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Article

Adverse birth outcomes of adolescent and young adult women diagnosed with cancer during pregnancy

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Abstract

Background: We examined adverse birth outcomes among adolescent and young adult women diagnosed with cancer (AYA women, ages 15-39 years) during pregnancy.

Methods: We linked data from the Texas Cancer Registry, vital records, and Texas Birth Defects Registry to identify all singleton births to AYA women diagnosed during pregnancy from January 1999 to December 2016. We compared prevalence of adverse live birth outcomes between AYA women and women without cancer (matched 1:4 on age, race and ethnicity, and year). Among AYA women, we used log-binomial regression to identify factors associated with these outcomes. Statistical tests were 2-sided.

Results: AYA women had 1271 singleton live births and 20 stillbirths. AYA women (n = 1291) were 33.3% Hispanic and 9.8% non-Hispanic Black and most commonly had breast (22.5%), thyroid (19.8%), and gynecologic (13.3%) cancers. Among live births, AYA women had a higher prevalence of low birth weight offspring (30.1% vs 9.0%), very preterm (5.7% vs 1.2%), and preterm birth (25.1% vs 7.2%); cesarean delivery (44.3% vs 35.2%); and low Apgar score (2.7% vs 1.5%), compared with women without cancer (n = 5084) (all $P < .05$). Prevalence of any birth defect by age 12 months did not statistically differ (5.2% vs 4.7%; $P = .48$), but live births to AYA women more often had heart and circulatory system defects (2.2% vs 1.3%; $P = .01$). In adjusted models, cancer type and chemotherapy were associated with adverse live birth outcomes.

Conclusions: AYA women diagnosed during pregnancy have higher prevalence of adverse birth outcomes and face difficult decisions in balancing treatment risks and benefits.

For adolescent and young adult women with cancer (ages 15-39 years, hereafter AYA women), the disease and its treatment disrupt development, including reproductive health and childbearing. Although rare, cancers diagnosed during pregnancy are becoming more common (1-3), accounting for approximately 1 in 1000 pregnancies (4). This likely reflects increasing incidence of cancer in AYA women and increasing maternal age at first birth. Thus, a growing number of AYA women and their providers face challenges balancing cancer, treatment, and potential impacts on pregnancy and offspring.

A robust evidence base of birth outcomes in this population can facilitate care planning and shared decision making when a woman is diagnosed during pregnancy. However, most studies comprise small samples and/or a single center (5-15); of the few large epidemiologic studies, most have been conducted in Europe (16-19). Although limited, these studies suggest higher prevalence of preterm birth but similar prevalence of birth defects among AYA women diagnosed during pregnancy compared with the general population. Results are mixed regarding other outcomes, including small for gestational age, low birth weight, and low Apgar score (2,16,17). To our knowledge, there are no population-based studies of birth outcomes to AYA women diagnosed during pregnancy in the United States, where access to care and clinical practice substantially differ from Europe. Therefore, the extent to which this growing population in the United States experiences adverse birth outcomes is unclear, and there is little information about factors associated with outcomes among these women.

We conducted a population-based study of birth outcomes of AYA women diagnosed with cancer during pregnancy over a 15-year period. Specifically, we addressed the following research questions.

1) What are the characteristics of AYA women diagnosed with cancer during pregnancy?
2) Does the prevalence of adverse live birth outcomes, including birth defects, differ between AYA women and women without cancer?

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3) Among AYA women diagnosed during pregnancy, what factors are associated with adverse live birth outcomes?

Methods

Study population

We identified all women diagnosed with cancer at age 15-39 years between January 1, 1999, and December 31, 2015, using population-based data from the Texas Cancer Registry (TCR; see Figure 1). As 1 of only 12 state registries funded by both the National Cancer Institute's Surveillance, Epidemiology, and End Results Program and the National Program of Cancer Registries, TCR meets Gold Certification criteria set by the North American Association of Central Cancer Registries (eg, case ascertainment exceeds 95%).

We linked data from TCR to 1) live birth and fetal death certificates from January 1, 1999, to December 31, 2016, and 2) the Texas Birth Defects Registry from January 1, 1999, to December 31, 2016. Texas requires fetal death certificates for fetuses weighing at least 350 grams or gestational age of at least 20 weeks (ie, stillbirth) (20). The Texas Birth Defects Registry is one of the largest active birth defects surveillance systems in the United States; staff members routinely visit all maternity hospitals, pediatric hospitals, birthing centers, and midwife facilities in Texas, as well as examine discharge log diagnostic codes, to identify birth defects in infants through age 12 months (21,22). Using Match*Pro (described at https://seer.cancer.gov/tools/matchpro/), the Texas Department of State Health Services linked records using probabilistic linkage, described elsewhere (20,23).

