Childbirth after adolescent and young adult cancer: a population-based study

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Abstract

Purpose Annually, > 45,000 US women are diagnosed with cancer during adolescence and young adulthood (AYA). Since 2006, national guidelines have recommended fertility counseling for cancer patients. We examined childbirth after AYA cancer by calendar period, cancer diagnosis, and maternal characteristics.

Methods We identified a cohort of women with an incident invasive AYA cancer diagnosis at ages 15–39 during 2000–2013 in North Carolina. Cancer records were linked with statewide birth certificates through 2014. Hazard ratios (HR) and 95% confidence intervals (CI) for first post-diagnosis live birth were calculated using Cox proportional hazards regression.

Results Among 17,564 AYA cancer survivors, 1989 had ≥ 1 birth after diagnosis during 98,397 person-years. The 5- and 10-year cumulative incidence of live birth after cancer was 10 and 15%, respectively. AYA survivors with a post-diagnosis birth were younger at diagnosis, had lower stage disease, and had less often received chemotherapy than those without a birth. The 5-year cumulative incidence of post-diagnosis birth was 10.0% for women diagnosed during 2007–2012, compared to 9.4% during 2000–2005 (HR = 1.01; 0.91, 1.12), corresponding to periods before and after publication of American Society of Clinical Oncology fertility counseling guidelines in 2006.

Conclusions Despite advances in fertility preservation options and recognition of fertility counseling as a part of high-quality cancer care, the incidence of post-diagnosis childbirth has remained stable over the last 15 years.

Implications for Cancer Survivors Our study uses statewide data to provide recent, population-based estimates of how often AYA women have biological children after a cancer diagnosis.

Keywords Neoplasms · Live birth · Adolescent · Young adult · Survivors

Introduction

The ability to have children after treatment is a leading concern for the > 45,000 female adolescents and young adults (AYA, defined by the National Cancer Institute as ages 15–39), who are diagnosed with cancer each year [1]. National guidelines from the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network, and the American Society for Reproductive Medicine recommend fertility counseling for AYA patients before cancer treatment [2–4]. Delivery of counseling is not universal, and > 50% of patients report needing more information on "realistic chances of having children in the future" before and after cancer treatment [5–10]. Having biological children is an important path to parenthood for AYA cancer survivors who may face difficulties meeting the medical screening requirements for adoption due to a prior cancer diagnosis [11].

Direct gonadotoxic effects of cancer treatment can occur from cytotoxic chemotherapy, ovarian radiation exposure, disruption of hypothalamic pituitary regulation, and structural changes from gynecologic surgery [2–4]. Fertility risks are also related to a woman's age at the time of treatment. Even in the absence of toxic therapies, time spent in active cancer

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treatment can disrupt relationships or may cause women to postpone childbearing plans to older ages when the chances of conceiving are lower.

Embryo and oocyte cryopreservation are accepted fertility preservation strategies for post-pubertal women. However, they are infrequently covered by insurance in the USA, and traditional techniques for harvesting mature oocytes can result in cancer treatment delays. Even in states with mandated infertility coverage, AYA cancer patients often do not qualify for coverage at the time services are needed because they are not infertile prior to cancer treatment. Costly medical advancements can exacerbate existing racial and economic disparities in cancer care and outcomes [12].

To examine the cumulative incidence of live birth after AYA cancer, and potential variation by tumor and maternal characteristics and calendar year, we conducted a population-based study in North Carolina.

