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ORIGINAL REPORT

Reproductive Patterns Among Childhood and Adolescent Cancer Survivors in Sweden: A Population-Based Matched-Cohort Study

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A B S T R A C T

Purpose

To compare the probability of a first live birth, age at time of birth, and time between diagnosis/referent date and birth between childhood and adolescent cancer survivors and an age-matched comparison group.

Materials and Methods

A total of 1,206 survivors was included in the study, together with 2,412 age-matched individuals from the general population. A Cox proportional hazards model was used to investigate first live birth after diagnosis/referent date. Data were stratified by sex, age at diagnosis, and diagnostic era (ie, diagnosis before 1988 *v* in 1988 or later).

Results

Overall, the probability of having a first live birth (hazard ratio [HR]) was significantly lower; men had lower HRs than women (HR, 0.65 *v* 0.79). There were no significant differences in the probability of having a first live birth among women diagnosed during adolescence (HR, 0.89), but the HR was lower among women with childhood cancers (HR, 0.47). Among male survivors, the situation was the opposite; men diagnosed during adolescence had lower HRs than survivors of childhood cancer (HR, 0.56 *v* 0.70). Examination of the data from the two diagnostic eras (before 1988 and 1988 or later) shows that the HR increased among female survivors after 1988 (HR, 0.71 *v* 0.90) and decreased among male survivors (HR, 0.72 *v* 0.59). A shorter time had elapsed between diagnosis/referent date and the birth of a first child among both male and female survivors compared with controls. In addition, female survivors were younger at time of birth.

Conclusion

The study demonstrates reduced probability of having a first live birth among cancer survivors diagnosed during childhood or adolescence; men were particularly vulnerable.

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INTRODUCTION

The treatment of cancer in childhood or adolescence is usually effective, and the 5-year survival rate for all cancers combined is approximately 80%.[1] However, modern cancer treatment may affect reproductive ability,[2-4] and survivors of childhood cancer may face fertility problems when they want to start a family. Research shows that childhood and adolescent cancer survivors are less likely to have children compared with their siblings[3-6] and the general population.[7,8] However, the studies to date have focused on treatment regimens, rather than on diagnostic groups, or have included data from survivors diagnosed across a long period of time, in some cases as far back as 1953.

The aim of this study was to investigate the probability of first live birth among childhood and adolescent cancer survivors compared with age-matched comparison group. Secondary aims were to determine age at time of first live birth and the time interval between diagnosis and first live birth.

MATERIALS AND METHODS

Data Sources

In this study, five population-based registries were used. The National Patient Register (NPR)[9] contains information about main and secondary diagnoses as well as procedures for all inpatients in Sweden. By using the NPR, all men and women born between 1973 and

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1977 who had been diagnosed with cancer in childhood or adolescence (age < 21 years) were identified. Data extended back to a time when the International Classification of Diseases (ICD) version 8 and 9 (ICD-8 and ICD-9) were used, so ICD-8 and ICD-9 codes were converted into ICD-10 terminology to obtain clear definitions.[10] However, unusual diagnostic groups in the chosen age span (eg, malignant neoplasm of the breast, lip, or skin, and malignant neoplasm of the digestive, respiratory and intrathoracic organs) were combined to form a single group—other malignant neoplasms—together with malignant neoplasms of ill-defined, secondary, and unspecified sites. Individuals who had received more than one diagnosis were included in each subset of the appropriate diagnostic group. The Total Population Register (TPR)[11] contains demographic information, such as marital status and migration. By using TPR, a comparison group was created from the general population that consisted of two age- and sex-matched individuals per case born on the same day. The individuals in the comparison group (controls) were assigned a referent date corresponding to the date of cancer diagnosis of the cancer survivor. The Swedish Medical Birth Register (MBR)[12] contains information about prenatal, delivery and neonatal care. The MBR does not contain any information about fatherhood, so the Multi-Generation Register,[13] which is a part of the TPR, was used to determine paternal linkage to the birth of a child registered in the MBR. Reproduction after cancer/referent date was defined as linked to the live birth of a child at age 13 years or older after a gestation in which the last menstruation coincided with the first cancer diagnosis/referent date or thereafter. We chose to start follow-up assessments at age 13 years, because that is the approximate average age of menarche in Sweden. Also, the youngest girls who gave birth in Sweden were 13 years old. The same cutoff age was chosen for boys for consistency. In addition, the Swedish Register of Education[14] was used to obtain information about the educational level of participants.