We identified AYA women diagnosed with cancer during pregnancy as those who had a singleton live birth or stillbirth for which the recorded gestational length was greater than the number of weeks between the date of cancer diagnosis and the date of delivery. For example, diagnosis date February 5, 2004, delivery date August 5, 2004, and gestational age 40 weeks. We excluded those missing gestational age. We also excluded multiple births because they comprised less than 2% of all births to women diagnosed with cancer during pregnancy (see Figure 1).

To compare live birth outcomes with the general population, we randomly selected up to 4 singleton live births to women without cancer from January 1, 1999, to December 31, 2016. Comparison births were frequency matched to births to AYA women by maternal age, maternal race and ethnicity, and delivery year.

Statistical analysis

We described characteristics of AYA women diagnosed with cancer during pregnancy, including age at diagnosis, race and ethnicity, cancer type, year of diagnosis, stage at diagnosis, trimester of diagnosis, parity, and receipt of surgery and chemotherapy. We combined race and ethnicity to include Hispanic (any race), non-Hispanic Asian or Pacific Islander, non-Hispanic Black, non-Hispanic Other, and non-Hispanic White. Non-Hispanic Other included American Indian or Alaska Native and "some other race" as coded by North American Association of Central Cancer Registries item #160 (https://datadictionary.naaccr.org/default.aspx?c=10&Version=23#160). We calculated gestational week of diagnosis by subtracting the number of weeks between diagnosis and delivery from gestational age and defined trimester of diagnosis as first (0-13 weeks), second (14-26 weeks), and third (≥27 weeks) trimester. TCR collects information on first course of treatment (ie, prior to disease progression or recurrence), including surgery, chemotherapy, and radiation therapy. Treatment missingness ranged from 4.2% (surgery) to 11.2% (chemotherapy); we did not examine radiation therapy because it was missing for the majority of the sample (58.9%).

Among singleton live births to AYA women and women without cancer, we estimated prevalence of very preterm (<32 weeks) and preterm (32 to <37 weeks) birth, low birth weight (<2500 grams), cesarean delivery, low Apgar score (<7), and any birth defect. We defined any birth defect using modified British Pediatric Association codes 740.000-759.000, based on the British Pediatric Association Classification of Diseases and developed by the National Center on Birth Defects and Developmental Disabilities (24). We also estimated prevalence of specific birth defect types (Supplementary Methods, available online). We compared prevalence in AYA women vs women without cancer using a χ^2 or Fisher exact test, as appropriate.

We used log binomial regression models to identify factors associated with preterm birth, low birth weight, and cesarean delivery among live births to AYA women. We additionally fit a model including receipt of surgery limited to AYA women with cancers for which surgery may be indicated (ie, excluding leukemia, lymphoma, other specified, unspecified). We did not fit a model for low Apgar score, because 22.9% of live births were missing data on this outcome, or for any birth defects, because of the small number of events (<70). We report adjusted prevalence ratios (aPR) and 95% confidence intervals (CIs).

The institutional review board at the University of Texas Health Science Center at Houston and Texas Department of State Health Services approved this study. Analyses were conducted in SAS version 9.4 (SAS Institute, Cary, NC, USA). Statistical tests were 2-sided; a *P*-value less than .05 indicated statistical significance.

Results

There were 56 113 AYA women diagnosed with cancer in Texas from January 1, 1999, to December 31, 2015. Among these women, 1291 singleton births occurred to those diagnosed with cancer during pregnancy, including 1271 live births and 20 stillbirths. Characteristics of AYA women diagnosed during pregnancy are summarized in Table 1. Nearly half of AYA women were racial and ethnic minorities: 33.3% Hispanic, 3.7% non-Hispanic Asian or Pacific Islander, and 9.8% non-Hispanic Black. Breast (22.5%), thyroid (19.8%), and gynecologic (13.3%) cancers were the most common cancer types. Median gestational age at diagnosis was 22 weeks (interquartile range = 13-29 weeks), and most AYA women were diagnosed in the second (40.3%) or third (35.9%) trimester.