Methods

We identified 17,564 women with an incident, invasive, first primary cancer at ages 15–39 years between January 1, 2000 and December 31, 2013 from the North Carolina Central Cancer Registry, a gold-certified North American Association of Central Cancer Registries (NAACCR) member within the Centers for Disease Control and Prevention's National Program of Cancer Registries. Cancer type groupings for commonly diagnosed AYA cancers (breast, thyroid, other head and neck carcinomas, gastrointestinal tract carcinomas, melanoma/skin carcinoma, soft tissue sarcomas, leukemias, non-Hodgkin lymphoma, Hodgkin lymphoma, and central nervous system and other intracranial and intraspinal neoplasms) were defined according to the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) site and histology codes using the AYA Site Recode ICD-O-3/WHO 2008 definitions [13]. We created a category of gynecologic malignancies to include AYA recodes for germ cell tumors of the ovary, carcinomas of the ovary, and carcinomas of the cervix and uterus. All other carcinomas of the genitourinary tract were defined as a separate category. Date of diagnosis, summary stage, race, and first course definitive treatments (including surgery, radiation, and chemotherapy) were abstracted from cancer registry records.

To identify births occurring after cancer diagnosis, records from the Central Cancer Registry were linked to North Carolina statewide vital records from 2000 to 2014 using a probabilistic linkage strategy in LinkPlus at the State Center for Health Statistics [14]. Variables used in the linkage included maternal name, date of birth, and social security number. Reliability estimates for these linkage variables are 98, 96, 97, 96, and 96% for social security number, date of birth, last name, first name, and middle name, respectively.

Infant date of birth, gestational weeks, and maternal parity were abstracted from birth certificates. We included all live births where the total recorded gestational length occurred after the cancer diagnosis date (i.e., births to women who were diagnosed during pregnancy were not included). However, women who were diagnosed with cancer during pregnancy ($N = 376$) contributed follow-up time, and additional live births that were conceived after the cancer diagnosis were considered post-diagnosis births. Records for 13 fetal deaths were not counted as live births. Women who experienced a fetal death were retained in analyses and could contribute one or more live births after a fetal death. Multiple post-diagnosis births to the same woman were identified and multiple gestations (i.e., twins, higher order births) were counted as a single birth event. Final analyses included 1989 first post-diagnosis births (of 2694 total births) to 17,564 AYA cancer survivors.

Statistical analysis

Hazards ratios (HR) and 95% confidence intervals (CI) for first post-diagnosis childbirth were estimated with Cox proportional hazards models. The Fine and Gray method was used to estimate the cumulative incidence of childbirth to account for death as a competing event [15]. Person-years were accrued from the date of diagnosis to date of first post-diagnosis childbirth, death, age 46, or December 31, 2014, whichever occurred first. In our data, age 45 years was the oldest maternal age observed among cancer survivors. The proportional hazards assumption was checked by visual inspection of log-log plots. In sensitivity analyses, we varied the start of follow-up to 1 and 2 years after cancer diagnosis and censored women at the date of fetal death.

For comparison to published general population birth rates in North Carolina in 2013 among women ages 15–45 [16], we calculated standardized birth ratios (SBRs) as the ratio of observed births among female AYA cancer survivors to the expected births among women without cancer, summed across strata of age and race/ethnicity. The number of expected births was calculated by multiplying the general population birth rate by the number of AYA cancer survivors in our cohort who were alive at that age at the end of 2013. Confidence intervals were calculated using Fisher's exact methods [17].

We also compared the 5-year cumulative incidence of childbirth for diagnosis years before and after the 2006 publication of ASCO recommendations regarding fertility counseling [18]. AYA women diagnosed with cancer during 2000–2005 and followed through 2007 were compared with women diagnosed during 2007–2012 and followed through 2014 to ensure equivalent follow-up time for both groups. Log-rank tests were used to compare the incidence curves. All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

Results

In total, 17,564 women contributed 98,397 person-years to our analysis (mean = 5.6 years, range <1–15 years). During this time, 1989 women had at least one identified live born child after their cancer diagnosis. Overall, the 5- and 10-year cumulative incidence of post-diagnosis live birth was 10 and 15%, respectively (Table 1). Childbirth was most common after melanoma and Hodgkin lymphoma (10-year cumulative incidence of 30 and 29%, respectively) and least common after breast, gynecologic, or gastrointestinal tract cancers (8, 6, and 6%, respectively).

