Fertility Preservation and Financial Hardship among Adolescent and Young Adult Women with Cancer

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ABSTRACT

Background: Financial hardship among adolescents and young adults (AYA) with cancer who receive gonadotoxic treatments may be exacerbated by the use of fertility services. This study examined whether AYA women with cancer who used fertility preservation had increased financial hardship.

Methods: AYA women with cancer in North Carolina and California completed a survey in 2018–2019. Cancer-related financial hardship was compared between women who cryopreserved oocytes or embryos for fertility preservation after cancer diagnosis ($n = 65$) and women who received gonadotoxic treatment and reported discussing fertility with their provider, but did not use fertility preservation ($n = 491$). Multivariable log-binomial regression was used to estimate prevalence ratios and 95% confidence intervals (CI).

Results: Women were a median age of 33 years at diagnosis and 7 years from diagnosis at the time of survey. Women who used fertility preservation were primarily ages 25 to 34 years at diagnosis (65%), non-Hispanic White (72%), and had at least a Bachelor's degree (85%). In adjusted analysis, use of fertility preservation was associated with 1.50 times the prevalence of material financial hardship (95% CI: 1.08–2.09). The magnitude of hardship was also substantially higher among women who used fertility preservation: 12% reported debt of ≥$25,000 versus 5% in the referent group.

Conclusions: This study provides new evidence that cryopreserving oocytes or embryos after cancer diagnosis for future family building is associated with increased financial vulnerability.

Impact: More legislation that mandates insurance coverage to mitigate hardships stemming from iatrogenic infertility could improve access to fertility preservation for young women with cancer.

Introduction

A cancer diagnosis can lead to adverse financial outcomes, especially in the United States, where adults with a history of cancer report higher out-of-pocket medical spending, more debt, and lower net worth compared with adults without cancer (1, 2). Cancer diagnosed as an adolescent or young adult (AYA) can be particularly financially disruptive due to variable insurance coverage and the unique developmental stages across this age spectrum, such as pursuing education and early career building (3). AYA cancer survivors are more likely to report problems paying medical bills; more likely to worry about health care costs; and more likely to delay or forgo medical care because of cost relative to adults with no cancer history (4, 5).

Concurrent with the financial stressors of a cancer diagnosis, AYAs may use costly fertility services if they are at risk of impaired fertility from gonadotoxic cancer treatment (6). Established fertility preservation procedures recommended by the American Society of Clinical Oncology and the National Comprehensive Cancer Network include sperm cryopreservation for men and oocyte or embryo cryopreservation for women (7, 8). Though the cost of sperm cryopreservation is not insignificant, oocyte or embryo cryopreservation is 10 to 30 times the cost ($10,000–$15,000)—not including storage and future treatment cycles to attempt pregnancy—contributing to a greater financial burden on women who want to preserve their fertility (9). These costs are borne out of pocket by many women with cancer given the lack of mandated insurance coverage for such procedures in most states across the United States (10–12).

For young women who have not started or completed family building at the time of their diagnosis, preserving fertility can result in financial and psychosocial stressors that add to those already present from a cancer diagnosis (6, 13). The combined burdens of cancer and a potential loss of fertility due to gonadotoxic treatment can lead to anxiety and distress (13). However, no studies to date have quantitatively assessed the extent to which fertility preservation may contribute to financial stress. In this study, we examined whether AYA women with cancer who used fertility preservation had increased financial hardship.

Materials and Methods

Study population

Women who were diagnosed with cancer as an AYA (ages 15–39 years) in North Carolina (2004–2015) or California (2004–2016) were invited to complete a survivorship survey in 2018–2019. Women were identified from the North Carolina Central Cancer Registry, or from

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Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

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the Kaiser Permanente Northern or Southern California (KPNC or KPSC) cancer registries. Eligible women were diagnosed with breast cancer, thyroid cancer, melanoma, gynecologic (cervical, ovarian, or uterine) cancer, or lymphoma—the five most common AYA cancers in women (14); and were alive and 18 years or older in 2018. KPNC and KPSC participants had to be enrolled in a KP health plan at the time of survey invitation. Cancer types were classified using the AYA Site Recode/World Health Organization 2008 definitions based on the International Classification of Diseases for Oncology, Third Edition (15). This study was approved by the Institutional Review Boards (IRB) at each study site.

Survey development and invitation

The survivorship survey was a 130-item online questionnaire assessing the effects of cancer diagnosis and treatment on life after diagnosis. Survey items were included in consultation with oncologists, epidemiologists, psychiatrists, and other public health experts. Cognitive interviews with nine AYA women with cancer in North Carolina were conducted to ensure adequate item clarity and comprehension. Eligible women ($n = 13{,}132$) were mailed invitation letters to complete the survey; reminder letters were sent to women who had not responded after 3 weeks. Women who completed the survey ($n = 1{,}679$) were entered into a drawing for one of 40 $50 Amazon gift cards (respondents from KPNC were ineligible for the drawing per IRB requirements). Additional details regarding the survey have been published previously (16).