As shown in Table 2, prevalence of low birth weight (prevalence ratio [PR] = 3.36, 95% CI = 2.97 to 3.79), cesarean delivery (PR = 1.26, 95% CI = 1.17 to 1.35), and low Apgar score (PR = 1.76, 95% CI = 1.12 to 2.78) was higher among live births to AYA women than women without cancer. Very preterm (5.7% vs 1.2%; PR = 4.95, 95% CI = 3.53 to 6.94) and preterm (25.1% vs 7.2%; PR = 3.51, 95% CI = 3.06 to 4.02) birth was also 2 or 3 times as prevalent in AYA women compared with women without cancer, and prevalence of preterm birth remained higher when limited to vaginal deliveries (22.1% AYA women vs 7.0% women without cancer).

Few birth defects were identified in liveborn offspring of AYA women through age 12 months (Table 3), and prevalence of any birth defect did not statistically differ between AYA women (5.2%) and women without cancer (4.7%; P = .48). There were very small numbers of specific types of birth defects, especially among

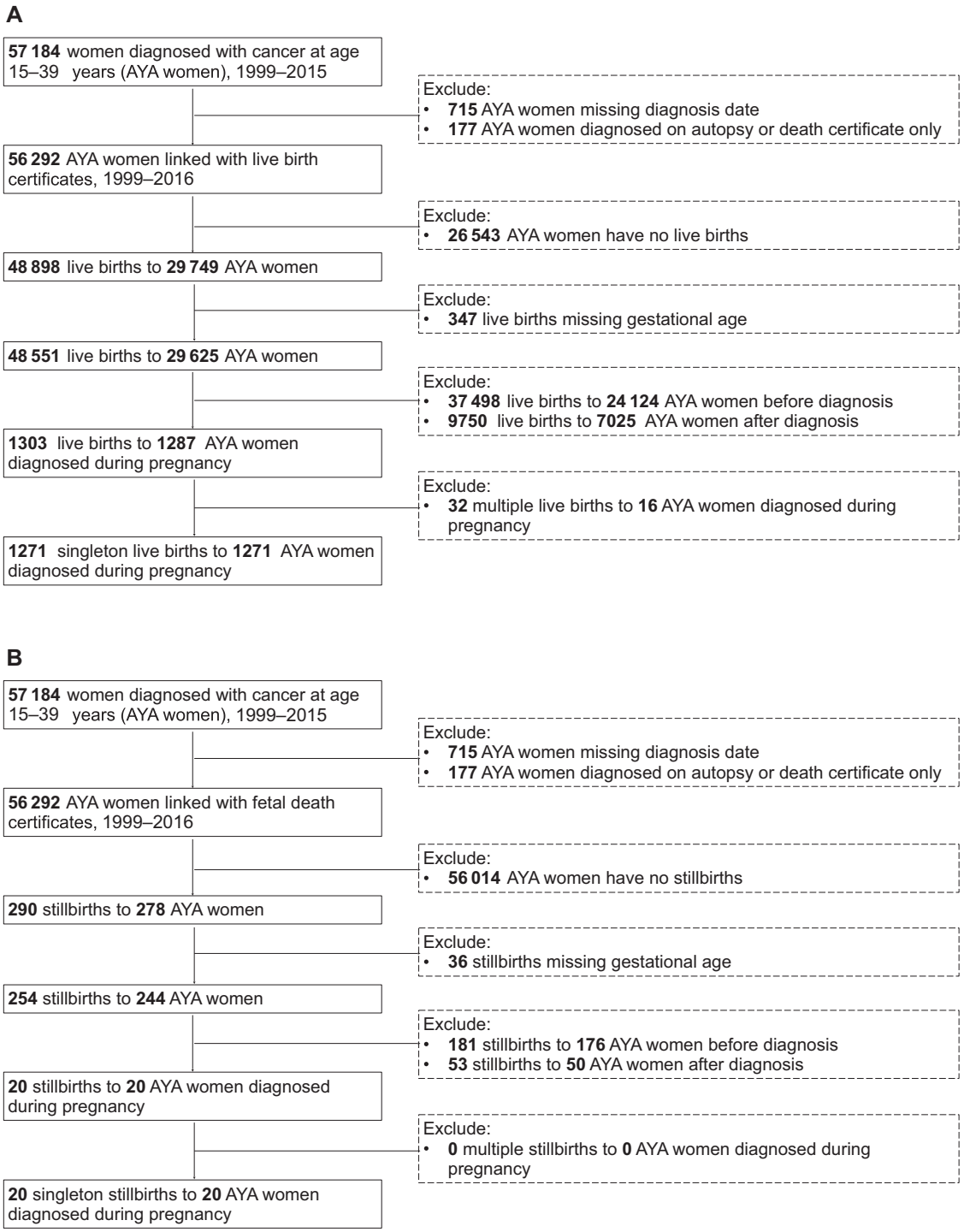

Figure 1. Study flow diagram depicting (**A**) singleton live births to adolescent and young adult (AYA) women diagnosed with cancer during pregnancy and (**B**) singleton stillbirths to AYA women.