Among women who had a post-diagnosis live birth, the mean time from diagnosis to birth was 3.6 years (SD = 2.4, range <1–13.6 years). The majority of women (72%) had one child after diagnosis, but as many as six children were reported. Of those who gave birth after a cancer diagnosis, approximately half (49%) had not had children before their cancer diagnosis (Table 2).

Compared to women diagnosed with melanoma, women with other cancer types were 25–77% less likely to have a live birth after diagnosis. Corresponding age-adjusted HRs for post-diagnosis childbirth ranged from 0.23 for gynecologic malignancies (CI 0.18, 0.28) to 0.75 for thyroid cancer (CI 0.66, 0.85) (Table 3). The cumulative incidence of post-diagnosis live birth was higher among women with younger ages at cancer diagnosis. Compared to women ages 30–34 at cancer diagnosis, those ages 20–24 were twice as likely to have a live birth after diagnosis (HR = 2.39; CI 2.11, 2.71), while those ages 35–39 at diagnosis were one fifth as likely to have a child by age 46 (HR = 0.21; CI 0.18, 0.25). After additional adjustment for cancer type, the HR for post-diagnosis childbirth among women ages 35–39 was virtually unchanged (0.22; CI 0.19, 0.26) and the combined category of age at diagnosis < 30 years was associated with a HR of 1.78 (CI 1.61, 1.98) for post-diagnosis childbirth compared to women ages 30–34 years at diagnosis (Table 3).

We also observed a pattern of lower cumulative incidence of post-diagnosis childbirth among women with more advanced stage disease. Compared to women with localized cancers at diagnosis, those with distant disease were 0.63 times as likely (CI 0.51, 0.78) (Table 3) to have a live birth after diagnosis. The 5- and 10-year cumulative incidence of childbirth after distant stage disease was 6 and 10%, respectively. Among women with distant stage disease, we observed no births after genitourinary, CNS, or soft tissue sarcoma; as few as 2–3 births after melanoma, breast, head and neck, or gastrointestinal cancer diagnoses; and as many as 43 births after Hodgkin lymphoma (*data not shown*).

In analyses that excluded gynecologic cancers, receipt of radiation without chemotherapy was not strongly associated with post-diagnosis live birth (HR = 0.91; 95% CI 0.79, 1.06) compared to surgery alone (Table 3). However, women with cancer types that were most likely to receive cranial or pelvic radiation, such as CNS tumors, gynecologic cancers, or Hodgkin lymphoma, were infrequently (< 5%) treated with radiation in the absence of chemotherapy. To evaluate potential associations with cranial radiation, we combined CNS tumors and head and neck cancers: compared to surgery alone, women who had radiation without chemotherapy had an age-adjusted HR of 0.82 (95% CI 0.50, 1.36) for post-diagnosis live birth, and women who had any chemotherapy had an HR of 0.53 (95% CI 0.32, 0.86) (*data not shown*). Consistent with our overall results, these findings suggest the potential for decreased risk of post-diagnosis live birth for radiation without chemotherapy that is intermediate between surgery alone and any chemotherapy, but estimates were not statistically significant. Too few women received radiation in the absence of chemotherapy to evaluate potential cranial and pelvic radiation for lymphomas specifically.

The cumulative incidence of childbirth associated with receipt of any chemotherapy was associated with an HR of 0.64 (95% CI 0.54, 0.77) (Table 3). Among women with gynecologic malignancies ($N = 2337$), we identified 105 post-diagnosis live births among women with cervical ($N = 52$), uterine ($N = 10$) or ovarian ($N = 11$) carcinomas, or germ cell ($N = 32$) neoplasms (*data not shown*).