In this study, the term cancer survivor refers to individuals diagnosed with cancer before age 21 years who survived beyond age 13 years. This study was approved by the Regional Ethical Review Board, Linköping, Sweden.

Statistical Analysis

The Pearson χ^2 or t test was used to investigate the relationship between variables. To determine if cancer in childhood or adolescence was related to having a child (measured as the hazard ratio [HR] for first live birth of a child), data were analyzed with a Cox proportional hazards model; age when becoming a parent was the time-dependent variable. The observation time for the first live birth after diagnosis/referent date started at the 13-year birthday or after the date of diagnosis/referent date. All participants were observed until date of death, permanent emigration, first childbirth, or December 31, 2012. Adjustments were made for the age of the mothers of participants at birth, the educational level of participants, the marital status of participants, and birth characteristics (ie, optimal [birthweight > 2,500 g, appropriate size for gestational age and delivered at weeks 37 to 42] *v* nonoptimal: birthweight ≤ 2,500 g, small size for gestational age and preterm]) of participants—all factors shown to have an impact on reproduction.[15,16] The analysis was performed on the whole group and also on each diagnostic group. Treatment strategies have changed over time from more to less intensive treatments, which resulted in reduced mortality.[17] To investigate possible differences in reproduction patterns over time, data were stratified into diagnosis before 1988 or diagnosis in 1988 or later—the same cut point used in a previous Norwegian study.[18] The cut point was set after an investigation of changes in treatment strategies for the most frequent malignancies among young adults (eg, a change to the use of fertility-sparing surgery and avoidance of abdominal radiation). Also, to account for the possible effect of age at time of diagnosis on having a child, data were stratified into two age groups: childhood (< 14 years) and adolescence (≥ 14 to 20 years). All analyses were done in relation to sex. Statistical analyses were conducted in SPSS (SPSS Statistics for Windows, version 22.0; IBM, Armonk, NY).

RESULTS

Out of the 516,576 individuals who were born in Sweden between 1973 and 1977, a total of 1,709 boys and girls were diagnosed with cancer before the age of 21 years (0.33%); of these, 1,206 (71%) were alive, were residents of Sweden after age 13 years, and consequently were included in the study. The majority of the survivors had been diagnosed during childhood (65.7%), and almost half (47.2%) had been diagnosed in 1988 or later (Table 1). Of the sample, 17.6% (n = 115 male and n = 97 female survivors) had received more than one cancer diagnosis. The most common malignancies among both male and female childhood cancer survivors were leukemia and CNS tumors. Among survivors diagnosed during adolescence, the most common malignancies among male survivors were CNS tumors (19%), malignancies in male genital organs (15%), and leukemia (12%); among female survivors diagnosed during adolescence, CNS tumors (18%), Hodgkin disease (15%), and bone tumors (15%) were most common. Compared with controls, survivors had fewer years of education and were less often married.

Reproduction Patterns Among Male Survivors

Among the 654 male survivors, 258 (39%) were linked to at least one live birth after diagnosis. Compared with controls, a shorter time passed between diagnosis/referent day and the first child born, but there were no significant differences in age at time of birth (Table 1). Adjusted models show that the relative probability of having a first live birth after being diagnosed with any form of cancer was 35% lower than the probability among controls (Table 2). Least likely to have a child were those who had been diagnosed with mesothelial and soft tissue tumors and CNS tumors, whereas those diagnosed with malignancies in the urinary tract and the male genitals were as likely to have a child as controls. In the total group, male survivors diagnosed during adolescence were less likely to be linked to a first live birth than those who were diagnosed during childhood (Table 3). However, the HR for first live birth after diagnosis of leukemia was lower among childhood cancer survivors than among those diagnosed during adolescence. Male survivors diagnosed with any cancer in 1988 or later were less likely to be linked to a first live birth than male survivors diagnosed before 1988 (Table 4). However, among those diagnosed with leukemia, the HR for first live birth showed a marked increase with time: the HR was half that of the comparison group with diagnosis before 1988 but was equal to the value for the comparison group with a diagnosis in 1988 or later.

Reproduction Patterns Among Female Survivors

Of the 552 female cancer survivors, 278 (50%) gave birth to at least one live child after diagnosis. A shorter time had elapsed between diagnosis/referent day and birth among female survivors than the comparison group, and the mean age at time of birth was lower among survivors than among controls (Table 1). The adjusted model showed that the HR for first live birth after being diagnosed with any form of cancer was 21% lower than that of controls (Table 2). Three diagnostic groups were associated with reduced HR; malignancy of the eye, CNS tumors, and leukemia.

