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Article

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A Reappraisal of Sex-Specific Cancer Survival Trends Among Adolescents and Young Adults in the United States

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Abstract

Background: Cancer survival among adolescents and young adults (AYAs) was previously reported as showing little or no improvement compared to younger or older counterparts. The role of the HIV/AIDS epidemic in the AYA survival deficit has not been evaluated.
Methods: Using cancer registry data from the Surveillance, Epidemiology, and End Results program (SEER 9), we examined sex-specific 5-year relative survival trends for children (0–14 years old), AYAs (15–39 years old), and older adults (40 years and older) diagnosed with cancer during 1973–2009 and followed through the end of 2014. The analysis was conducted with and without Kaposi sarcoma (KS) and lymphomas, and by two time periods: 1973–1977 (before the human immunodeficiency virus/acquired immunodeficiency syndrome [HIV/AIDS] epidemic) and 2005–2009 (after the HIV/AIDS epidemic waned).
Results: A total of 3 209 721 invasive cancer cases were included in the study (27 646 children, 213 930 AYAs, and 2 968 145 older adults; 24 803 children, 178 741 AYAs, and 2 844 062 older adults when KS and lymphoma cases were excluded). We found that 5-year relative survival for AYAs exceeded that of children and older adults before the onset of the HIV/AIDS epidemic (eg, during 1973–1979, 0.58–0.67 among male AYAs as compared with 0.47–0.61 for male children and 0.36–0.42 for male older adults; among female AYAs, the numbers were 0.73–0.77 as compared with 0.51–0.65 for female children and 0.52–0.55 for female older adults); substantially declined during 1983–1997 when HIV/AIDS lacked effective treatment among male AYAs; and returned to be higher than most age groups by the late 1990s after HIV/AIDS was controlled. Nonetheless, comparison of survival improvement between 1973–1977 and 2005–2009 demonstrated less progress in AYAs than other age groups, which was due to AYAs' better baseline survival and larger survival gains among children and older adults in recent years.
Conclusions: Apart from the temporary impact of HIV/AIDS, survival among AYA cancer patients has shown sustained improvement and superiority relative to other age groups. However, these encouraging findings do not negate the distinctive challenges in cancer diagnosis, treatment, and survivorship faced by AYAs.

Cancer is the most common cause of death due to disease among adolescents and young adults (AYAs), defined by the US National Cancer Institute as 15–39 years old (1). Each year about 70 000 cancer cases are diagnosed among AYAs in the United States, approximately six times the incidence of cancer among children under age 15 (2). Furthermore, during a life stage characterized by dramatic physical and psychosocial development, AYA cancer patients experience a multitude of distinctive challenges, including differing cancer and host biology, delayed diagnosis, limited access to optimal treatment and age-appropriate services, excess treatment-related toxicity, and low levels of participation in clinical trials (3,4).

An earlier report based on data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program for the period of 1975–1997 showed AYA cancer patients had the least improvement in 5-year relative survival

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as compared to both younger and older age groups (5). During that period, survival even worsened for some older AYAs (5). Two subsequent reports using updated SEER data suggest a more complex scenario. For example, since the early 1970s, AYA survival continued to improve for leukemia, kidney cancer, and testicular cancer, but not for cervical cancer, head and neck cancer, or rhabdomyosarcoma (6,7). These reports also recognized the dramatic improvement in survival among AYA males with Kaposi sarcoma (KS) and non-Hodgkin lymphoma, two major cancer types closely associated with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), following the introduction of "highly active antiretroviral therapy" in 1996 (now referred to as "combination antiretroviral therapy" or cART) (8,9). However, the impact of the HIV/AIDS epidemic on overall cancer survival among AYAs has not been fully examined.

Therefore, we undertook this analysis of AYA cancer survival using the most recent SEER data release (10) and adjusting for the historical impact of HIV/AIDS. We hypothesized that previous reports of inferior AYA cancer survival improvement reflected the temporary impact of poor survival among HIV/AIDS-related cancers (ie, KS and lymphomas) before the availability of antiretroviral therapy. We further hypothesized that AYA cancer survival regained its pre-HIV/AIDS momentum once HIV/AIDS was more effectively controlled with cART.

Methods

Data Source and Inclusion Criteria

We used all invasive cancer data (including bladder in situ cases) from the nine SEER registries for 1973–2014 (10) to evaluate the survival of AYA cancer patients (15–39 years old) in comparison with children (0–14 years) and older adults (40 years and older). We grouped age at diagnosis into 5-year age intervals (0–4, 5–9, 10–14, . . ., 55–59, ≥60), as well as broadly aggregated age groups of interest (0–14, 15–39, and ≥40). Histology codes from the *International Classification of Disease for Oncology, 3rd Edition* were used to identify HIV/AIDS-associated cancers: KS (9140) and lymphomas [9590–9729, 9823, 9827, and 9837; including non-Hodgkin and Hodgkin, as both could be related to HIV/AIDS (11,12)].

Survival Analysis

We used SEER*Stat software Version 8.3.4 (10) to calculate 5-year relative survival among those diagnosed with cancer during 1973–2009 in this dataset; thus every patient would have had full 5-year or longer survival time by the end of 2014. Relative survival is defined as the ratio of the observed probability of survival of cancer patients to the expected probability of survival in a comparable set of cancer-free individuals matched by age, race, sex, and year (13). It is a net survival measure representing cancer survival in the absence of other competing causes of death by taking into account the mortality experience in the general population. Two sets of 5-year relative survival were calculated by sex, age, and year of diagnosis for all cancers combined: including and excluding KS and lymphomas, to assess the impact of HIV/AIDS on cancer survival in different population groups.

To evaluate cancer survival improvement over time, we compared the 5-year relative survival by sex and age between the beginning and ending years of the 1973–2009 diagnostic period, as well as between the average 5-year relative survival for the periods of 1973–1977 (before the onset of the HIV/AIDs epidemic in early 1980s) and 2005–2009 (after the HIV/AIDS epidemic was controlled by cART implementation in 1996) to have more statistical stability in the evaluation that is free from the impact of the HIV/AIDS epidemic. The survival improvement was measured by the ratio of the survival probability in the ending year or period divided by the corresponding one from the beginning year or period.