Exposure, outcome, and covariate assessment

Use of fertility preservation was self-reported "freezing embryos or eggs after your diagnosis but before starting cancer treatment that may harm fertility (e.g.: chemotherapy)," or "after you completed treatment for cancer." The latter group is not typically considered to have used "fertility preservation" because cryopreservation occurred after cancer treatment (potentially gonadotoxic or not) but are included here given that these women are still relevant in understanding the financial hardship of cryopreserving oocytes or embryos after cancer diagnosis. During the years of cancer diagnoses included in this analysis (2004–2016), cryopreservation of oocytes or embryos was the only recommended, nonexperimental method of fertility preservation for women (7). The primary referent group included women who received potentially gonadotoxic cancer treatment—chemotherapy for any cancer, radiation for gynecologic cancers or lymphoma, or surgery for gynecologic cancers—and who also discussed fertility with their health care provider ("after diagnosis, but before you started treatment, did you ever have a discussion with a health care provider about the effect cancer treatment could have on your future fertility or ability to have children?"), but never used fertility preservation (before or after diagnosis).

Material financial hardship was defined as borrowing money, incurring debt, or filing for bankruptcy because of cancer, its treatment, or the lasting effects of that treatment. Psychologic financial hardship was defined as worrying about paying medical bills related to cancer. These survey items were from the Medical Expenditure Panel Survey Experiences with Cancer supplement and had undergone prior cognitive testing (17).

Education, employment, marital status, caregiving roles, and health insurance were self-reported in the survey. Age and year of diagnosis, cancer type, and SEER summary stage were obtained from the North Carolina Central Cancer Registry or the KPNC or KPSC cancer registries. Race and ethnicity and cancer treatment were obtained from both self-report in the survey and cancer registry data. Race and ethnicity are social constructs and interpreted in analysis as one factor that may influence a woman's access to fertility preservation and her financial vulnerability after cancer diagnosis due to structural inequities in health care and economic power (18).

Statistical analysis

Women who either used fertility preservation after cancer diagnosis ($n = 65$), or received gonadotoxic cancer treatment and discussed fertility with their health care provider but did not use fertility preservation ($n = 491$) were compared in primary analysis (**Fig. 1**). Log-binomial regression was used to estimate prevalence ratios (PR) and 95% CIs for material and psychologic financial hardship. Confounders were identified *a priori* using directed acyclic graphs and included state, age at diagnosis, cancer type, stage, cancer treatment, race and ethnicity, education, health insurance at diagnosis, marital status at diagnosis, and caregiving for children at diagnosis. Because of lack of model convergence, health insurance could not be included as a covariate (all women who used fertility preservation had private insurance), and women with melanoma ($n < 5$) or thyroid cancer ($n < 5$) were excluded. Effect measure modification on the multiplicative scale by each of the included covariates was assessed by examining overlap in subgroup-specific 95% CIs and the *P* value for interaction. Modification analysis was exploratory only given the small subgroup sample sizes.

Sensitivity analysis

Using broad covariate categorization, the fully adjusted model lacked positivity (i.e., there were cell sizes of zero in the fertility preservation group when the data were stratified by all combinations of theoretical confounders; ref. 19). Given this nonpositivity, in addition to the full model, we present estimates for two reduced models. First, reduced model 1 in which covariates were selected one at a time based on their influence to the model (i.e., the largest percent change in the PR). The first covariate was included on the basis of its influence relative to the unadjusted model; the second covariate was included on the basis of its influence relative to the model containing the first covariate, and so forth. All models were restricted to the same sample as the full model ($n = 525$), which excluded women with missing covariate data and women with melanoma or thyroid cancer. Covariate selection continued until positivity was violated. Covariates in reduced model 1 for material hardship included state and caregiving for children. Covariates in reduced model 1 for psychologic hardship included state, age at diagnosis, and race and ethnicity. Second, reduced model 2 included the maximum number of theoretical confounders without violating positivity; every combination of confounders was examined, adding one variable at a time until the model lacked positivity. The maximum number of confounders that could be included was three, which was achieved in four different adjustment sets: (i) state, age at diagnosis, and stage; (ii) state, cancer type, and race and ethnicity; (iii) state, age at diagnosis, and race and ethnicity; and (iv) state, education, and marital status.