In univariate analyses, Black women appeared less likely to have a live birth after AYA cancer (HR = 0.82; 95% CI 0.73, 0.92) (Table 3). However, this association was not apparent after adjustment for age at diagnosis and cancer type (HR = 1.03; 95% CI 0.91, 1.17). Women who were diagnosed with cancer during pregnancy were also more likely to conceive and deliver an additional live born child after their cancer treatment (HR = 1.49; 95% CI 1.20–1.84), although this estimate should be interpreted as a time-averaged summary measure due to evidence of non-proportional hazards within the first 2.5 years after diagnosis.

The patterns of association reported in Table 3 were unchanged in sensitivity analyses that varied the start of follow-up from 1 to 2 years after cancer diagnosis or censored at the date of fetal death. During the first year after cancer diagnosis, 87 AYAs gave birth, and 501 in the second year after diagnosis. Among the 13 women with an identified post-diagnosis fetal death, 5 had a subsequent live birth.

The cumulative incidence of childbirth after AYA cancer among women diagnosed in 2007–2012 (and followed through 2014) compared to 2000–2005 (followed through 2007), which corresponds to the time period before and after the 2006 publication of ASCO recommendations regarding fertility counseling, was not statistically different (HR = 1.01; 95% CI 0.91, 1.12, Table 3) [18]. The 5-year cumulative incidence of post-diagnosis childbirth was 10.0% for women diagnosed during 2007–2012, compared to 9.4% during 2000–2005. This finding was repeated in analyses restricted to each cancer type group (*data not shown*). The cumulative

Table 1 Characteristics of women diagnosed with adolescent or young adult cancer according to post-diagnosis childbirth, North Carolina 2000–2014

	AYA women with cancer		AYA women with ≥ 1 live birth after cancer	5-year cumulative incidence of post-diagnosis live birth	10-year cumulative incidence of post-diagnosis live birth
	N	%	*N*	%	%
Total AYA women	17,564	100%	1989	10.0%	15.0%
Cancer type					
Melanoma/skin carcinoma	2026	12%	486	21.6%	29.6%
Thyroid	2684	15%	458	15.5%	23.2%
Breast	4445	25%	245	4.6%	8.0%
Hodgkin lymphoma	756	4%	172	18.9%	29.0%
Non-Hodgkin lymphoma	682	4%	100	13.0%	18.9%
Gynecologic (cervical/uterine/ovarian)	2337	13%	105	3.8%	5.9%
Soft tissue sarcomas	476	3%	68	11.7%	18.9%
CNS and intracranial/spinal neoplasms	540	3%	63	10.0%	15.8%
Genitourinary tract carcinomas[a]	510	3%	41	7.1%	11.3%
Gastrointestinal tract carcinomas	1097	6%	51	4.7%	6.3%
Head and neck carcinomas[b]	290	2%	43	13.1%	19.7%
Leukemias	492	3%	36	6.4%	10.6%
Other	1229	7%	121	8.8%	12.8%
Race					
White	13,050	75%	1571	10.5%	15.9%
African-American	3688	21%	326	8.1%	11.9%
Other	736	4%	79	9.9%	14.2%
Missing/unknown	90		13	16.0%	22.0%
Age at diagnosis, years					
15–19	791	5%	184	15.9%	32.0%
20–24	1546	9%	432	22.0%	36.2%
25–29	2744	16%	603	19.9%	27.8%
30–34	4640	26%	573	11.8%	15.2%
35–39	7843	45%	197	2.5%	3.1%
Summary stage					
Localized	9605	55%	1338	12.4%	18.3%
Regional	4769	27%	396	7.3%	11.0%
Distant	2414	14%	163	5.8%	9.7%
Unstaged	771	4%	92	9.2%	15.7%
Cancer treatment					
Surgery only	6860	41%	1010	13.2%	18.7%
Radiation, no chemotherapy	2213	13%	315	12.7%	19.7%
Chemotherapy	7576	46%	547	6.0%	10.3%
Unknown	915		117	11.9%	16.0%
Cancer diagnosed during pregnancy					
No	17,188	98%	1901	9.7%	14.7%
Yes	376	2%	88	22.2%	31.1%