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Table 1. Total case counts and 5-year relative survival in males by 5-year age group and diagnostic year, all invasive cancers including and excluding Kaposi sarcoma (KS) and lymphomas, SEER 9 registries

	5-year relative survival by age group												
Diagnostic year	0–4 y	5–9 y	10–14 y	15–19 y	20–24 y	25–29 y	30–34 y	35–39 y	40–44 y	45–59 y	50–54 y	55–59 y	≥60 y
Including KS and lymphomas, N	6941	3870	4196	7009	11 099	17 107	23 838	31 786	44 636	70 982	117 515	172 337	1 151 099
1973	0.47	0.58	0.54	0.55	0.62	0.69	0.58	0.48	0.45	0.39	0.38	0.36	0.35
1974	0.50	0.41	0.47	0.46	0.62	0.71	0.65	0.56	0.49	0.41	0.39	0.37	0.38
1975	0.53	0.52	0.48	0.56	0.67	0.67	0.67	0.59	0.50	0.43	0.40	0.40	0.39
1976	0.52	0.59	0.54	0.62	0.64	0.68	0.67	0.57	0.52	0.45	0.41	0.41	0.40
1977	0.56	0.52	0.60	0.60	0.65	0.71	0.67	0.61	0.52	0.42	0.40	0.41	0.41
1978	0.66	0.60	0.56	0.59	0.65	0.73	0.67	0.58	0.50	0.42	0.40	0.41	0.41
1979	0.59	0.63	0.57	0.61	0.69	0.73	0.68	0.60	0.51	0.42	0.41	0.41	0.41
1980	0.63	0.67	0.58	0.71	0.75	0.69	0.71	0.60	0.48	0.45	0.42	0.42	0.41
1981	0.64	0.57	0.59	0.61	0.77	0.74	0.72	0.60	0.53	0.47	0.42	0.44	0.43
1982	0.67	0.64	0.60	0.69	0.72	0.75	0.69	0.61	0.56	0.45	0.44	0.42	0.42
1983	0.61	0.68	0.72	0.73	0.69	0.73	0.66	0.60	0.54	0.45	0.46	0.42	0.44
1984	0.64	0.70	0.65	0.63	0.72	0.65	0.58	0.56	0.52	0.46	0.44	0.43	0.44
1985	0.70	0.66	0.59	0.68	0.71	0.67	0.59	0.57	0.48	0.49	0.46	0.43	0.46
1986	0.67	0.72	0.60	0.75	0.74	0.66	0.59	0.51	0.52	0.47	0.46	0.45	0.48
1987	0.77	0.68	0.59	0.71	0.74	0.63	0.56	0.52	0.50	0.50	0.49	0.48	0.50
1988	0.70	0.68	0.62	0.74	0.72	0.62	0.53	0.47	0.49	0.46	0.46	0.48	0.51
1989	0.75	0.71	0.74	0.71	0.70	0.63	0.54	0.48	0.51	0.47	0.45	0.47	0.53
1990	0.76	0.84	0.76	0.73	0.77	0.64	0.52	0.50	0.51	0.49	0.51	0.50	0.56

(continued)

Table 1. (continued)

	5-year relative survival by age group												
Diagnostic year	0–4 y	5–9 y	10–14 y	15–19 y	20–24 y	25–29 y	30–34 y	35–39 y	40–44 y	45–59 y	50–54 y	55–59 y	≥60 y
1991	0.73	0.75	0.74	0.79	0.74	0.59	0.52	0.49	0.51	0.50	0.51	0.54	0.61
1992	0.77	0.78	0.81	0.72	0.76	0.61	0.53	0.51	0.51	0.51	0.56	0.59	0.65
1993	0.73	0.74	0.74	0.72	0.79	0.63	0.56	0.53	0.52	0.55	0.58	0.61	0.63
1994	0.81	0.81	0.73	0.73	0.75	0.70	0.55	0.59	0.54	0.56	0.60	0.60	0.61
1995	0.75	0.80	0.77	0.75	0.75	0.72	0.63	0.57	0.59	0.58	0.59	0.62	0.61
1996	0.83	0.79	0.76	0.81	0.74	0.77	0.70	0.66	0.61	0.62	0.63	0.63	0.61
1997	0.78	0.84	0.75	0.76	0.82	0.78	0.73	0.70	0.60	0.62	0.64	0.63	0.62
1998	0.78	0.79	0.80	0.75	0.78	0.84	0.75	0.73	0.65	0.63	0.65	0.66	0.62
1999	0.80	0.76	0.75	0.73	0.83	0.80	0.77	0.71	0.66	0.61	0.65	0.68	0.64
2000	0.81	0.80	0.78	0.72	0.83	0.82	0.78	0.72	0.67	0.64	0.67	0.70	0.65
2001	0.84	0.80	0.76	0.79	0.82	0.79	0.79	0.71	0.71	0.66	0.68	0.70	0.66
2002	0.84	0.74	0.77	0.76	0.80	0.81	0.81	0.77	0.70	0.66	0.70	0.71	0.66
2003	0.80	0.81	0.86	0.83	0.81	0.82	0.80	0.74	0.72	0.67	0.68	0.70	0.65
2004	0.84	0.80	0.83	0.79	0.84	0.83	0.80	0.76	0.73	0.67	0.69	0.71	0.66
2005	0.83	0.83	0.78	0.85	0.84	0.82	0.83	0.79	0.74	0.68	0.69	0.70	0.66
2006	0.83	0.87	0.84	0.81	0.83	0.82	0.80	0.76	0.75	0.70	0.70	0.73	0.68