AYA women, but heart and circulatory system defects were more common in offspring of AYA women (2.2% vs 1.3%; $P = .01$); these included pulmonary atresia, atrial septal defects, and tricuspid atresia. Notably, prevalence of heart and circulatory system defects was similar among AYA women who received chemotherapy and those who did not (2.1% vs 2.4%), although numbers were very small.

Table 4 illustrates factors associated with preterm birth, low birth weight, and cesarean delivery among live births to AYA women. Cancer type was associated with all 3 outcomes, to a varying degree and magnitude. For example, AYA women with gastrointestinal cancers had a particularly high likelihood of preterm birth (aPR = 5.29, 95% CI = 3.39 to 8.26) and low birth weight (aPR = 2.39, 95% CI = 1.72 to 3.32) compared with women with thyroid cancers. Similarly, women with central nervous system (CNS) or gynecologic cancers had higher prevalence of preterm birth, low birth weight, and cesarean section. Receipt of chemotherapy was associated with preterm birth (aPR = 1.82,

Table 1. Characteristics of 1291 adolescent and young adult (ages 15-39 years at diagnosis) women diagnosed with cancer during pregnancy, Texas Cancer Registry, 1999-2015

Characteristics	No. (%)
Age at diagnosis, y	
15-19	53 (4.1)
20-24	199 (15.4)
25-29	355 (27.5)
30-34	408 (31.6)
35-39	276 (21.4)
Race and ethnicity	
Hispanic, any race	427 (33.3)
Non-Hispanic Asian or Pacific Islander	48 (3.7)
Non-Hispanic Black	126 (9.8)
Non-Hispanic White	673 (52.4)
Non-Hispanic Other[a]	10 (0.8)
Missing	—
Cancer type[b]	
Breast	291 (22.5)
Central nervous system	37 (2.9)
Genitourinary	23 (1.8)
Gastrointestinal	44 (3.4)
Gynecologic	171 (13.3)
Head and neck	25 (1.9)
Leukemias	74 (5.7)
Lymphomas	101 (7.8)
Sarcomas	49 (3.8)
Melanoma and skin	98 (7.6)
Thyroid	255 (19.8)
Other specified	55 (4.3)
Unspecified	68 (5.3)
Year of diagnosis	
1999-2001	153 (11.9)
2002-2004	151 (11.7)
2005-2007	241 (18.7)
2008-2010	260 (20.1)
2011-2013	303 (23.5)
2014-2015	183 (14.2)
Stage at diagnosis[c]	
Local	566 (50.9)
Regional	348 (31.3)
Distant	198 (17.8)
Missing	179
Trimester of diagnosis	
First trimester	307 (23.8)
Second trimester	520 (40.3)
Third trimester	464 (35.9)
Received surgery	
Yes	784 (63.4)
No	453 (36.6)
Missing	54
Received chemotherapy	
Yes	381 (33.3)
No	765 (66.8)
Missing	145
Parity	
Nulliparous	402 (31.4)
Primiparous	880 (68.6)
Missing	—

[a] Non-Hispanic Other includes American Indian or Alaska Native and "some other race" as coded by North American Association of Central Cancer Registries item #160. "—" denoted because Texas Department of State Health Services prohibits reporting small (n < 10) cells. AYA = adolescent and young adult women diagnosed with cancer.
[b] Defined using the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) site and histology codes and according to the AYA Site Recode ICD-O-3/World Health Organization 2008 (described at https://seer.cancer.gov/ayarecode/aya-who2008.html).
[c] Defined using Surveillance, Epidemiology, and End Results summary stage.

95% CI = 1.53 to 2.17) and low birth weight (aPR = 1.36, 95% CI = 1.17 to 1.58). Findings were similar in the model including receipt of surgery (Supplementary Table 1, available online), with surgery not associated with any outcome.

