYAs has caught up to survival in older adults, but survival for breast cancer in AYAs still lags behind that in older adults (Tables 1 and 3) (Fig. 1). The progress in colorectal cancer is due, at least in part, to the increased awareness of the worse survival observed in AYAs across all stages of disease,[17] and the delivery of better therapies to this age group.[18]

However, the majority of cancers have not demonstrated survival progress in AYAs comparable to that achieved in either younger or older patients. From the 1990s to the last decade, there was a lack of statistical evidence for progress in 20 of 34 (59%) cancer types in AYAs. Many of the cancers demonstrating survival improvement during the 1970s and 1980s, such as osteosarcoma, chondrosarcoma, and high-grade astrocytomas, have shown little to no evidence of survival progress since that time.[6] Survival also improved markedly less in AYAs compared with children for AML and medulloblastoma/PNET. In addition, survival improved less in AYAs than in older adults for hepatic carcinoma, AML, high-grade and low-grade astrocytoma, ALL, pancreatic carcinoma, gastric carcinoma, renal carcinoma, cancer of the oral cavity and pharynx, Hodgkin lymphoma, ovarian cancer, fibromatous sarcoma, other soft tissue sarcoma, and thyroid carcinoma. That fibromatous sarcomas and thyroid carcinoma have not experienced significant improvements in survival is likely due to the fact that their survival rates

were already too high to demonstrate such an incremental increase statistically.

Several factors are believed to have influenced the lack of survival improvement noted for AYAs. Historically, AYAs have been less likely to have health insurance than children and older adults,[19] and health insurance influences health outcomes. In particular, being uninsured is associated with the presentation of metastatic disease, being undertreated, and poorer survival.[20] Progress in outcomes also may have been constrained by the lower participation in and access to clinical trials,[21] and the poorer understanding of the unique biological characteristics of cancers in AYAs.[22]

AYAs have a lower survival than younger or older patients for several cancers. As of the most recent data, the 5-year relative survival rates for children with ALL (90%) and AML (66%) were significantly better than those of AYAs diagnosed with the same diseases (52% and 50%, respectively). In addition, the 5-year relative survival rate was >20% less for AYAs compared with children for RMS (43% in AYAs and 69% in children) and Ewing sarcoma (54% in AYAs and 77% in children). Compared with older adults, the 5-year relative survival after breast cancer was somewhat lower in AYAs (86% in AYAs and 91% in older adults). A worse prognosis in AYAs compared with older patients for breast cancer and in AYAs compared with younger patients for ALL, RMS, Ewing sarcoma, and AML suggests that the biology of some cancers differs in AYAs from what otherwise appears to be the same cancer in older or younger patients.

Molecular, epidemiologic, and therapeutic outcome comparisons offer clues to the distinctiveness in most of the common cancers of AYAs, including leukemias; lymphomas; sarcomas; melanoma; and carcinomas of the breast, colorectum, and nasopharynx.[14,17,18] Some cancer types may simply have worse survival with increasing patient age, as was suggested recently for papillary thyroid cancer.[23] A starting point for improvement in survival should be that the biology of cancers in AYAs and certainly of the host are different from that of other age groups, and these differences suggest a need to tailor treatment strategies. Laboratory and clinical investigations to compare biology by patient age are in their infancy and must become a research priority.

The current study is subject to some limitations. Because at least 5 years of follow-up are necessary to calculate relative survival trends, the current analyses were limited to patients diagnosed through 2006 and thus more recent changes in survival were not presented. In addition, due to small numbers of AYA patients with some cancer types/histologies, survival for all types of cancers that occur among AYAs are not presented. In addition, for those cancer sites presented, the substantially larger number of older adults than AYAs can result in APCs being statistically significant for older adults but not AYAs (ie, AYA survival trends have more variability). Therefore, the magnitude of the APCs, not just the statistical significance, should be considered when interpreting these findings.

Conversely, a major strength of the current study is the inclusion of a large number of patients from population-based cancer registries, comprising approximately 15% of the US population, who received their care across all types of institutions, thereby increasing the generalizability of the current study findings. Furthermore, with the expansion of the AYA age range from 15 to 29 years to 15 to 39 years and the shift in the distribution of types of cancer (ie, more carcinomas among individuals aged 30-39 years), to the best of our knowledge, these analyses are among the first to explore expanding the AYA recode site list for carcinomas.

The findings from the current study suggest that there have been improvements in the survival of several cancer types that occur frequently in AYAs, including melanoma, CML, AML, NHL, Hodgkin lymphoma, myeloma, Kaposi sarcoma, colorectal cancer, and breast cancer. However, survival is not improving to the same extent in AYAs as in children or older adults for several cancers. Further investment in exploring the distinct biology of tumors in AYAs, and of their hosts, must be a priority in AYA oncology.

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