2007	0.83	0.87	0.82	0.81	0.81	0.83	0.83	0.80	0.74	0.70	0.71	0.73	0.68
2008	0.86	0.84	0.81	0.82	0.85	0.84	0.84	0.80	0.74	0.73	0.71	0.72	0.67
2009	0.82	0.77	0.86	0.84	0.84	0.84	0.81	0.77	0.76	0.72	0.72	0.72	0.67
Survival ratio 2009 : 1973	1.74	1.33	1.59	1.53	1.35	1.22	1.40	1.60	1.69	1.85	1.89	2.00	1.91
Excluding KS and lymphomas, N	6679	3258	3229	5200	8285	12 486	16 982	23 910	37 229	64 016	110 274	164 757	1 112 041
1973	0.46	0.57	0.44	0.44	0.56	0.70	0.57	0.47	0.45	0.38	0.37	0.36	0.35
1974	0.48	0.41	0.44	0.42	0.59	0.69	0.63	0.53	0.48	0.40	0.39	0.36	0.38
1975	0.55	0.53	0.43	0.50	0.61	0.67	0.64	0.57	0.48	0.41	0.39	0.39	0.39
1976	0.53	0.57	0.52	0.54	0.62	0.66	0.65	0.55	0.52	0.44	0.40	0.40	0.40
1977	0.57	0.52	0.60	0.56	0.64	0.72	0.67	0.59	0.51	0.41	0.39	0.41	0.41
1978	0.68	0.62	0.52	0.53	0.63	0.72	0.65	0.57	0.48	0.41	0.39	0.40	0.41
1979	0.60	0.57	0.50	0.55	0.68	0.72	0.65	0.59	0.50	0.41	0.41	0.41	0.41
1980	0.63	0.62	0.52	0.69	0.71	0.67	0.71	0.58	0.48	0.44	0.41	0.41	0.42
1981	0.64	0.57	0.53	0.59	0.74	0.73	0.72	0.60	0.52	0.46	0.41	0.43	0.43
1982	0.68	0.63	0.58	0.63	0.73	0.75	0.70	0.61	0.55	0.44	0.43	0.41	0.42
1983	0.60	0.60	0.69	0.71	0.68	0.75	0.70	0.63	0.54	0.45	0.45	0.42	0.44
1984	0.64	0.64	0.59	0.57	0.72	0.70	0.67	0.58	0.53	0.46	0.43	0.42	0.44
1985	0.71	0.61	0.56	0.66	0.73	0.79	0.71	0.67	0.49	0.49	0.45	0.43	0.46
1986	0.66	0.72	0.52	0.72	0.77	0.81	0.76	0.64	0.57	0.47	0.45	0.44	0.48
1987	0.77	0.65	0.54	0.64	0.78	0.78	0.76	0.66	0.56	0.52	0.48	0.47	0.50
1988	0.70	0.68	0.55	0.72	0.73	0.80	0.74	0.64	0.56	0.46	0.45	0.48	0.52
1989	0.75	0.69	0.74	0.69	0.73	0.82	0.77	0.66	0.59	0.49	0.45	0.47	0.53
1990	0.75	0.83	0.71	0.67	0.81	0.81	0.75	0.67	0.59	0.52	0.51	0.50	0.56
1991	0.72	0.74	0.71	0.77	0.79	0.77	0.75	0.66	0.59	0.53	0.52	0.55	0.62
1992	0.76	0.77	0.81	0.70	0.76	0.79	0.75	0.67	0.59	0.53	0.56	0.60	0.65
1993	0.73	0.72	0.71	0.69	0.83	0.82	0.77	0.69	0.59	0.57	0.58	0.61	0.63
1994	0.81	0.80	0.71	0.69	0.77	0.85	0.73	0.71	0.61	0.59	0.59	0.60	0.61
1995	0.75	0.77	0.75	0.71	0.76	0.83	0.78	0.68	0.63	0.59	0.59	0.62	0.61
1996	0.83	0.78	0.72	0.77	0.78	0.83	0.79	0.72	0.63	0.62	0.63	0.63	0.62
1997	0.77	0.83	0.72	0.73	0.79	0.77	0.77	0.70	0.60	0.62	0.64	0.63	0.63
1998	0.78	0.78	0.77	0.73	0.79	0.85	0.77	0.75	0.65	0.62	0.65	0.66	0.62
1999	0.80	0.73	0.70	0.68	0.83	0.80	0.81	0.72	0.66	0.60	0.65	0.68	0.65
2000	0.81	0.78	0.71	0.72	0.82	0.82	0.79	0.74	0.66	0.64	0.67	0.69	0.65
2001	0.84	0.79	0.72	0.77	0.81	0.82	0.80	0.72	0.71	0.65	0.68	0.71	0.66
2002	0.83	0.71	0.75	0.71	0.79	0.80	0.81	0.78	0.69	0.65	0.69	0.71	0.66
2003	0.80	0.79	0.84	0.79	0.79	0.83	0.80	0.75	0.71	0.66	0.68	0.70	0.65
2004	0.84	0.78	0.83	0.79	0.82	0.82	0.80	0.77	0.73	0.67	0.69	0.71	0.66
2005	0.83	0.81	0.77	0.82	0.81	0.84	0.83	0.79	0.72	0.67	0.69	0.70	0.66
2006	0.82	0.86	0.80	0.80	0.82	0.83	0.79	0.76	0.74	0.69	0.69	0.73	0.68
2007	0.82	0.86	0.79	0.78	0.80	0.81	0.83	0.79	0.74	0.69	0.70	0.73	0.69
2008	0.87	0.85	0.77	0.80	0.83	0.83	0.84	0.79	0.74	0.72	0.70	0.72	0.67
2009	0.82	0.74	0.85	0.82	0.84	0.84	0.82	0.77	0.76	0.71	0.72	0.71	0.68
Survival ratio 2009 : 1973	1.78	1.30	1.93	1.86	1.50	1.20	1.44	1.64	1.69	1.87	1.95	1.97	1.94