In addition, women who used fertility preservation after cancer diagnosis were compared with two different referent groups to assess the referent group's influence on the effect estimates (**Fig. 1**). Referent group 2 included women who received gonadotoxic treatment and reported not having completed their desired family size at diagnosis, or were unsure ["when you were diagnosed with cancer, had you completed your desired family size [had as many children as you hoped to have)?"], but did not use fertility preservation ($n = 431$). Referent

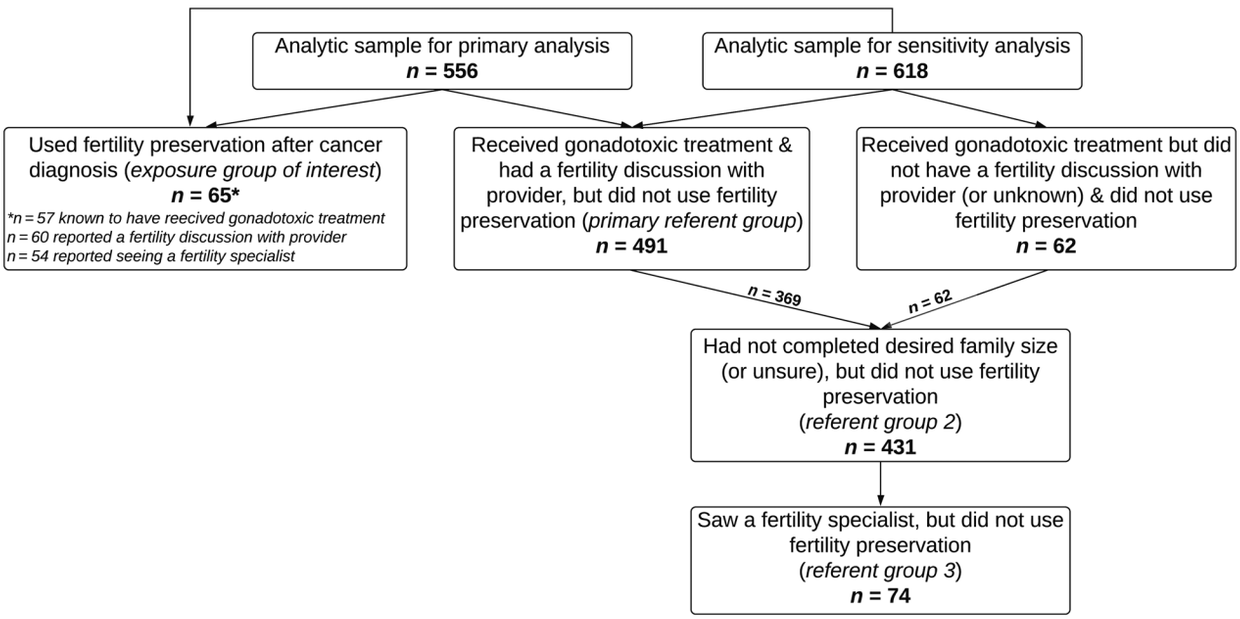

Figure 1.
Study participant flow diagram showing the selection of participants for primary analysis and sensitivity analysis, including the selection of the exposed group of interest and referent groups.

group 3 included women who received gonadotoxic treatment and saw a fertility specialist after cancer diagnosis ("after diagnosis, but before you started treatment, did you see a fertility specialist to talk about fertility preservation?"; vs. only discussing fertility with their provider, as in the primary referent group) but did not use fertility preservation ($n = 74$). The primary referent group and referent groups 2 and 3 were identified *a priori* as the most relevant comparator groups, given that these women were potentially at risk of impaired fertility and expressed some form of interest in fertility after cancer. Effect estimates for analyses with referent groups 2 and 3 include the unadjusted model, the full theoretical model which lacked positivity, and reduced model 1 which included covariates in order of magnitude of influence on the effect estimate until nonpositivity occurred. Analyses were conducted using SAS version 9.4.

Data availability

The data underlying this article cannot be shared publicly due to the privacy of individuals that participated in the study. The corresponding author can be contacted regarding sharing of a deidentified dataset with appropriate IRB approval.

Results

Study sample characteristics

Primary analysis included 556 women who either used fertility preservation after cancer diagnosis or did not use fertility preservation but received gonadotoxic treatment and discussed fertility with their health care provider (**Table 1**). Overall, 55.8% of women were diagnosed in North Carolina and 44.2% were diagnosed in California. Women were a median age of 33 years at diagnosis and 7 years from diagnosis at the time of the survey (range: 3–15 years). The majority of women were diagnosed with breast cancer (54.3%), followed by lymphoma (23.7%) and gynecologic cancer (20.5%). Few women were diagnosed with thyroid cancer ($n < 5$) or melanoma ($n < 5$).