Table 1. Characteristics of Cancer Survivors and Controls

Characteristic	Men			Women		
	Patients (n = 654)	Controls (n = 1,308)	*P*	Patients (n = 552)	Controls (n = 1,104)	*P*
Mean (SD) age at diagnosis, years	10.7 (6.2)	NA		11.0 (6.1)	NA	
No. (%) by age group at diagnosis						
Childhood (< 14 years)	433 (66.2)	NA		360 (65.2)	NA	
Adolescence (≥ 14-20 years)	221 (33.8)			192 (34.8)		
No. (%) by diagnostic era						
< 1988	352 (53.8)	NA		289 (52.4)	NA	
≥ 1988	302 (46.2)			263 (47.6)		
No. (%) by educational level, years			.003			< .001
9-10	89 (14.6)	118 (9.3)		56 (11.0)	48 (4.5)	
11-13	287 (47.1)	622(49.1)		216 (42.5)	431 (40.3)	
≥ 14	233 (38.3)	526 (41.5)		236 (46.5)	591 (55.2)	
No. (%) by relationship status			< .001			< .001
Married/registered partner	133 (20.3)	398 (30.4)		114 (20.7)	436 (39.5)	
Unmarried	521 (79.7)	910 (69.6)		438 (79.3)	668 (60.5)	
No. (%) with children			< .001			< .001
Yes	258 (39.4)	824 (63.0)		278 (50.4)	875 (75.1)	
No	396 (60.6)	484 (37.0)		275 (49.6)	275 (24.0)	
Age at first live birth, years			.650			< .001
Mean (SD)	30.1 (4.2)	33.0 (3.6)		27.6 (4.9)	32.1 (3.73)	
Range (min to max)	18-39	18-39		16-39	18-39	
Observation time to first live birth, years			< .001			< .001
Mean (SD)	20.0 (7.2)	22.5 (7.5)		16.2 (7.7)	21.0 (7.3)	
Range (min to max)	0-38	0-39		0-35	3-35	

Abbreviations: NA, not applicable; SD, standard deviation.

In the other diagnostic groups, the HR for having a first live birth was equal to that of controls, or the groups were too small or skewed to allow detection of any difference. Diagnosis with any cancer during childhood was associated with a lower HR than diagnosis during adolescence (Table 3). However, those who were diagnosed with leukemia during childhood had a slightly higher HR than those who were diagnosed during adolescence. The HR for first live birth increased with time: the HR was almost one third lower in survivors than controls among those diagnosed before 1988 but was equal to that of the comparison group among those diagnosed in 1988 or later (Table 4).

DISCUSSION

The overall probability of a first live birth was significantly lower among cancer survivors than among the age-matched comparison group. There have been some studies published about population-

Table 2. Adjusted Models for HRs of First Live Birth After Cancer Diagnosis

Cancer site	Women		Men	
	No. of Patients	HR (95% CI)	No. of Patients	HR (95% CI)
Leukemia	118	0.69 (0.49 to 0.96)*	124	0.60 (0.42 to 0.86)†
Brain and CNS	117	0.50 (0.35 to 0.73)‡	108	0.43 (0.28 to 0.67)‡
Bone and articular cartilage	62	0.93 (0.60 to 1.43)	86	0.51 (0.34 to 0.76)†
Hodgkin disease	40	1.24 (0.77 to 1.99)	53	0.75 (0.45 to 1.23)
Genital organs	27	0.93 (0.50 to 1.71)	52	1.04 (0.66 to 1.65)
Non-Hodgkin lymphoma	11	—	45	0.60 (0.35 to 1.03)
Thyroid and other endocrine glands	66	0.99 (0.66 to 1.49)	37	0.85 (0.46 to 1.55)
Mesothelial and soft tissue	30	0.73 (0.38 to 1.40)	37	0.17 (0.07 to 0.40)‡
Urinary tract	49	0.99 (0.64 to 1.54)	35	1.05 (0.60 to 1.82)
Eye	18	—	29	0.71 (0.34 to 1.47)
Other malignant neoplasms	111	1.19 (0.88 to 1.61)	163	0.76 (0.58 to 1.00)
All diagnoses combined	552	0.82 (0.72 to 0.95)†	654	0.68 (0.59 to 0.79)‡

NOTE. Some patients had more than one cancer diagnosis, so numbers for all diagnoses cannot be summarized across individual rows. Em dash represents comparisons for which models were not possible because of small sample size and/or skewed distribution.
Abbreviation: HR, hazard ratio.
*Significant at $P < .05$.
†Significant at $P < .01$.
‡Significant at $P < .001$.