Table 2. Total case counts and 5-year relative survival in females by 5-year age group and diagnostic year, all invasive cancers including and excluding Kaposi sarcoma (KS) and lymphomas, SEER 9 registries

	5-year relative survival by age group												
Diagnostic year	0–4 y	5–9 y	10–14 y	15–19 y	20–24 y	25–29 y	30–34 y	35–39 y	40–44 y	45–59 y	50–54 y	55–59 y	≥60 y
Including KS and lymphomas, N	5929	3017	3693	6324	11 436	20 606	33 246	51 479	77 774	107 866	133 119	154 820	937 997
1973	0.44	0.47	0.61	0.71	0.76	0.77	0.75	0.70	0.64	0.65	0.62	0.58	0.45
1974	0.65	0.55	0.64	0.70	0.78	0.77	0.72	0.73	0.66	0.67	0.63	0.59	0.48
1975	0.60	0.64	0.60	0.72	0.76	0.79	0.73	0.71	0.70	0.66	0.64	0.60	0.49
1976	0.64	0.62	0.59	0.77	0.77	0.79	0.77	0.72	0.69	0.67	0.64	0.60	0.48
1977	0.59	0.63	0.69	0.79	0.81	0.80	0.77	0.73	0.71	0.65	0.63	0.59	0.48
1978	0.67	0.58	0.71	0.76	0.81	0.82	0.80	0.70	0.70	0.65	0.64	0.57	0.49
1979	0.69	0.63	0.57	0.79	0.77	0.78	0.77	0.70	0.70	0.65	0.62	0.56	0.48
1980	0.59	0.66	0.66	0.76	0.86	0.83	0.74	0.73	0.71	0.65	0.60	0.58	0.48
1981	0.69	0.75	0.63	0.75	0.79	0.82	0.76	0.73	0.71	0.68	0.60	0.59	0.48
1982	0.72	0.75	0.72	0.73	0.80	0.82	0.76	0.75	0.70	0.68	0.61	0.58	0.48
1983	0.71	0.69	0.72	0.76	0.81	0.81	0.75	0.75	0.70	0.68	0.63	0.58	0.49
1984	0.68	0.67	0.61	0.79	0.83	0.81	0.77	0.75	0.71	0.69	0.63	0.59	0.50
1985	0.72	0.75	0.74	0.85	0.87	0.83	0.76	0.72	0.74	0.68	0.66	0.60	0.51
1986	0.72	0.72	0.71	0.84	0.88	0.83	0.79	0.77	0.71	0.70	0.67	0.60	0.52
1987	0.73	0.72	0.69	0.86	0.83	0.80	0.80	0.77	0.75	0.71	0.65	0.61	0.53
1988	0.74	0.78	0.87	0.83	0.86	0.81	0.80	0.77	0.76	0.72	0.67	0.62	0.54
1989	0.66	0.72	0.76	0.80	0.87	0.84	0.78	0.76	0.76	0.72	0.68	0.63	0.53
1990	0.73	0.62	0.68	0.81	0.87	0.83	0.82	0.75	0.77	0.74	0.67	0.62	0.54
1991	0.78	0.75	0.78	0.81	0.85	0.83	0.79	0.79	0.77	0.75	0.69	0.63	0.54
1992	0.80	0.68	0.79	0.79	0.83	0.82	0.81	0.80	0.78	0.74	0.69	0.65	0.54
1993	0.80	0.80	0.80	0.82	0.85	0.84	0.81	0.81	0.78	0.74	0.70	0.65	0.54
1994	0.74	0.86	0.79	0.83	0.85	0.82	0.82	0.79	0.78	0.75	0.71	0.66	0.54
1995	0.74	0.85	0.81	0.86	0.85	0.83	0.80	0.80	0.79	0.77	0.73	0.69	0.54
1996	0.80	0.78	0.84	0.89	0.89	0.87	0.82	0.81	0.80	0.77	0.72	0.68	0.55
1997	0.79	0.75	0.85	0.80	0.88	0.87	0.81	0.82	0.79	0.78	0.75	0.69	0.55
1998	0.78	0.73	0.79	0.86	0.84	0.85	0.82	0.81	0.81	0.77	0.75	0.71	0.56
1999	0.82	0.81	0.83	0.88	0.86	0.86	0.86	0.82	0.81	0.79	0.76	0.71	0.56
2000	0.80	0.82	0.83	0.80	0.85	0.87	0.84	0.83	0.81	0.81	0.76	0.72	0.57
2001	0.80	0.89	0.84	0.84	0.90	0.87	0.84	0.83	0.81	0.78	0.77	0.72	0.58
2002	0.84	0.85	0.81	0.87	0.83	0.87	0.87	0.84	0.82	0.80	0.76	0.73	0.58
2003	0.87	0.83	0.89	0.86	0.88	0.90	0.86	0.86	0.83	0.80	0.75	0.73	0.57
2004	0.85	0.77	0.85	0.83	0.90	0.89	0.86	0.86	0.83	0.79	0.77	0.73	0.57
2005	0.81	0.81	0.86	0.88	0.85	0.87	0.85	0.86	0.84	0.81	0.77	0.74	0.58
2006	0.90	0.86	0.86	0.86	0.89	0.89	0.88	0.86	0.84	0.82	0.78	0.75	0.58
2007	0.85	0.79	0.84	0.86	0.89	0.88	0.90	0.86	0.85	0.82	0.78	0.74	0.59
2008	0.82	0.74	0.91	0.89	0.91	0.91	0.88	0.88	0.85	0.82	0.79	0.74	0.59
2009	0.83	0.82	0.85	0.91	0.91	0.88	0.88	0.85	0.85	0.82	0.78	0.75	0.60
Survival ratio 2009 : 1973	1.89	1.74	1.39	1.28	1.20	1.14	1.17	1.21	1.33	1.26	1.26	1.29	1.33
Excluding KS and lymphomas, N	5792	2786	3059	4764	9209	18 088	30 816	49 001	74 886	104 336	128 671	149 470	898 382
1973	0.44	0.47	0.57	0.67	0.76	0.77	0.75	0.70	0.64	0.65	0.62	0.58	0.46
1974	0.63	0.55	0.63	0.65	0.80	0.77	0.72	0.73	0.66	0.67	0.63	0.60	0.49
1975	0.60	0.66	0.58	0.69	0.76	0.79	0.72	0.71	0.70	0.66	0.64	0.61	0.49
1976	0.65	0.60	0.57	0.73	0.78	0.79	0.78	0.72	0.69	0.67	0.64	0.60	0.49
1977	0.59	0.62	0.66	0.75	0.80	0.79	0.77	0.73	0.71	0.64	0.63	0.59	0.48
1978	0.67	0.58	0.67	0.72	0.80	0.82	0.80	0.70	0.70	0.65	0.64	0.57	0.49
1979	0.70	0.63	0.56	0.75	0.77	0.78	0.78	0.69	0.70	0.64	0.62	0.56	0.48
1980	0.59	0.67	0.64	0.75	0.87	0.84	0.73	0.72	0.71	0.65	0.60	0.58	0.48
1981	0.69	0.73	0.59	0.72	0.79	0.82	0.76	0.73	0.71	0.68	0.60	0.59	0.48
1982	0.73	0.76	0.70	0.70	0.81	0.82	0.76	0.75	0.69	0.69	0.61	0.58	0.48
1983	0.72	0.70	0.70	0.75	0.80	0.81	0.74	0.75	0.70	0.68	0.63	0.58	0.49
1984	0.69	0.65	0.61	0.75	0.81	0.80	0.77	0.74	0.71	0.68	0.63	0.59	0.51
1985	0.72	0.77	0.71	0.86	0.85	0.83	0.76	0.72	0.75	0.68	0.66	0.60	0.52
1986	0.71	0.73	0.67	0.81	0.88	0.82	0.80	0.77	0.71	0.70	0.67	0.60	0.53
1987	0.72	0.72	0.67	0.86	0.81	0.81	0.80	0.77	0.75	0.71	0.65	0.61	0.53
1988	0.75	0.76	0.88	0.83	0.84	0.81	0.81	0.77	0.76	0.72	0.67	0.62	0.54
1989	0.65	0.71	0.70	0.78	0.86	0.84	0.78	0.77	0.76	0.72	0.68	0.62	0.53
1990	0.74	0.61	0.65	0.81	0.86	0.82	0.81	0.75	0.77	0.74	0.67	0.62	0.55
1991	0.79	0.75	0.76	0.79	0.85	0.83	0.80	0.79	0.77	0.75	0.69	0.63	0.54
1992	0.80	0.67	0.78	0.77	0.83	0.82	0.81	0.80	0.78	0.74	0.69	0.65	0.54
1993	0.80	0.78	0.77	0.81	0.84	0.84	0.81	0.81	0.78	0.74	0.70	0.65	0.54
1994	0.74	0.85	0.77	0.79	0.84	0.81	0.82	0.79	0.78	0.76	0.71	0.66	0.55
1995	0.75	0.84	0.81	0.85	0.86	0.83	0.81	0.79	0.79	0.77	0.73	0.69	0.54
1996	0.81	0.78	0.81	0.87	0.89	0.86	0.83	0.81	0.80	0.77	0.72	0.68	0.55

(continued)

Table 2. (continued)

Diagnostic year	5-year relative survival by age group												
	0–4 y	5–9 y	10–14 y	15–19 y	20–24 y	25–29 y	30–34 y	35–39 y	40–44 y	45–59 y	50–54 y	55–59 y	≥60 y
1997	0.79	0.74	0.82	0.77	0.87	0.87	0.82	0.82	0.79	0.77	0.75	0.69	0.55
1998	0.78	0.73	0.78	0.82	0.82	0.86	0.83	0.81	0.81	0.77	0.75	0.71	0.56
1999	0.83	0.81	0.81	0.85	0.87	0.86	0.86	0.82	0.81	0.79	0.76	0.71	0.56
2000	0.80	0.80	0.80	0.77	0.83	0.88	0.84	0.82	0.81	0.81	0.76	0.72	0.57
2001	0.80	0.87	0.84	0.83	0.90	0.87	0.84	0.83	0.81	0.78	0.77	0.72	0.57
2002	0.84	0.83	0.81	0.86	0.83	0.88	0.86	0.84	0.82	0.79	0.76	0.72	0.57
2003	0.86	0.83	0.87	0.85	0.87	0.89	0.86	0.85	0.83	0.80	0.75	0.72	0.56
2004	0.85	0.78	0.85	0.78	0.89	0.90	0.86	0.85	0.83	0.79	0.76	0.72	0.57
2005	0.81	0.81	0.85	0.88	0.84	0.86	0.84	0.86	0.83	0.81	0.77	0.74	0.57
2006	0.90	0.84	0.85	0.86	0.89	0.88	0.87	0.85	0.84	0.82	0.78	0.74	0.57
2007	0.84	0.78	0.83	0.83	0.87	0.87	0.89	0.86	0.84	0.82	0.78	0.74	0.58
2008	0.82	0.73	0.90	0.86	0.91	0.91	0.88	0.87	0.86	0.82	0.78	0.74	0.59
2009	0.83	0.82	0.82	0.91	0.90	0.87	0.88	0.85	0.85	0.81	0.78	0.74	0.60
Survival ratio 2009 : 1973	1.89	1.74	1.44	1.36	1.18	1.13	1.17	1.21	1.33	1.25	1.26	1.28	1.30