The fertility preservation group had a greater proportion of women who were younger (40.0% were ages ≤29 years vs. 24.4% in the no fertility preservation group); diagnosed in more recent calendar years (63.1% were diagnosed in 2013–2016 vs. 42.4% in the no fertility preservation group); were non-Hispanic Asian (18.5% vs. 6.9%); had a Bachelor's degree or higher (84.6% vs. 70.8%); were employed at diagnosis (92.3% vs. 81.8%); and were never married at diagnosis (32.3% vs. 22.0%). No women who used fertility preservation were non-Hispanic Black (vs. 8.4% in the referent group), or were uninsured or insured with nonprivate insurance (vs. 8.6% in the referent group). The type of fertility preservation used was roughly evenly distributed: 53.8% of women used embryo cryopreservation and 49.2% used oocyte cryopreservation (two women reported both embryo and oocyte cryopreservation).

Financial hardship overall and by use of fertility preservation

Overall, 28% of women reported any cancer-related material financial hardship (36.9% among the fertility preservation group and 27.3% among the no fertility preservation group; **Table 2**). Material hardship included borrowing money or going into debt or filing for bankruptcy because of cancer. In the fully adjusted model, use of fertility preservation was associated with 1.50 times the prevalence of material financial hardship compared with the primary referent group (95% CI: 1.08–2.09). The magnitude of hardship was substantially higher among women who used fertility preservation: 12% reported debt of ≥$25,000, compared with 5% in the referent group. No differences were observed in the prevalence of psychologic financial hardship in the fully adjusted model (52% in both groups; fully adjusted PR = 1.04, 95% CI: 0.82–1.34).

Effect modification was examined by several variables of interest (**Table 3**); however, subgroup sample sizes were small and thus these

Table 1. Sample characteristics of AYA women diagnosed with cancer in North Carolina and California, 2004–2016, overall and by use of fertility preservation ($n = 556$).

	Overall, $n = 556$		Used FP, $n = 65$		Fertility discussion but no FP,[a] $n = 491$	
	n	%[b]	*n*	%[b]	*n*	%[b]
State						
North Carolina	310	55.8	27	41.5	283	57.6
California (KPNC/KPSC)	246	44.2	38	58.5	208	42.4
Mean age at survey, years (SD)	39.7	(6.2)	36.9	(4.9)	40.1	(6.3)
Median age at diagnosis, years (IQR)	33.0	(7.0)	31.0	(8.0)	34.0	(7.0)
Age at diagnosis, years						
15–24	51	9.2	6	9.2	45	9.2
25–29	95	17.1	20	30.8	75	15.3
30–34	181	32.5	22	33.8	159	32.4
35–39	229	41.2	17	26.2	212	43.2
Year of cancer diagnosis						
2004–2006	82	14.7	5	7.7	77	15.7
2007–2009	110	19.8	6	9.2	104	21.2
2010–2012	115	20.7	13	20.0	102	20.8
2013–2016	249	44.8	41	63.1	208	42.4
Cancer type[c]						
Breast	302	54.3	38	58.5	264	53.8
Lymphoma	132	23.7	14	21.5	118	24.0
Gynecologic (cervical, uterine, ovarian)	114	20.5	9	13.8	105	21.4
Thyroid	<5	<0.9	<5	<7.7	<5	<1.0
Melanoma	<5	<0.9	<5	<7.7	<5	<1.0
SEER summary stage[c]						
In situ	<5	<0.9	<5	<7.7	<5	<1.0
Localized	236	44.2	31	47.7	205	43.7
Regional	252	47.2	30	46.2	222	47.3
Distant	44	8.2	<5	<7.7	40	8.5
Unknown	22	4.0	0	0	22	4.5
Cancer treatment[c]						
Any chemotherapy (with or without radiation)	457	82.2	52	80.0	405	82.5
Radiation without chemotherapy, or surgery only	99	17.8	13	20.0	86	17.5
Race and ethnicity						
Hispanic	68	12.2	6	9.2	62	12.6
Non-Hispanic Asian	46	8.3	12	18.5	34	6.9
Non-Hispanic Black	41	7.4	0	0	41	8.4
Non-Hispanic White	385	69.2	47	72.3	338	68.8
Non-Hispanic all other races[d]	16	2.9	0	0	16	3.3
Education						
High school graduate or less	27	4.9	0	0	27	5.5
Some college or associate degree	126	22.7	10	15.4	116	23.7
≥Bachelor's degree	402	72.4	55	84.6	347	70.8
Unknown	1	0.2	0	0	1	0.2
Employment status at diagnosis						
Employed (full- or part-time)	460	83.0	60	92.3	400	81.8
Not employed	94	17.0	5	7.7	89	18.2
Unknown	2	0.4	0	0	2	0.4
Marital status at diagnosis						
Married or living with partner	402	72.3	44	67.7	358	72.9
Never married	129	23.2	21	32.3	108	22.0
Divorced, separated, or widowed	25	4.5	0	0	25	5.1
Caregiver for child(ren) at diagnosis						
Yes	236	42.4	8	12.3	228	46.4
No	320	57.6	57	87.7	263	53.6
Health insurance at diagnosis[c]						
Any private insurance	514	92.4	65	100.0	449	91.4
Military or Veteran's Benefits	<5	<0.9	0	0	<5	<1.0
Medicaid or other public assistance program	17	3.1	0	0	17	3.5
Other insurance, not otherwise specified	<5	<0.9	0	0	<5	<1.0
Not insured	22	4.0	0	0	22	4.5