[a] Not including cervical/uterine or ovarian

[b] Not including thyroid

incidence curves appeared to separate toward the end of follow-up with a suggested higher incidence of childbirth in the more recent time period, but this difference was not statistically significant (log-rank $p = 0.2$) (Fig. 1). We repeated analyses restricted to women treated with chemotherapy as a group that may be especially targeted for fertility counseling,

Table 2 Characteristics of 1989 women diagnosed with adolescent or young adult cancer and ≥ 1 post-diagnosis live birth, North Carolina 2000–2014

	N	%
	1989	100%
Time between cancer diagnosis and first post-diagnosis live birth		
< 2	588	30%
2–< 3	441	22%
3–< 5	519	26%
5+	441	22%
Mean (SD)	3.6	(2.4)
Number of post-diagnosis births[a]		
1	1425	72%
2	455	23%
3	86	4%
4	16	1%
5	5	0%
6	2	0%
Parity at first post-diagnosis birth		
0	973	49%
1	585	29%
2	278	14%
3+	152	8%
Missing	1	0%

Among the 1989 first post-diagnosis live births to AYA cancer survivors, 58 were multiple births (2.9% of total; 56 twins, 2 triplets)

[a] *N* = 2694 births to 1989 women

but saw little difference in childbirth after AYA cancers over time (HR = 1.09; 95% CI 0.89, 1.35, adjusted for age and cancer type) (*data not shown*).

In 2013, the age- and race-adjusted birth rate among AYA cancer survivors was 55% of that in the general population (SBR = 0.55; 95% CI 0.49, 0.62). Across cancer type groups, the SBRs comparing cancer survivors to the general population were 0.25 (95% CI 0.14, 0.41) after gynecologic cancer, 0.42 (95% CI 0.29, 0.59) after breast cancer, 0.50 (95% CI 0.25, 0.89) after non-Hodgkin lymphoma, 0.59 (95% CI 0.46, 0.75) after thyroid cancer, 0.63 (95% CI 0.41, 0.94) after Hodgkin lymphoma, and 0.89 (95% CI 0.69, 1.12) after melanoma.

Discussion

Our study provides population-based data on childbirth after an AYA cancer diagnosis during the 2000s in North Carolina. Childbirth after AYA cancer was inversely associated with age at cancer diagnosis, disease stage, and receipt of chemotherapy (compared to surgery alone). After accounting for age and cancer type, racial group was not associated with post-diagnosis childbirth. The incidence of post-diagnosis childbirth remained unchanged in recent years, despite increasing recognition over the last decade that fertility counseling is a cornerstone of high-quality cancer care for AYAs.

Recognized risk factors for infertility after cancer treatment include alkylating agent-based chemotherapy, cranial radiation (due to disruption of hypothalamic pituitary regulation), pelvic radiation (due to ovarian/uterine exposure), and gynecologic surgery. Fertility risks are also related to a woman's age at the time of cancer treatment, and the duration and dose intensity of therapy [19]. These risks are reflected, in part, by the lower cumulative incidence of childbirth after cancers diagnosed at older ages or treated with chemotherapy observed in our study.

Previous studies of childbirth after cancer in other countries have reported similar findings by cancer type. In Norway, among women diagnosed with cancer at ages 16–45 during 1967–2004, post-diagnosis live births were identified among 3% of women diagnosed with breast cancer, 11% of those with gynecologic cancers, 16% with non-Hodgkin lymphoma, 29% with melanoma, 33% with thyroid cancer, and 35% with Hodgkin lymphoma [15, 20, 21]. In Finland, among women ages 15–34 years at cancer diagnosis in 1953–2004, 6% of women had a child after their breast cancer diagnosis, 19% after non-Hodgkin lymphoma, 25% after Hodgkin lymphoma, and 27% after thyroid cancer. Unlike earlier reports, our data came from a more recent time period that reflects contemporary treatment protocols.