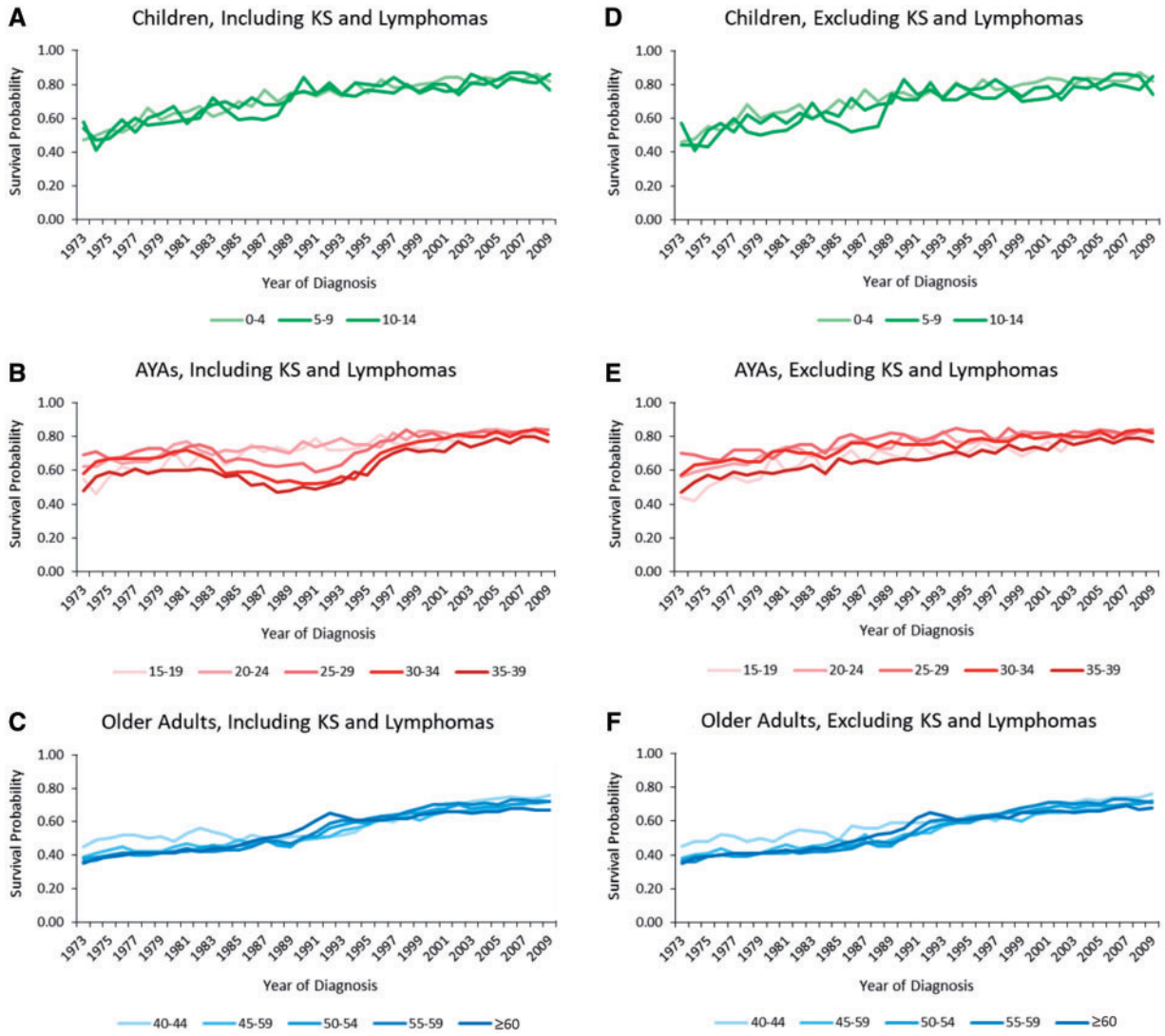

Figure 1. Time trends of 5-year relative survival in males by 5-year age group. Data were from the SEER 9 registries, 1973–2009. Survival probability of all invasive cancers including Kaposi sarcoma (KS) and lymphomas are shown in (**A**) children age 0–14 years, (**B**) adolescents and young adults (AYAs) age 15–39 years, and (**C**) older adults age 40 to ≥60 years, respectively. Survival probability of all invasive cancers excluding KS and lymphomas are shown in (**D**) children age 0–14 years, (**E**) AYAs age 15–39 years, and (**F**) older adults age 40 to ≥60 years, respectively.