Table 3. Adjusted Models for HRs of First Live Birth After Cancer Diagnosis, Reported by Age at Diagnosis

	Women				Men			
	Childhood Diagnosis		Adolescent Diagnosis		Childhood Diagnosis		Adolescent Diagnosis	
Cancer site	No. of Patients	HR (95% CI)	No. of Patients	HR (95% CI)	No. of Patients	HR (95% CI)	No. of Patients	HR (95% CI)
Leukemia	99	0.76 (0.53 to 1.10)	19	0.55 (0.21 to 1.46)	97	0.52 (0.35 to 0.77)*	27	1.58 (0.60 to 4.18)
Brain and CNS	82	0.46 (0.29 to 0.74)*	35	0.61 (0.33 to 1.12)	67	0.41 (0.23 to 0.72)*	41	0.44 (0.22 to 0.88)†
Bone and articular cartilage	34	1.19 (0.66 to 2.17)	28	—	35	0.82 (0.46 to 1.47)	1	0.30 (0.17 to 0.56)‡
Hodgkin disease	11	3.81 (1.43 to 10.19)*	29	0.89 (0.51 to 1.57)	28	0.85 (0.42 to 1.73)	25	0.68 (0.33 to 1.42)
Genital organs	9	—	18	0.95 (0.46 to 1.97)	19	1.93 (0.87 to 4.26)	33	0.81 (0.44 to 1.49)
Non-Hodgkin lymphoma	9	3.41 (1.11 to 10.49)†	2	—	39	0.57 (0.32 to 1.04)	6	0.35 (0.05 to 2.53)
Thyroid and other endocrine glands	45	0.90 (0.54 to 1.50)	21	1.15 (0.56 to 2.35)	26	0.94 (0.44 to 2.04)	11	0.60 (0.21 to 1.70)
Mesothelial and soft tissue	13	0.61 (0.21 to 1.79)	17	—	12	0.66 (0.20 to 2.14)	25	0.08 (0.02 to 0.27)‡
Urinary tract	43	0.90 (0.56 to 1.44)	6	—	32	1.14 (0.64 to 2.05)	3	—
Eye	18	—	0	—	27	0.74 (0.34 to 1.58)	2	—
Other malignant neoplasms	67	1.31 (0.88 to 1.95)	44	1.17 (0.73 to 1.89)	116	0.94 (0.69 to 1.28)	47	0.46 (0.25 to 0.87)†
All diagnoses combined	360	0.79 (0.66 to 0.95)*	192	0.90 (0.71 to 1.13)	433	0.74 (0.62 to 0.88)*	221	0.59 (0.45 to 0.76)‡

NOTE. Age at diagnosis was dichotomized into childhood (< 14 years) or adolescence (≥ 14-20 years). Some patients had more than one cancer diagnosis, so numbers cannot be summarized across individual rows. Em dash represents comparisons for which models were not possible because of small sample size and/or skewed distribution.

Abbreviation: HR, hazard ratio.

*Significant at $P < .01$.

†Significant at $P < .05$.

‡Significant at $P < .001$.

based reproduction rates among young cancer survivors, but only a few studies focused on survivors of cancer during childhood and adolescence. Three of these are based on data from the Childhood Cancer Survivors Study conducted among individuals diagnosed with cancer at age 20 years or younger.[3-5] The results show the same patterns of lower probability of parenthood among survivors, and the probability to have ever sired a pregnancy or to have had a live birth was lower among men than among women. The Childhood Cancer Survivors Study showed that, among male survivors of childhood cancer, alkylating agents and cisplatin were associated with a decreased likelihood of siring a pregnancy, whereas chemotherapy-specific effects on pregnancy among female survivors were few.[5] Surgery directed at the reproductive organs or nearby systems that does not cause permanent infertility can cause fertility problems, such as erectile or ejaculation dysfunction, obstructions in the oviducts, or damage to the cervix or uterus.[2,19,20] In addition, surgery and radiation therapy in connection with brain tumors may affect the hypothalamic-pituitary-gonadal axis and cause subsequent disruption of pubertal development, menstrual cycles, and spermatogenesis. In addition to its toxic impact on spermatogenesis and the follicle pool, radiation therapy directed at the pelvic area may cause scar tissue that restricts uterine capacity and reduces blood flow, which may lead to implantation problems, miscarriage, and premature labor.[2] However, it is not only the oncologic treatment that may have a negative impact on reproductive rates among cancer survivors. It has also been established that psychosocial aspects, such as fear of cancer recurrence,[21,22] worries about genetic risk for the future child,[21,23,24] and—among female survivors—concerns about health issues in connection with pregnancy and childbirth,[22,25] can have an impact on the motivation of survivors to have children. In addition, research shows that survivors of childhood cancer are less likely to marry[8,26] or have a life partner[27] and, therefore, might be less likely to have children.