Among more contemporary studies, in Australia, 24% of all women diagnosed with cancer at ages 15–39 during 1982–2007 had an identified post-diagnosis live birth [22]. In Canada, 5-year survivors who were diagnosed with cancer at ages 20–34 during 1992–1999 and who did not experience a cancer recurrence had a higher proportion of live births after cancer—from 23% after breast cancer to 43% after Hodgkin lymphoma [23]. In our data, restricting analyses to 5-year survivors did not substantially increase the cumulative incidence of childbirth; however, we were unable to account for women who may have experienced a cancer recurrence.

In 2013, the birth rate we observed after all AYA cancers was 0.55 times the general North Carolina population birth rate for women ages 15–45 [24]. This too is in range with reports from Norway and Canada where the HR for childbirth after cancer compared to the general population was 0.3–0.5 after breast cancer [15, 23], 0.6–0.7 after Hodgkin lymphoma [15, 23], and 0.3–0.6 after gynecologic cancers [15].

In the USA, information about pregnancy risks after a cancer diagnosis frequently comes from studies of adult survivors of *childhood* cancers [25–28]. Reproductive outcomes after a childhood cancer diagnosis may not accurately reflect risks among AYAs. The most common cancer sites among AYA women (including breast, thyroid, melanoma, gynecologic malignancies, and lymphoma) are distinct from common

Table 3 Hazard ratios (HR) and 95% confidence intervals (CI) for childbirth after adolescent or young adult (AYA) cancer, North Carolina 2000–2014

	No. AYAs with ≥ 1 live birth after cancer	Person-years[a]	Univariate HR (95% CI)	Age-adjusted HR (95% CI)[b]	Age and cancer type-adjusted HR (95% CI)[b]
Cancer type					
Melanoma/skin carcinoma	486	11,923	1	1	1
Thyroid	458	15,520	0.71 (0.63, 0.81)	0.75 (0.66, 0.85)	0.75 (0.66, 0.85)
Breast	245	25,898	0.23 (0.20, 0.27)	0.40 (0.34, 0.47)	0.40 (0.34, 0.47)
Hodgkin lymphoma	172	4708	0.91 (0.76, 1.08)	0.71 (0.60, 0.85)	0.71 (0.60, 0.84)
Non-Hodgkin lymphoma	100	3624	0.68 (0.55, 0.84)	0.72 (0.58, 0.90)	0.72 (0.58, 0.90)
Gynecologic (cervical/uterine/ovarian)	105	14,248	0.18 (0.15, 0.23)	0.23 (0.18, 0.28)	0.23 (0.18, 0.28)
Soft tissue sarcomas	68	2516	0.66 (0.51, 0.85)	0.62 (0.48, 0.81)	0.62 (0.48, 0.81)
CNS and intracranial/spinal neoplasms	63	2844	0.55 (0.42, 0.71)	0.48 (0.37, 0.63)	0.48 (0.37, 0.63)
Genitourinary tract carcinomas [c]	41	2813	0.35 (0.26, 0.49)	0.56 (0.41, 0.77)	0.56 (0.41, 0.77)
Gastrointestinal tract carcinomas	51	4984	0.25 (0.19, 0.34)	0.37 (0.27, 0.49)	0.37 (0.27, 0.49)
Head and neck carcinomas[d]	43	1632	0.64 (0.47, 0.88)	0.74 (0.54, 1.01)	0.74 (0.54, 1.01)
Leukemias	36	2085	0.44 (0.31, 0.62)	0.39 (0.28, 0.54)	0.39 (0.28, 0.54)
Other	121	5602	0.53 (0.44, 0.65)	0.56 (0.46, 0.69)	0.56 (0.46, 0.69)
Race					
White	1571	75,056	1	1	1
African-American	326	19,051	0.82 (0.73, 0.92)	0.87 (0.77, 0.98)	1.03 (0.91, 1.17)
Other	79	3886	0.97 (0.77, 1.21)	0.95 (0.76, 1.19)	1.07 (0.85, 1.34)
Age at diagnosis					
15–19	184	4582	1.91 (1.61, 2.25)	1.91 (1.61, 2.25)	1.78 (1.61, 1.98)
20–24	432	8584	2.39 (2.11, 2.71)	2.39 (2.11, 2.71)	
25–29	603	15,299	1.90 (1.69, 2.13)	1.90 (1.69, 2.13)	
30–34	573	27,736	1	1	1
35–39	197	42,195	0.21 (0.18, 0.25)	0.21 (0.18, 0.25)	0.22 (0.19, 0.26)
Summary stage[e]					
Localized	1338	58,479	1	1	1
Regional	396	26,314	0.65 (0.58, 0.73)	0.70 (0.62, 0.78)	0.72 (0.64, 0.82)
Distant	127	7377	0.77 (0.64, 0.92)	0.67 (0.56, 0.80)	0.63 (0.51, 0.78)
Cancer treatment[f, g]					
Surgery only	941	32,617	1	1	1
Radiation, no chemotherapy	315	12,077	0.89 (0.79, 1.01)	0.88 (0.77, 0.99)	0.91 (0.79, 1.06)
Chemotherapy	486	33,527	0.51 (0.46, 0.57)	0.59 (0.53, 0.66)	0.64 (0.54, 0.77)
Cancer diagnosed during pregnancy[h]					
No	1858	94,731	1	1	1
Yes	88	2034	2.20 (1.78, 2.72)	1.64 (1.33, 2.03)	1.49 (1.20, 1.84)
Cancer diagnosis year[i]					
2000–2005	600	28,644	1	1	1
2007–2012	776	34,655	1.07 (0.96, 1.19)	1.03 (0.92, 1.14)	1.01 (0.91, 1.12)