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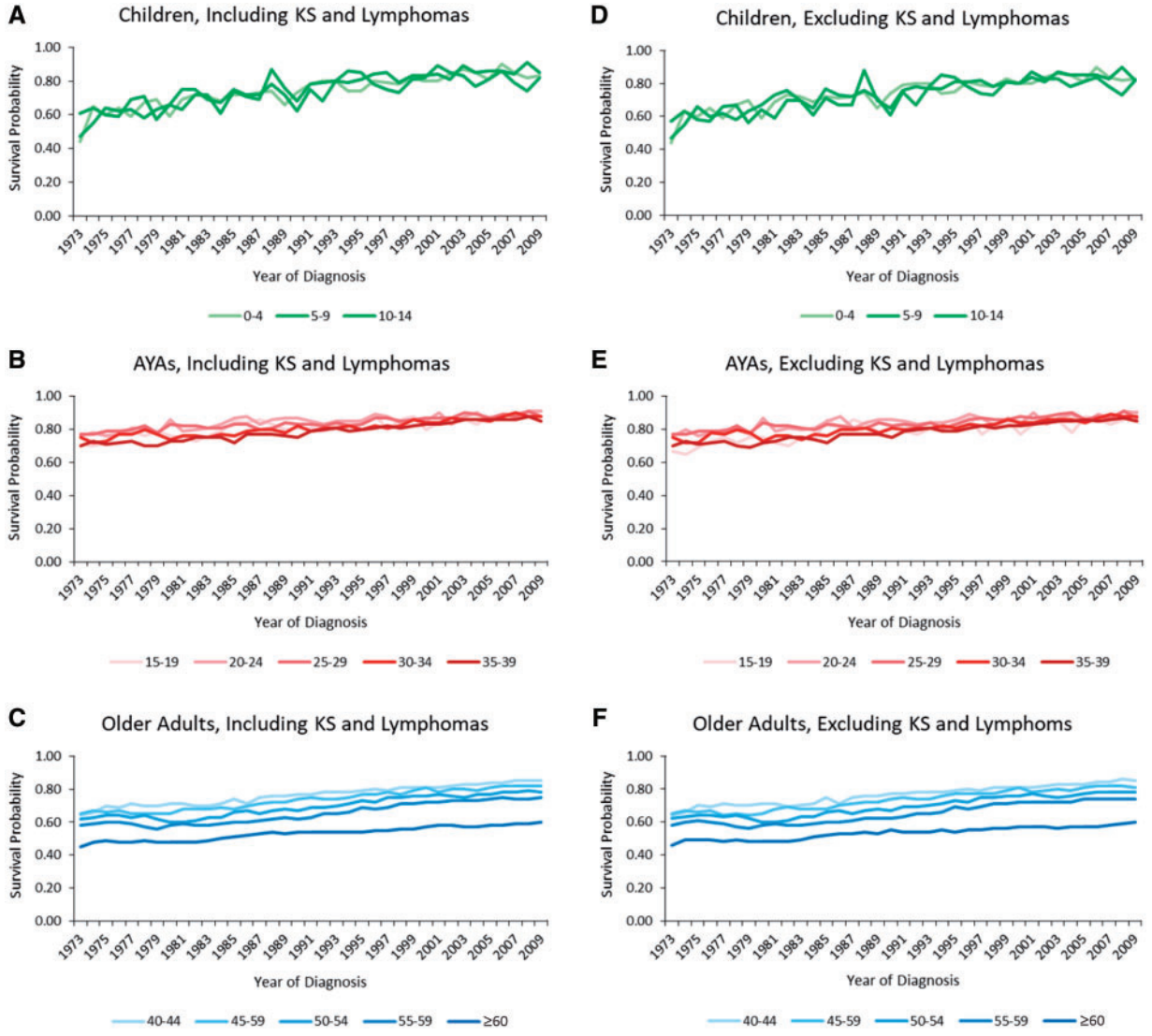

Figure 2. Time trends of 5-year relative survival for females by 5-year age group. Data were from the SEER 9 registries, 1973–2009. Survival probability of all invasive cancers including Kaposi sarcoma (KS) and lymphomas are shown in (**A**) children age 0–14 years, (**B**) adolescents and young adults (AYAs) age 15–39 years, and (**C**) older adults age 40 to ≥60 years, respectively. Survival probability of all invasive cancers excluding KS and lymphomas are shown in (**D**) children age 0–14 years, (**E**) AYAs age 15–39 years, and (**F**) older adults age 40 to ≥60 years, respectively.

Results

A total of 3 209 721 invasive cancer cases were included in the study, with 27 646 children, 213 930 AYAs, and 2 968 145 older adults. Exclusion of KS and lymphoma resulted in case count reduction 24 803 in children, 178 741 in AYAs, and 2 844 062 in older adults.

AYAs displayed better overall cancer survival than children or older adults in the 1970s, based on both the 5-year age grouping (Tables 1 and 2 and Figures 1 and 2) and the three broad age groups (Table 3 and Figure 3). For example, during 1973–1979, the overall 5-year relative survival among male AYAs ranged from 0.58 to 0.67 as compared to 0.47–0.61 for male children and 0.36–0.42 for male older adults; among female AYAs the numbers were 0.73–0.77 as compared with 0.51–0.65 for female children and 0.52–0.55 for female older adults (Table 3). The 5-year relative survival for all cancers combined including KS and lymphomas has been improving since the early 1970s across all female age groups (Table 2 and Figure 2, A–C; Table 3 and Figure 3, B) and for male children and older males (Table 1 and Figure 1, A and C; Table 3 and Figure 3, A). For male AYAs there was a deficit in 5-year relative survival among those 25–39 years old (Table 1 and Figure 1, B; Table 3 and Figure 3, A) during 1983–1997, a period that corresponds to the initial uncontrolled HIV/AIDS epidemic, prior to the availability of effective cART. After excluding KS and lymphomas, this male AYA survival deficit disappeared (Table 1 and Figure 1, E; Table 3 and Figure 3, C), which demonstrates the negative impact of uncontrolled HIV/AIDS on the overall cancer survival among male AYAs during this time period. Inclusion or exclusion of KS and lymphomas did not result in noticeable changes in the survival probability for males of either younger or older age groups (Figure 1, A, D, C, F; Figure 3, A and C), or for females of any age group (Figures 2, A–F; Figure 3, B and D). Apart from the dip in survival probabilities

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Table 3. Five-year relative survival by sex, broad age group, and diagnostic year, all invasive cancers including and excluding Kaposi sarcoma (KS) and lymphomas, SEER 9 registries