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Table 1. Sample characteristics of AYA women diagnosed with cancer in North Carolina and California, 2004–2016, overall and by use of fertility preservation ($n = 556$). (Cont'd)

	Overall, $n = 556$		Used FP, $n = 65$		Fertility discussion but no FP,[a] $n = 491$	
	n	%[b]	*n*	%[b]	*n*	%[b]
Type of fertility preservation[e]						
Oocyte cryopreservation	32	5.8	32	49.2	–	–
Embryo cryopreservation	35	6.3	35	53.8	–	–

Abbreviations: FP, fertility preservation; IQR, interquartile range; KPNC, Kaiser Permanente Northern California; KPSC, Kaiser Permanente Southern California; SD, standard deviation.

[a]Women who discussed fertility with their health care provider and also received gonadotoxic treatment, which included chemotherapy for any cancer; radiation for gynecologic cancers and lymphoma; or surgery for gynecologic cancers.

[b]Percentages exclude missing values.

[c]Exact numbers not reported, or categories were combined, because the North Carolina Central Cancer Registry required cells <5 to be suppressed.

[d]Non-Hispanic all other races include American Indian or Alaska Native, other race not otherwise specified, and multiracial.

[e]Two women reported both oocyte and embryo cryopreservation.

observations should be interpreted as exploratory only. Using fertility preservation was associated with higher likelihood of material hardship for women diagnosed in California or at older ages, and for those who reported not being a caregiver for children. Women diagnosed with gynecologic cancers also had an increased prevalence of material hardship in association with use of fertility preservation. No suggestions of effect modification were observed for psychologic hardship.

Sensitivity analysis

In analyses to address the nonpositivity in the fully adjusted model, results remained similar across different reduced models (**Table 4**). For material hardship, PRs ranged from 1.49 to 1.65 (vs. 1.39 in the unadjusted model and 1.50 in the fully adjusted model), with all 95% CIs excluding the null value. For psychologic hardship, PRs ranged from 1.03 to 1.14 (vs. 1.00 in the unadjusted model and 1.04 in the fully adjusted model), with all 95% CIs including the null value.

In analyses to assess the influence of the referent group on the observed associations, results remained substantively similar (Supplementary Tables S1A and S1B). Compared with women who received gonadotoxic treatment and reported that their family size was not complete at diagnosis, or were unsure (referent group 2), or compared with women who received gonadotoxic treatment and saw a fertility specialist (referent group 3), fertility preservation was associated with increased material hardship: PRs (95% CIs) ranged from 1.28 (0.91–1.81) in the unadjusted model with referent group 2 to 1.67 (1.04–2.70) in the reduced model with referent group 3. No differences were observed between women who used fertility preservation and either referent group for psychologic hardship.

Discussion

This analysis provides new evidence that cryopreserving oocytes or embryos after cancer diagnosis is associated with increased material

Table 2. Prevalence of cancer-related financial hardship by use of fertility preservation among a sample of AYA women diagnosed with cancer in North Carolina and California, 2004–2016 ($n = 556$).

	Used FP, $n = 65$		Fertility discussion but no FP,[a] $n = 491$		Unadjusted PR[b] (95% CI)	Fully adjusted PR[c] (95% CI)
	n	%	*N*	%		
Material financial hardship[d]	24	36.9	134	27.3	1.39 (0.99–1.97)	1.50 (1.08–2.09)
Borrowed money or went into debt	24	36.9	128	26.1	—	—
<$10,000	6	9.2	55	11.2	—	—
$10,000–$24,999	9	13.8	41	8.4	—	—
≥$25,000	8	12.3	25	5.1	—	—
Filed for bankruptcy[e]	<5	<7.7	13	2.6	—	—
Psychologic financial hardship[f]	34	52.3	256	52.1	1.00 (0.78–1.28)	1.04 (0.82–1.34)

Abbreviations: CI, confidence interval; FP, fertility preservation; PR, prevalence ratio.

[a]Women who discussed fertility with their health care provider and also received gonadotoxic treatment, but did not use fertility preservation.

[b]Unadjusted models are restricted to the same sample as the full model (i.e., excluding women with missing covariate data and women with melanoma or thyroid cancer); $n = 61$ included in the FP group and $n = 464$ included in the no FP group.