Discussion

Our findings in a large, diverse population-based sample of AYA women diagnosed with cancer during pregnancy demonstrate higher prevalence of low birth weight, very preterm and preterm birth, cesarean delivery, and low Apgar score compared with women without cancer, as expected. We observed no difference in the prevalence of any birth defect in liveborn offspring through age 12 months, but offspring of AYA women more often had heart and circulatory system defects, although rare. There were also 20 stillbirths to AYA women, higher than that expected in the general population over approximately the same period, as reported elsewhere (20). A diagnosis of cancer during pregnancy presents AYA women and their providers with difficult decisions as they must balance risks to the fetus with risks to the mother of a delayed or different course of treatment. Decisions may include termination or continuation of pregnancy; delaying chemotherapy until the second trimester; using different therapies than those recommended for women who are not pregnant; delaying some treatment to postpartum to minimize risks to the fetus; and/or, for women diagnosed in the third trimester, delivering early to initiate treatment. This balancing act underscores the importance of shared decision making to incorporate women's values and preferences, including access to safe and legal abortion in accordance with guidelines (25), and a multidisciplinary approach to managing cancer during pregnancy. Additional research on maternal and cancer outcomes of AYA women diagnosed during pregnancy will be critical in guiding shared decision making (26-29).

A lower proportion of live births in our study occurred in women diagnosed during the first trimester, similar to other large European studies (16,18). This may reflect miscarriages, terminations, or delays in prenatal care. Miscarriages in this population have ranged from 2% to 4% (11,30), whereas terminations have varied widely from 5% to 22% (10,11,18,30,31) in larger studies of women diagnosed with cancer during pregnancy. In a large, international cohort of women diagnosed during pregnancy, an overwhelming majority of terminations were due to start of oncological treatment or poor maternal prognosis (18). Although we report stillbirths, we were not able to examine miscarriages or terminations because they are not uniformly collected at the population level in Texas; however, many AYA women in our study were diagnosed with regional or distant-stage cancer in the first trimester and therefore had to critically consider their prognosis and need for immediate treatment. Texas is 1 of 12 states that banned abortion in July 2022 (32,33), with no exceptions for medically necessary treatment, and more than 75 health-care organizations have since released a joint statement supporting rights of patients and providers to access and offer abortion care (34,35). As of this writing, Texans may legally obtain abortion in other states, but for women diagnosed with cancer during pregnancy, added logistics and expenses required for negotiating long-distance travel (36,37) may delay treatment initiation.

The high burden of adverse live birth outcomes among AYA women diagnosed during pregnancy reinforces the importance of multidisciplinary care that incorporates oncology, maternal-fetal medicine, obstetrics, and perinatology—in a setting with access to neonatal intensive care units and psychosocial supports (38,39). Increasing evidence implicates preterm birth as the primary driver of neonatal complications and mortality in this population, regardless of whether women received chemotherapy during pregnancy (16,38,40). Preterm birth also remained higher among AYA women in our study when limited to vaginal

Table 2. Prevalence of adverse live birth outcomes of adolescent and young adult women diagnosed with cancer during pregnancy compared with women without cancer

Birth outcome	AYA women (n = 1271) n (%)	Women without cancer (n = 5084) n (%)	PR (95% CI)[a]	P
Birth weight, g				
<2500	378 (30.1)	451 (9.0)	3.36 (2.97 to 3.79)	<.01
2500-3999	842 (67.1)	4200 (83.5)	0.80 (0.77 to 0.84)	<.01
≥4000	35 (2.8)	377 (7.5)	0.37 (0.26 to 0.52)	<.01
Missing	16	56		
Gestational age				
<32 wk	73 (5.7)	59 (1.2)	4.95 (3.53 to 6.94)	<.01
32-37 wk	319 (25.1)	364 (7.2)	3.51 (3.06 to 4.02)	<.01
≥37 wk	879 (69.2)	4661 (91.7)	0.75 (0.73 to 0.78)	<.01
Delivery method				
Cesarean	561 (44.3)	1784 (35.2)	1.26 (1.17 to 1.35)	<.01
Vaginal	706 (55.7)	3282 (64.8)	0.86 (0.82 to 0.91)	<.01
Missing	4			
Apgar score				
<7	26 (2.7)	59 (1.5)	1.76 (1.12 to 2.78)	.02
≥7	953 (97.3)	3852 (98.5)	0.99 (0.98 to 1.00)	.04
Missing	292	1173		
Birth defect				
Any	66 (5.2)	240 (4.7)	1.10 (0.84 to 1.43)	.48
None	1205 (94.8)	4844 (95.3)	1.00 (0.98 to 1.01)	.49

[a] Unadjusted prevalence ratio shown in table; in these models, cancer is the independent variable, and each live birth outcome is the dependent variable. AYA = adolescent and young adult women diagnosed with cancer; CI = confidence interval; PR = prevalence ratio.