Diagnostic Year	Including KS and lymphomas						Excluding KS and lymphomas					
	Males			Females			Males			Females		
	0–14 y	15–39 y	≥40 y	0–14 y	15–39 y	≥40 y	0–14 y	15–39 y	≥40 y	0–14 y	15–39 y	≥40 y
1973	0.52	0.58	0.36	0.51	0.73	0.52	0.48	0.55	0.36	0.49	0.73	0.52
1974	0.47	0.61	0.38	0.62	0.74	0.54	0.45	0.59	0.38	0.61	0.74	0.54
1975	0.52	0.64	0.39	0.61	0.74	0.55	0.51	0.61	0.39	0.61	0.73	0.55
1976	0.55	0.63	0.41	0.62	0.76	0.54	0.54	0.61	0.40	0.61	0.76	0.55
1977	0.56	0.65	0.41	0.64	0.77	0.53	0.56	0.64	0.41	0.62	0.76	0.53
1978	0.61	0.64	0.41	0.65	0.77	0.54	0.62	0.63	0.41	0.65	0.76	0.54
1979	0.60	0.67	0.42	0.64	0.75	0.52	0.56	0.64	0.42	0.65	0.74	0.53
1980	0.62	0.68	0.42	0.63	0.77	0.52	0.60	0.66	0.42	0.62	0.76	0.53
1981	0.61	0.69	0.43	0.69	0.76	0.53	0.60	0.68	0.43	0.68	0.76	0.53
1982	0.64	0.68	0.43	0.73	0.77	0.53	0.64	0.68	0.43	0.73	0.77	0.53
1983	0.66	0.67	0.45	0.71	0.77	0.53	0.62	0.68	0.44	0.71	0.76	0.53
1984	0.66	0.61	0.44	0.66	0.77	0.54	0.63	0.65	0.44	0.66	0.77	0.55
1985	0.66	0.62	0.46	0.73	0.77	0.56	0.65	0.71	0.46	0.73	0.76	0.56
1986	0.67	0.60	0.47	0.72	0.80	0.56	0.66	0.72	0.47	0.71	0.80	0.57
1987	0.70	0.58	0.50	0.71	0.80	0.57	0.69	0.72	0.50	0.71	0.79	0.57
1988	0.68	0.56	0.50	0.79	0.80	0.58	0.67	0.71	0.51	0.78	0.79	0.58
1989	0.73	0.56	0.52	0.69	0.79	0.58	0.73	0.73	0.52	0.68	0.79	0.58
1990	0.78	0.57	0.55	0.69	0.79	0.59	0.76	0.73	0.55	0.68	0.79	0.59
1991	0.74	0.56	0.59	0.78	0.80	0.59	0.72	0.73	0.60	0.77	0.80	0.59
1992	0.78	0.57	0.63	0.77	0.81	0.59	0.78	0.72	0.64	0.76	0.81	0.59
1993	0.73	0.59	0.61	0.80	0.82	0.59	0.72	0.75	0.62	0.79	0.82	0.59
1994	0.79	0.62	0.60	0.78	0.81	0.60	0.78	0.75	0.61	0.77	0.81	0.60
1995	0.77	0.64	0.60	0.79	0.81	0.61	0.76	0.74	0.61	0.79	0.81	0.61
1996	0.80	0.71	0.62	0.81	0.83	0.61	0.79	0.77	0.62	0.80	0.83	0.61
1997	0.79	0.74	0.62	0.80	0.83	0.62	0.77	0.75	0.63	0.78	0.83	0.62
1998	0.79	0.76	0.63	0.77	0.83	0.63	0.78	0.78	0.63	0.77	0.82	0.63
1999	0.77	0.76	0.65	0.82	0.85	0.63	0.75	0.77	0.65	0.82	0.84	0.63
2000	0.80	0.76	0.66	0.81	0.84	0.64	0.78	0.77	0.66	0.80	0.83	0.64
2001	0.80	0.76	0.67	0.84	0.84	0.64	0.79	0.77	0.67	0.83	0.84	0.64
2002	0.80	0.79	0.67	0.83	0.85	0.65	0.79	0.79	0.67	0.83	0.85	0.65
2003	0.82	0.79	0.66	0.86	0.87	0.64	0.80	0.79	0.66	0.86	0.86	0.64
2004	0.83	0.80	0.67	0.84	0.87	0.65	0.82	0.79	0.67	0.84	0.86	0.64
2005	0.82	0.82	0.67	0.82	0.86	0.66	0.81	0.82	0.67	0.82	0.85	0.65
2006	0.84	0.80	0.69	0.88	0.87	0.66	0.82	0.79	0.69	0.87	0.87	0.66
2007	0.84	0.81	0.70	0.83	0.88	0.66	0.83	0.80	0.69	0.82	0.87	0.66
2008	0.84	0.82	0.69	0.83	0.89	0.67	0.84	0.82	0.69	0.81	0.88	0.66
2009	0.82	0.81	0.69	0.83	0.87	0.67	0.81	0.81	0.69	0.82	0.87	0.67
Survival ratio 2009 : 1973	1.58	1.41	1.91	1.63	1.19	1.30	1.68	1.47	1.91	1.68	1.19	1.29

between 1983 and 1997 among AYA males due to the onset of the HIV/AIDS epidemic, AYAs of both sexes experienced improved 5-year relative survival throughout 1973–2009. Female AYAs showed consistently higher survival than either male AYAs or females of other age groups (Tables 1–3 and Figures 1–3).

Survival improved from 1973–1977 to 2005–2009 for every age group in both sexes (Table 4 and Figure 4, A, B). Although age-specific 5-year relative survival improved by 21%–49% for male AYAs and 13%–20% for female AYAs, their magnitudes of improvement are smaller than those for children (57%–61% for males and 35%–43% for females) and older adults (50%–85% for males and 23%–25% for females) (Table 4). As a result, although AYAs with cancer consistently maintained the highest survival in both time periods, their survival superiority during 1973–1977 diminished substantially by 2005–2009, as survival improvement in both children and older adults outpaced that of AYAs (Figure 4, A, B).

Discussion

We evaluated 5-year relative survival by sex and age over time among patients diagnosed with invasive cancer during 1973–2009 from the SEER 9 registries, a population-based source representing the experience throughout the United States. These data covered the time periods before, during, and following the HIV/AIDS epidemic, allowing us to observe the impact of HIV/AIDS on cancer survival through inclusion and exclusion of KS and lymphomas, two major HIV/AIDS-associated malignancies. We found superior cancer survival among AYAs of both sexes throughout the 1970s as compared to younger and older patients, which was also noted by an earlier report (7). However, such survival advantage disappeared in AYA males during the 1980s-1990s, a time associated with the burgeoning HIV/AIDS epidemic in the United States. By excluding KS and lymphomas from the sex-age-specific analysis, we were able to show that this observed decline in cancer survival among AYAs was (1)

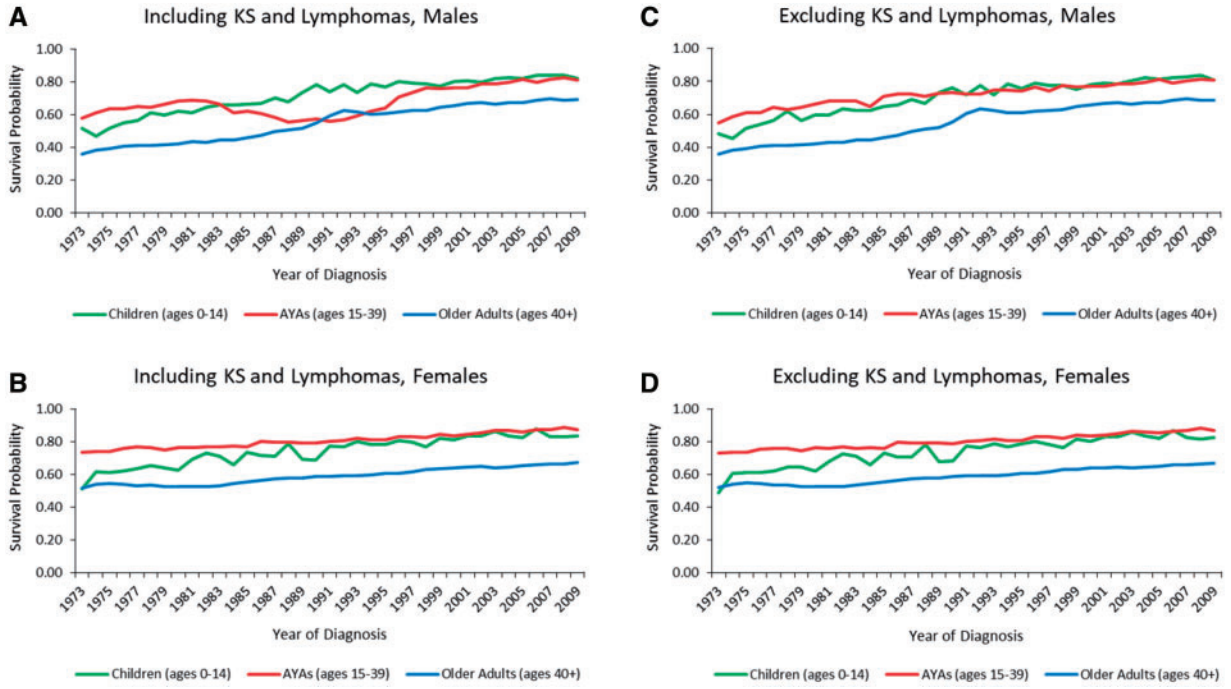

Figure 3. Time trends of 5-year relative survival by age group and sex. Data were from the SEER 9 registries, 1973–2009. Analyses for probability of survival from all invasive cancers including Kaposi sarcoma (KS) and lymphomas are shown for (**A**) males and (**B**) females. Analyses for probability of survival from all invasive cancers excluding KS and lymphomas are shown for (**C**) males and (**D**) females. AYA = adolescents and young adults.