[c]The fully adjusted model excludes women who were missing data for any model covariates and women with melanoma ($n < 5$) or thyroid cancer ($n < 5$) due to lack of model convergence; $n = 61$ included in the FP group and $n = 464$ included in the no FP group. Covariates included in the fully adjusted model were study state, age group at diagnosis, cancer type, SEER summary stage, cancer treatment, race and ethnicity, education, marital status at diagnosis, and caregiving for children at diagnosis.

[d]Cancer-related material financial hardship is defined as borrowing money, going into debt, or filing for bankruptcy because of cancer or its treatment.

[e]Exact numbers not reported because the North Carolina Central Cancer Registry required cells <5 to be suppressed.

[f]Cancer-related psychologic financial hardship is defined as worrying about medical bills related to cancer.

Table 3. Exploratory assessment of effect modification for the association between fertility preservation use and cancer-related financial hardship among a sample of AYA women diagnosed with cancer in North Carolina and California, 2004–2016 ($n = 556$).

	Sample sizes		Material financial hardship[a]		Psychologic financial hardship[b]	
	Used FP ($n = 65$)	Fertility discussion but no FP ($n = 491$)	PR (95% CI)[c]	$P_{interaction}$	PR (95% CI)[c]	$P_{interaction}$
State						
North Carolina	27	283	1.32 (0.87–2.01)	—	1.08 (0.87–1.34)	—
California (KPNC/KPSC)	38	208	1.94 (1.07–3.52)	0.30	1.37 (0.83–2.26)	0.39
Age at diagnosis, years						
15–29	26	120	1.05 (0.56–2.00)	—	0.92 (0.63–1.36)	—
30–34	22	159	1.38 (0.75–2.54)	0.56	1.10 (0.73–1.66)	0.55
35–39	17	212	1.75 (1.01–3.04)	0.24	0.93 (0.55–1.57)	0.98
Cancer type[d]						
Breast	38	264	1.44 (0.97–2.14)	—	1.09 (0.81–1.46)	—
Lymphoma	14	118	0.56 (0.15–2.10)	0.18	0.83 (0.44–1.56)	0.44
Gynecologic (cervical, uterine, ovarian)	9	105	2.65 (1.33–5.30)	0.13	1.08 (0.59–2.00)	0.98
SEER summary stage						
In situ or localized	31	207	1.53 (0.90–2.61)	0.49	1.04 (0.72–1.50)	0.65
Regional or distant	34	262	1.19 (0.75–1.89)	—	0.92 (0.66–1.29)	—
Race and ethnicity						
Non-Hispanic White	47	338	1.34 (0.91–1.96)	—	1.06 (0.83–1.36)	—
All other races and ethnicities[e]	18	153	1.33 (0.59–2.97)	0.98	0.71 (0.33–1.53)	0.32
Education						
<Bachelor's degree	10	143	1.38 (0.71–2.65)	0.85	1.18 (0.77–1.81)	0.54
≥Bachelor's degree	55	347	1.48 (0.98–2.23)	—	1.00 (0.75–1.34)	—
Marital status at diagnosis						
Married or living with partner	44	358	1.37 (0.74–2.52)	—	0.85 (0.61–1.19)	—
Not married	21	133	1.34 (0.88–2.06)	0.96	1.36 (0.96–1.93)	0.06
Caregiver for child(ren) at diagnosis						
Yes	57	263	1.14 (0.46–2.84)	—	1.26 (0.73–2.19)	—
No	8	228	1.64 (1.09–2.47)	0.47	0.94 (0.71–1.24)	0.34

Abbreviations: CI, confidence interval; FP, fertility preservation; KPNC, Kaiser Permanente Northern California; KPSC, Kaiser Permanente Southern California; PR, prevalence ratio.

[a]Cancer-related material financial hardship is defined as borrowing money, going into debt, or filing for bankruptcy because of cancer or its treatment.

[b]Cancer-related psychologic financial hardship is defined as worrying about medical bills related to cancer.

[c]Regression models include the covariate of interest and the interaction term(s) between fertility preservation use and that covariate. Observations with missing data were excluded (SEER summary stage: $n = 22$ excluded from the no fertility preservation group; Education: $n = 1$ excluded from the no fertility preservation group).

[d]The cancer type model excludes women with melanoma ($n < 5$) or thyroid cancer ($n < 5$) due to small sample sizes.

[e]All other races and ethnicities include Hispanic ($n = 68$), non-Hispanic Asian ($n = 46$), non-Hispanic Black ($n = 41$), and non-Hispanic all other races ($n = 16$), which included American Indian or Alaska Native, other race not otherwise specified, and multi-racial.

financial hardship beyond the financial hardship associated with a cancer diagnosis and treatment alone. Overall, more than one in four women in our study sample reported a cancer-related material hardship—borrowing money, going into debt, or filing for bankruptcy because of their cancer. Notably, these adverse financial outcomes were significantly more prevalent among women who used fertility preservation, and the magnitude of material hardship was substantially higher, though no differences between groups were observed for psychologic financial hardship. Our study is the first, to our knowledge, to examine the association between fertility preservation use and financial hardship after cancer diagnosis, and adds new insights regarding identifying and removing the economic barriers around fertility preservation for individuals with cancer. Such data are currently lacking in the literature and challenging to collect for a number of reasons, including that fertility preservation in cases of iatrogenic infertility is not a covered service for the majority of women in the United States, so administrative claims cannot be used to comprehensively capture use of these services.