Table 3. Prevalence of birth defects among live singleton births to adolescent and young adult women diagnosed with cancer during pregnancy and women without cancer

Birth defect type	AYA women (n = 1271)		Women without cancer (n = 5084)		
	No. (%)	(95% CI)	No. (%)	(95% CI)	P
Any birth defect	66 (5.2)	(4.0 to 6.4)	240 (4.7)	(4.1 to 5.3)	.48
Structural birth defect[a]					
Central nervous system	—	—	24 (0.5)	(0.3 to 0.7)	.72
Eye or ear	—	—	29 (0.6)	(0.4 to 0.8)	.38
Heart and circulatory system	28 (2.2)	(1.4 to 3.0)	65 (1.3)	(1.0 to 1.6)	.01
Respiratory system	—	—	10 (0.2)	(0.1 to 0.3)	>.99
Clefts	—	—	—	—	.68
Gastrointestinal system	—	—	28 (0.6)	(0.4 to 0.8)	>.99
Genitourinary system	13 (1.0)	(0.5 to 1.6)	69 (1.4)	(1.0 to 1.7)	.34
Musculoskeletal system	24 (1.9)	(1.1 to 2.6)	78 (1.5)	(1.2 to 1.9)	.37
Skin, hair, or nails	—	—	15 (0.3)	(0.2 to 0.5)	>.99
Other	0 (0.0)	(0.0)	—	—	.59
Chromosomal anomaly	—	—	14 (0.3)	(0.1 to 0.4)	.75

[a] Structural defects include only those diagnosed in offspring without a chromosomal anomaly. "—" denoted because Texas Department of State Health Services prohibits reporting small (n < 10) cells. AYA = adolescent and young adult women diagnosed with cancer.

deliveries. Accordingly, European guidelines and expert panels (41-43) recommend extending pregnancy as long as possible in women with cancer, whereas US guidelines do not address this issue. Given that disease- and treatment-related factors likely contributed to adverse outcomes, our findings support guidelines that strongly encourage referral to tertiary cancer centers specializing in cancer treatment during pregnancy (39). However, access to cancer and obstetrics care varies widely in the United States, and many AYAs may not have access to specialized centers.

Given the large study sample and active, statewide surveillance system used to ascertain birth defects in Texas, our findings represent some of the most robust evidence to date of structural or functional anomalies among offspring of AYA women diagnosed with cancer during pregnancy. We observed a higher prevalence of heart and circulatory system defects among liveborn offspring of AYA women compared with women without cancer, although rare in both groups. Prior population-based studies reporting no difference in birth defects between women with and without cancer did not examine specific types of birth defects, which differ in etiology (17,18,44-46). Further research is warranted to understand factors contributing to higher prevalence in offspring of AYA women. In addition, more information concerning developmental disorders diagnosed in offspring during early childhood, when a number of congenital anomalies become manifest (eg, cerebral palsy), is critically needed.

Findings of adjusted models suggest cancer-related factors contribute to preterm birth, low birth weight, and cesarean delivery among live births to AYA women. Prevalence of these outcomes in women diagnosed with thyroid cancer during pregnancy was near identical to women without cancer, whereas prevalence was much higher in AYA women diagnosed with

Table 4. Factors associated with preterm birth, low birth weight, and cesarean delivery among live singleton births to adolescent and young adult women diagnosed with cancer during pregnancy