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Table 4. Five-year relative survival by sex, age group, and time period, all invasive cancers, SEER 9 registries*

Population groups	Age groups, y	5-Year relative survival				Survival ratio	
		1973–1977		2005–2009		2005–2009 : 1973–1977	
		Males	Females	Males	Females	Males	Females
Children	0–4	0.52	0.59	0.83	0.84	1.61	1.43
	5-9	0.53	0.59	0.83	0.80	1.58	1.35
	10–14	0.52	0.63	0.82	0.87	1.57	1.38
AYAs	15–19	0.56	0.74	0.83	0.88	1.49	1.18
	20–24	0.64	0.78	0.83	0.89	1.30	1.14
	25-29	0.69	0.79	0.83	0.89	1.21	1.13
	30–34	0.65	0.75	0.82	0.88	1.26	1.17
	35–39	0.57	0.72	0.78	0.86	1.38	1.20
Older adults	40–44	0.50	0.68	0.75	0.85	1.50	1.24
	45–49	0.42	0.66	0.71	0.82	1.68	1.24
	50–54	0.40	0.63	0.70	0.78	1.78	1.24
	55–59	0.39	0.60	0.72	0.74	1.85	1.25
	≥60	0.39	0.48	0.67	0.59	1.75	1.23

*AYA = adolescents and young adults.

negated; (2) principally limited to AYA males who were disproportionately burdened by HIV/AIDS in the United States (14,15); and (3) transient, with resolution by the early 2000s after cART entered wide clinical use, providing highly effective treatment for HIV/AIDS (14,15).

Our analysis demonstrated that cancer survival has been rising in all age groups for both males and females including AYAs. In fact, AYAs consistently exhibited better survival than other age groups when HIV/AIDS-related cancers were excluded and after HIV/AIDS was effectively controlled. This finding concurs with a recent report that concluded AYAs have generally good outcomes after cancer diagnosis, noting their better overall health, greater ability to recover from cancer treatment, and lower mortality from other causes compared to older adults (16). Across age groups, females consistently displayed better survival than males, which was important information that was previously masked when the analysis was not sex specific (5).

Our analysis does indicate that the magnitude of survival improvement was smaller in AYAs than in either children or older adults and smaller in females than in males. This is explained by a combination of higher baseline survival of both AYAs and females, respectively, and more substantial increases in survival in both children and older adults (illustrated in Figure 4). Special emphasis on childhood cancer since the 1950s

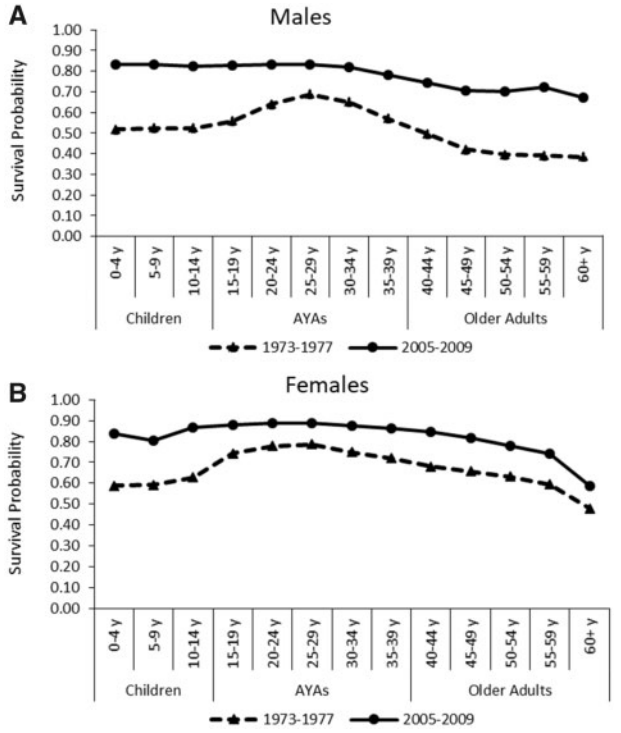

Figure 4. Comparison of 5-year relative survival for all invasive cancers by sex and age group, 1973–1977 vs 2005–2009. Data from the SEER 9 registries, 1973–2009, were analyzed. Age-specific 5-year relative survival during 1973–1977 and 2005–2009 are plotted separately for (**A**) males and (**B**) females. AYA = adolescents and young adults.

and passage of the National Cancer Act of 1971 have been credited for the dramatic improvement in cancer survival in children and older adults, respectively (3,5,7). Hence, in analyzing comparative survival trends for AYAs, it is important to be cognizant that less relative *improvement* does not necessarily correspond to poorer absolute *survival*.

These findings support our hypothesis and provide both an explanation for the historical observation of inferior survival improvement for AYAs and evidence that AYA cancer survival is, in fact, largely superior to other age groups and steadily improving. In addition, our findings reveal at least two more insights. First, reporting survival improvement alone, whether it is measured by absolute or relative differences in survival probabilities between two time periods or by annual percent change in survival, provides only partial information for evaluating progress. Actual survival probabilities by year or time period supplement measures of survival improvement to form a more complete assessment. Second, cancer risk and survival differ not only by age, but also by sex, particularly among AYAs. Therefore, informative assessment of survival should be sex specific as well. These two insights help ensure the most complete, accurate, and informative cancer survival data are available to aid the development of research and treatment priorities, and to direct resources most appropriately.

In reevaluating the previously reported poorer survival improvement in AYA cancer patients in comparison with other age groups considering the impact of HIV/AIDS, we followed a similar analytical scope as used in the previous report, although we added the age-specific analysis. This approach brought about two limitations of our study: We only examined survival at 5 years after diagnosis, and for all cancers combined. Challenges associated with long-term survival after 5 years are of particular importance for AYAs as they move through the different stages of life. The aggregate survival of all cancers combined does not necessarily represent or reveal survival of specific cancer types. Future efforts focusing on the long-term survival experience by cancer type will likely produce valuable new information.

Our analysis conveys a hopeful message that overall cancer survival among AYAs continues to exceed that of other age groups. In this sense, the future for AYA oncology looks bright. However, this does not negate other serious challenges facing this population, including differences in cancer and host biology, impaired access to appropriate cancer treatment, low participation in cancer clinical trials, increased susceptibility to acute and long-term treatment-related toxicity, and the need for intensive psychosocial support and long-term survivorship care. Additional AYA-focused cancer-specific research is needed in these areas to gain a better understanding of factors influencing cancer-specific outcomes and long-term survival.

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