Assessment of effect measure modification for the association between fertility preservation and financial hardship was limited in our study due to small subgroup sample sizes, but our data suggest areas for further research. Though there was no evidence of modification by race or ethnicity, we could not examine all racial and ethnic categories, and we did observe a lower prevalence of fertility preservation use among women who were Hispanic or non-Hispanic Black. Further exploration of whether fertility preservation after cancer is associated with greater material hardship among racial and ethnic groups that experience socioeconomic inequality would provide needed data to better address these vulnerabilities through clinical or policy interventions. In addition, some variability in the association was observed by cancer site; women with gynecologic cancers had the highest prevalence of material hardship associated with fertility preservation, followed by women with breast cancer, while women with lymphoma appeared to have an inverse association, though estimates are imprecise and should only be interpreted as exploratory. Given the differences in cancer care costs by cancer site (20), further study of cancer site as a potential modifier of the association between fertility preservation and material hardship is warranted.

The prevalence of material and psychologic financial hardship observed among all women in our study (28% and 52%, respectively)

Table 4. Sensitivity analysis to address the nonpositivity in the fully adjusted model on the prevalence of cancer-related financial hardship by use of fertility preservation among a sample of AYA women diagnosed with cancer in North Carolina and California, 2004–2016 ($n = 556$).

	Unadjusted PR[a] (95% CI)	Fully adjusted PR[b] (95% CI)	Reduced model 1, adjusted PR[c] (95% CI)	Reduced model 2a, adjusted PR[d] (95% CI)	Reduced model 2b, adjusted PR[e] (95% CI)	Reduced model 2c, adjusted PR[f] (95% CI)	Reduced model 2d, adjusted PR[g] (95% CI)
Material financial hardship[h]	1.39 (0.99–1.97)	1.50 (1.08–2.09)	1.65 (1.20–2.28)	1.50 (1.08–2.10)	1.49 (1.08–2.04)	1.54 (1.10–2.14)	1.57 (1.15–2.14)
Psychologic financial hardship[i]	1.00 (0.78–1.28)	1.04 (0.82–1.34)	1.08 (0.89–1.32)	1.03 (0.85–1.25)	1.14 (0.95–1.37)	1.08 (0.89–1.32)	1.13 (0.93–1.38)

Abbreviations: CI, confidence interval; FP, fertility preservation; PR, prevalence ratio.

[a]Referent group is women who discussed fertility with their health care provider and also received gonadotoxic treatment, but did not use fertility preservation. Unadjusted models are restricted to the same sample as the full model (i.e., excluding women with missing covariate data and women with melanoma or thyroid cancer); $n = 61$ included in the FP group and $n = 464$ included in the no FP group.

[b]The fully adjusted model excludes women who were missing data for any model covariates and women with melanoma ($n < 5$) or thyroid cancer ($n < 5$) due to lack of model convergence; $n = 61$ included in the FP group and $n = 464$ included in the no FP group. Covariates included in the full adjusted model were study state, age group at diagnosis, cancer type, SEER summary stage, cancer treatment, race and ethnicity, education, marital status at diagnosis, and caregiving for children at diagnosis.

[c]See the Statistical Analysis section for covariate selection methodology for the reduced models. Reduced model 1 for material financial hardship included study state and caregiving for children at diagnosis. Reduced model 1 for psychological financial hardship included study state, age group at diagnosis, and race and ethnicity. The reduced models are restricted to the same sample as the full model ($n = 525$).

[d]Reduced model 2a includes study state, age group at diagnosis, and SEER summary stage.

[e]Reduced model 2b includes study state, cancer type, and race and ethnicity.

[f]Reduced model 2c includes study state, age group at diagnosis, and race and ethnicity.

[g]Reduced model 2d includes study state, education, and marital status at diagnosis.

[h]Cancer-related material financial hardship is defined as borrowing money, going into debt, or filing for bankruptcy because of cancer or its treatment.