Factor	Preterm birth[a] (n = 1261)	Low birth weight[b] (n = 1245)	Cesarean delivery[c] (n = 1257)
	aPR[d] (95% CI)	aPR[d] (95% CI)	aPR[d] (95% CI)
Maternal age, y[e]			
15-19	1.07 (0.78 to 1.47)	1.19 (0.88 to 1.63)	0.81 (0.59 to 1.11)
20-24	1.15 (0.91 to 1.44)	1.18 (0.98 to 1.41)	0.84 (0.70 to 1.01)
25-29	0.98 (0.79 to 1.21)	0.99 (0.84 to 1.17)	0.93 (0.80 to 1.07)
30-34	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
35-39	1.12 (0.91 to 1.38)	0.96 (0.80 to 1.14)	1.16 (1.01 to 1.34)
Race and ethnicity			
Hispanic, any race	0.95 (0.81 to 1.12)	1.08 (0.94 to 1.24)	1.01 (0.89 to 1.14)
Non-Hispanic Asian or Pacific Islander	0.87 (0.58 to 1.30)	0.98 (0.70 to 1.35)	0.99 (0.73 to 1.33)
Non-Hispanic Black	0.88 (0.68 to 1.14)	1.03 (0.85 to 1.25)	0.97 (0.80 to 1.18)
Non-Hispanic White	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Non-Hispanic Other[f]	0.80 (0.25 to 2.59)	0.96 (0.43 to 2.14)	1.43 (0.85 to 2.42)
Trimester of diagnosis			
First trimester	1.06 (0.84 to 1.33)	0.92 (0.77 to 1.09)	0.96 (0.83 to 1.12)
Second trimester	1.15 (0.98 to 1.35)	1.01 (0.88 to 1.15)	1.03 (0.91 to 1.16)
Third trimester	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Cancer type			
Breast	2.60 (1.67 to 4.03)	1.61 (1.24 to 2.09)	1.07 (0.86 to 1.33)
Central nervous system	4.16 (2.43 to 7.13)	1.85 (1.26 to 2.72)	1.84 (1.39 to 2.44)
Genitourinary	2.63 (1.20 to 5.73)	1.42 (0.81 to 2.46)	1.18 (0.73 to 1.91)
Gastrointestinal	5.29 (3.39 to 8.26)	2.39 (1.72 to 3.32)	1.53 (1.14 to 2.06)
Gynecologic	4.14 (2.72 to 6.31)	1.97 (1.54 to 2.52)	1.74 (1.44 to 2.11)
Head and neck	3.69 (1.93 to 7.04)	1.88 (1.19 to 2.99)	1.18 (0.74 to 1.87)
Leukemias	3.91 (2.48 to 6.16)	1.80 (1.33 to 2.44)	1.44 (1.09 to 1.89)
Lymphomas	2.78 (1.74 to 4.44)	1.57 (1.17 to 2.11)	1.30 (1.00 to 1.69)
Sarcomas	3.48 (2.08 to 5.82)	1.84 (1.31 to 2.58)	1.57 (1.16 to 2.13)
Melanoma and skin	1.10 (0.54 to 2.21)	1.17 (0.81 to 1.68)	0.94 (0.69 to 1.28)
Thyroid	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Other	1.28 (0.70 to 2.36)	1.30 (0.95 to 1.79)	1.24 (0.97 to 1.59)
Year of diagnosis	0.99 (0.97 to 1.00)	1.00 (0.98 to 1.01)	1.00 (0.99 to 1.01)
Received chemotherapy[g]			
Yes	1.82 (1.53 to 2.17)	1.36 (1.17 to 1.58)	1.05 (0.92 to 1.19)
No	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Parity			
Nulliparous	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Primiparous	0.97 (0.82 to 1.14)	0.92 (0.80 to 1.05)	0.92 (0.82 to 1.05)

[a] Adjusted model of preterm birth includes 1261 AYA women (4 missing parity, 6 missing race and ethnicity). aPR = adjusted prevalence ratio; AYA = adolescent and young adult women diagnosed with cancer; CI = confidence interval.
[b] Adjusted model of low birth weight includes 1245 AYA women (4 missing parity, 6 missing race and ethnicity, 16 missing birth weight).
[c] Adjusted model of cesarean delivery includes 1257 AYA women (4 missing parity, 6 missing race and ethnicity, 4 missing delivery type).
[d] All models adjusted for maternal age, race and ethnicity, trimester of diagnosis, cancer type, year of diagnosis, receipt of chemotherapy, and parity.
[e] Maternal age at cancer diagnosis.
[f] Non-Hispanic Other includes American Indian or Alaska Native and "some other race" as coded by North American Association of Central Cancer Registries item #160.
[g] Women missing information on receipt of chemotherapy (n = 143) included in the model as "no"; results unchanged when these women are excluded from the model.

gastrointestinal, CNS, and gynecologic cancers and leukemia during pregnancy. This was the case even after adjusting for surgery and/or chemotherapy, suggesting disease burden may contribute to adverse birth outcomes independent of treatment. For women with gastrointestinal and gynecologic cancers, these findings support the intuition that cancers occurring in the abdominal region and/or affecting organs involved in pregnancy may influence birth outcomes. For example, although cesarean delivery at 37 weeks may be indicated for women diagnosed with gynecologic cancers to facilitate hysterectomy, these women were nonetheless substantially more likely than women with thyroid cancer to deliver before 37 weeks and regardless of receipt of surgery. Higher likelihood of adverse live birth outcomes in women with gastrointestinal cancers is consistent with our prior work establishing a higher risk of stillbirth in survivors of gastrointestinal cancers (20). Factors affecting maternal condition, such as neurologic symptoms in women with CNS tumors or systemic disease in women with leukemia, may also play a role.