[a] Person-years contributed by 17,564 women with an AYA cancer diagnosis, including 1989 with ≥ 1 post-diagnosis live birth

[b] Adjusted for age as < 30, 30–34, 35–39 (due to few young age breast cancers) and cancer type

[c] Not including cervical/uterine/ovarian cancers

[d] Not including thyroid cancer

[e] Excludes women with leukemia; no women with a leukemia diagnosis were in the regional disease category

[f, g] Excludes women with gynecologic cancer (based on differences between gynecologic surgery and surgery for other cancer types) and leukemia (no women with a leukemia diagnosis were in the radiation without chemotherapy category)

[h] Excludes women with head and neck cancers because only two women were diagnosed during pregnancy

[i] Follow-up though 2007 for cancers diagnosed in 2000–2005; through 2014 for cancers diagnosed in 2007–2012

childhood cancers (e.g., leukemias, central nervous system tumors) [29]. Further, accepted fertility preservation strategies (embryo and oocyte cryopreservation) require harvesting mature oocytes, and are therefore not feasible before puberty [3, 18]. These techniques are expensive and rarely covered by insurance [30], and could exacerbate existing racial and economic disparities in cancer care and outcomes [3, 18]. In our study, we lacked data on economic indicators, but observed no association between Black race and childbirth after AYA cancer after adjustment for age and cancer type.