[i]Cancer-related psychologic financial hardship is defined as worrying about medical bills related to cancer.

are similar to those reported in recent nationally representative samples from the 2011–2016 Medical Expenditure Panel Survey and the 2013–2016 National Health Interview Survey (NHIS), and consistently higher relative to adults with no cancer history: 25% to 43% of adults ages 18 to 64 years with a history of cancer reported material hardship and 34% to 54% reported psychologic hardship (1, 21). Among adults with a history of AYA cancer from the 2010–2018 NHIS, 37% reported material hardship and 47% reported psychologic hardship (4). In our study, fertility preservation was associated with increased material hardship, but not increased psychologic hardship, which may be related to how that domain within the financial hardship construct is defined, namely, the distress or concern related to costs of *cancer care* (5). Women do experience psychologic distress related to fertility and parenthood after a cancer diagnosis (22–24), as well as feelings of guilt associated with the costs of fertility preservation (25), which are not captured in the broad cancer-related psychologic financial hardship measure used in our study. Given that more than one in four women in our sample experienced material hardship and more than one in two women experienced psychologic hardship, our findings reinforce the need for adequate financial navigation and psychosocial services starting from diagnosis and into posttreatment survivorship—needs that often go unmet for AYAs (26–28).

To help AYAs in relation to financial navigation and financial support after cancer diagnosis, information should be readily available and provided to patients regarding the costs of fertility services—including the costs of fertility preservation and the costs of storing and using frozen oocytes or embryos to attempt pregnancy in the future (sometimes requiring multiple assisted reproductive technology cycles; refs. 6, 13). Such counseling and support for patients, especially those who are interested in future family building, may lead to more informed decision making (29, 30), lower fertility-related decision regret (31), and improved quality of life (32).

In addition, increasing the number of states that mandate insurance coverage for fertility preservation in cases of iatrogenic infertility has the potential to lessen the cooccurring financial hardship of a cancer diagnosis and loss of fertility. At the time of this research, neither state in this analysis had such mandates. As of 2021, 11 states do have mandates that cover individuals with cancer, including California, which enacted a law in 2019. However, who is covered by these laws varies by state; for instance, California's law does not include coverage for individuals with Medi-Cal or other state-sponsored health insurance (11). California's law deems fertility preservation a basic health care service in cases when a covered treatment may cause iatrogenic infertility (11). Classifying fertility preservation as a "basic health care service"—rather than an elective procedure—aligns with the justification for the federal Women's Health and Cancer Rights Act of 1998 that provides reimbursement for breast reconstructive surgery after a mastectomy (10, 33, 34).

The strengths of our study include the relevance of the sampling frame to address the study question: women in our study lived in two states that did not mandate insurance coverage for fertility preservation in cases of iatrogenic infertility during the study years. Our findings highlight the financial vulnerability experienced by women living in the 39 states currently without such mandates (11). In addition, we used high-quality data on cancer-related characteristics obtained from the North Carolina Central Cancer Registry and the KPNC and KPSC cancer registries, including stage and cancer treatment. The survey also encompassed a wide range of survivorship topics, allowing us to measure and account for other relevant covariates, such as caregiving roles.

There are several limitations to our study. We were unable to account for income or other indicators of socioeconomic position aside from education. If women who used fertility preservation had a higher baseline level of financial resources at the time of diagnosis—a hypothesis supported by the higher levels of education observed in the fertility preservation group—our data may underestimate the financial impact of these services after cancer. In addition, we lacked data on the amount of out-of-pocket spending for fertility preservation, and the reported material hardship could not be attributed to specific sources of expenditures or losses of income, be it cancer treatment bills, disrupted employment, fertility services, or otherwise. Our response rate was low (13%), and we have previously shown that response varied by cancer type, race and ethnicity, stage, and cancer treatment (16). We could not assess survey participation by noncancer characteristics, though we hypothesize that women with financial hardship may have been less likely to participate. But given that the survey encompassed a broad range of survivorship topics, it is unlikely that participation was influenced by fertility preservation use. The low response rate contributed to the lack of positivity in our fully adjusted model with *a priori* confounders. However, the reduced models presented in sensitivity analyses were substantively similar to the fully adjusted estimates and support our main findings. Finally, our findings may not be generalizable to women living in states with laws that mandate fertility preservation coverage for individuals with cancer.

Cryopreservation of oocytes or embryos after cancer diagnosis was associated with increased material financial hardship related to cancer. More widespread insurance coverage for fertility preservation could expand access to services, decrease adverse financial outcomes, and improve long-term cancer survivorship.

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Authors' Contributions

C. Meernik: Conceptualization, formal analysis, writing–original draft, writing–review and editing. **J.E. Mersereau:** Writing–review and editing. **C.D. Baggett:** Data curation, writing–review and editing. **S.M. Engel:** Writing–review and editing. **L.M. Moy:** Project administration, writing–review and editing. **N.T. Cannizarro:** Project administration, writing–review and editing. **M. Peavey:** Writing–review and editing. **L.H. Kushi:** Funding acquisition, writing–review and editing. **C.R. Chao:** Funding acquisition, writing–review and editing. **H.B. Nichols:** Conceptualization, funding acquisition, writing–review and editing.

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