We observed associations between receipt of chemotherapy and preterm birth and low birth weight, even when adjusting for cancer type, that warrant further study. Chemotherapy is not recommended during the first trimester but is generally considered safe in the second and third trimesters, though different agents may be recommended than for women who are not pregnant (39,47-49). We did not have information on dates, type, or dose of chemotherapy, and it is therefore not clear if and how these factors may have contributed to preterm birth and low birth weight. For example, women diagnosed in the third trimester or women requiring urgent treatment, such as those with leukemias, may have delivered early to initiate chemotherapy. Additional research is needed to inform clinical practice given limited evidence about the impact of certain chemotherapeutic agents on the developing fetus (18,25,47-49).

Results of our study point to the need for high-quality communication and shared decision making between AYA women and their providers as they must concurrently manage the physical

and psychological burden of cancer, treatment, a high-risk pregnancy, and delivery complications. Shared decision making is especially important in clinically nuanced situations for which the balance between benefits and harms of treatment decisions depend on individual values and preferences (50). In the case of cancer diagnosed during pregnancy, balancing risks of delaying or modifying treatments to protect the fetus vs benefits of beginning cancer treatment as soon as possible to protect the mother depends highly on an AYA woman's values and preferences (51). Shared decision making involves discussing treatment options and supporting a woman's autonomy with a personalized treatment plan, appropriate multidisciplinary team (38,52), and access to reproductive services, including abortion (34), and psychosocial supports (53-55).

To our knowledge, ours is the first population-based study in the United States—and with the largest sample of AYA women to date—to examine birth outcomes of AYA women diagnosed with cancer during pregnancy. We included all singleton live births and stillbirths to AYA women diagnosed with cancer during pregnancy in Texas over a 15-year period, and findings therefore reflect the diverse ages, cancer types, and races and ethnicities of this population. We lacked detailed information on treatment, including information on type, dose, and timing of chemotherapy and receipt of radiation. However, radiation is contraindicated during pregnancy (39), and we expect few AYA women received it during pregnancy. We also lacked information on miscarriages, terminations, and maternal conditions and circumstances associated with adverse birth outcomes (eg, hypertension, psychosocial distress related to cancer, prior birth outcomes, spontaneous or induced preterm birth). Population-based or clinical studies with detailed treatment information are needed to further understand mechanisms contributing to the adverse birth outcomes we observed.

AYA women diagnosed with cancer during pregnancy experience a disproportionate burden of adverse birth outcomes, illustrating the dilemmas they and their providers face in balancing care for cancer and pregnancy. Optimizing outcomes for these women and their families requires shared decision making, sensitive communication, access to legal and safe abortion, multidisciplinary care, and supporting a woman's autonomy to make informed and value-concordant decisions about her body when faced with both pregnancy and cancer.

Data availability

The data underlying this article are provided by the Texas Cancer Registry, Cancer Epidemiology and Surveillance Branch, Texas Department of State Health Services, 1100 West 49th Street, Austin, TX 78756 (www.dshs.texas.gov/tcr); the Texas Birth Defects Epidemiology & Surveillance, Texas Department of State Health Services, 1100 West 49th Street, Austin, TX 78676 (www.dshs.texas.gov/texas-birth-defects-epidemiology-surveillance); and the Center for Health Statistics, Texas Department of State Health Services, 1100 West 49th Street, Austin, TX 78756 (https://www.dshs.texas.gov/chs/).

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Andrea Betts, PhD, MPH (Conceptualization; Methodology; Supervision; Writing—original draft; Writing—review & editing), L. Aubree Shay, PhD, MSW (Writing—original draft; Writing—review & editing), Philip J. Lupo, PhD, MPH (Conceptualization; Funding acquisition; Methodology; Writing—review & editing), Sandi L. Pruitt, PhD, MPH (Conceptualization; Funding acquisition; Methodology; Writing—original draft; Writing—review & editing), Michael E. Roth, MD (Methodology; Writing—review & editing), Marlyn A. Allicock, PhD, MPH (Writing—original draft; Writing—review & editing), Barbara A. Cohn, PhD (Methodology; Writing—review & editing), and Caitlin C. Murphy, PhD, MPH (Conceptualization; Data curation; Formal analysis; Funding acquisition; Methodology; Writing—original draft; Writing—review & editing).

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Conflicts of interest

Dr Betts reports consulting for Substack; Dr Murphy reports consulting for Freenome; Dr Pruitt reports consulting for Pfizer. All other authors have no conflicts of interest to disclose.

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