In our analysis, approximately half of AYA women who had a child after their cancer diagnosis had not had children previously. Some studies suggest that women who have children at the time of cancer diagnosis may be less likely to made be aware of [31], or use [31, 32] fertility preservation options. Approximately a third of all identified post-diagnosis births

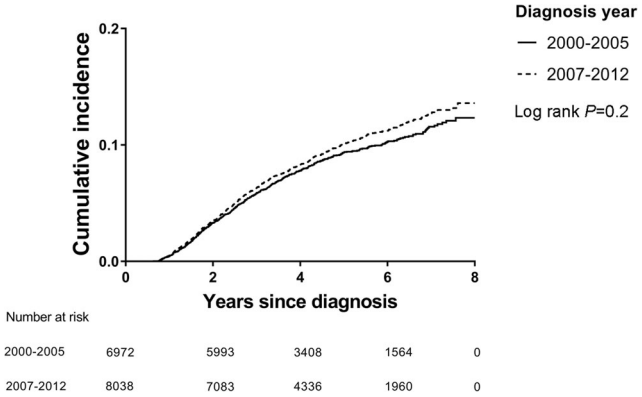

Fig. 1 Cumulative incidence of childbirth after adolescent or young adult cancer diagnosis by years since cancer diagnosis and according to calendar periods before and after the 2006 publication of ASCO recommendation statements for fertility counseling in cancer patients. Women diagnosed during 2000–2005 were followed through 2007; women diagnosed during 2007–2012 were followed through 2014 to ensure an equal amount of follow-up (max = 8 years) in both time periods

occurred within 2 years of cancer diagnosis. These were often births to women with melanoma ($N = 166$) or thyroid cancer ($N = 143$), but all cancer type groups had births within this 2-year window, including AYAs diagnosed with lymphoma (NHL: $N = 27$; HL: $N = 46$) or breast cancer ($N = 52$). Recommendations for attempting pregnancy after a cancer diagnosis are not uniform and can vary from waiting 6 months after treatment with radioactive iodine for thyroid cancer [33], to waiting 2–5 years after breast cancer or other malignancies [34, 35]. AYA cancer survivors may be at particular risk for inaccurate assumptions of infertility [36]. In the Fertility Information Research Study (FIRST), a prospective, web-based cohort of 295 women ages 18–44, nearly as many women reported use of emergency contraception (10%) as reported pregnancy after cancer diagnosis (11%). Overall, 64% of AYA survivors in the FIRST study were at risk of unintended pregnancy, and among 32 post-diagnosis pregnancies, 16% were unintended [37]. In our study, we cannot distinguish births that results from unintended versus planned pregnancies, but the relatively high proportion of births within 2 years of diagnosis suggests that this may be an important issue to consider.

We could not identify post-diagnosis live births among AYAs who left North Carolina after their cancer diagnosis. However, in census data for 2000–2010, most moves in North Carolina were within-county—7% of women overall moved out of state [38]. The North Carolina Central Cancer Registry is a gold-certified North American Association of Central Cancer Registries (NAACCR) member; however, validation information is not available for treatment data and misclassification may occur. Cancer registry treatment variables also do not include specific chemotherapy agents, including alkylating agent-based therapies, or radiation field or dose. Cancer recurrence information is also not available from the cancer registry. In 2011, a revised birth certificate included fields for infertility treatments—but recent reports indicate that only 37% of IVF-conceived births are accurately identified with this birth certificate item [39]. Additionally, we were unable to assess the impact of parity prior to diagnosis in our analyses, as this information was not available for women without a birth during the study period, or of sterilization procedures (e.g., tubal ligation, hysterectomy) that occurred either before or after cancer treatment.

An estimated 60% of AYA women with a cancer diagnosis want to preserve their ability to have children after treatment [9, 40]. National guidelines recommend fertility counseling before cancer treatment [3, 4, 18], but a majority of AYAs report needing more information on fertility and reproductive outcomes both before and after treatment [5, 6, 41–43]. Our study uses statewide data in North Carolina to provide recent, population-based estimates of how often AYA women go on to have biological children after a cancer diagnosis.

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Compliance with ethical standards

Conflict of interest BL is a research consultant to the Society for Assisted Reproductive Technology. HN, CA, KR, KB, SE, and JM have no conflicts to declare.

Research involving human participants All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent This study was approved by the Institutional Review Board at the University of North Carolina Chapel Hill (No. 15–2484). For this type of study, formal informed consent is not required.

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