This study found a lower HR for first live birth among female survivors who were diagnosed during childhood compared with those who were diagnosed during adolescence (HR, 0.47 *v* 0.89), but this finding is not in line with an earlier Finnish study, in which the reproduction rates were the same in both age groups.[6] The difference could be explained by a higher proportion of childhood cancer survivors with a diagnosis of CNS tumors in this study, because survivors of CNS tumors had the lowest HR among female survivors (HR, 0.43). An additional explanation could be that women diagnosed during adolescence may have had the opportunity to undergo fertility preservation by cryopreservation of oocytes. However, during the time span when the girls were diagnosed (1973 to 1998), this procedure was not common in Sweden, and fertility preservation by cryopreservation of ovarian tissue was even rarer.[28]

Among male survivors, those who were diagnosed during childhood (< 14 years) had a higher HR for first live birth than those who were diagnosed during adolescence (≥ 14 to 20 years; HR, 0.70 *v* 0.56). These findings differ from those reported in two earlier studies, in which adolescent cancer survivors had higher reproduction rates than childhood cancer survivors.[6,8] Sperm banking has been available for at least half a century for pubertal and postpubertal men, whereas the possibilities for prepubertal male patients are limited.[29] Despite this difference, the study showed a lower HR for first live birth among men diagnosed during adolescence. The difference between the age groups could

Table 4. Adjusted HRs of First Live Birth After Cancer Diagnosis Reported by Diagnostic Era

	Women				Men			
	Diagnosed Before 1988		Diagnosed in 1988 or After		Diagnosed Before 1988		Diagnosed in 1988 or After	
Cancer site	No. of Patients	HR (95% CI)	No. of Patients	HR (95% CI)	No. of Patients	HR (95% CI)	No. of Patients	HR (95% CI)
Leukemia	86	0.66 (0.44 to 0.97)*	32	0.80 (0.39 to 1.67)	84	0.48 (0.32 to 0.74)†	40	1.35 (0.67 to 2.74)
Brain and CNS	52	0.38 (0.21 to 0.69)†	65	0.61 (0.38 to 0.98)*	43	0.49 (0.25 to 0.98)*	65	0.41 (0.23 to 0.72)†
Bone and articular cartilage	27	1.45 (0.75 to 2.80)	35	0.74 (0.40 to 1.34)	23	1.01 (0.51 to 1.99)	63	0.36 (0.21 to 0.61)‡
Hodgkin disease	9	4.57 (1.52 to 13.71)†	31	1.00 (0.58 to 1.74)	20	0.68 (0.28 to 1.65)	33	0.77 (0.41 to 1.44)
Genital organs	7	—	20	1.06 (0.54 to 2.09)	12	1.45 (0.44 to 4.71)	40	1.17 (0.68 to 2.01)
Non-Hodgkin lymphoma	8	3.36 (1.03 to 10.92)*	3	—	38	0.61 (0.34 to 1.11)	7	0.24 (0.04 to 1.53)
Thyroid and other endocrine glands	41	0.82 (0.46 to 1.43)	25	1.35 (0.72 to 2.52)	25	0.81 (0.36 to 1.82)	12	0.84 (0.32 to 2.22)
Mesothelial and soft tissue	9	0.89 (0.28 to 2.90)	21	0.66 (0.29 to 1.47)	5	—	32	0.13 (0.05 to 0.33)‡
Urinary tract	41	0.79 (0.48 to 1.30)	8	5.32 (1.52 to 18.59)†	31	1.11 (0.62 to 1.99)	4	—
Eye	18	—	0	—	26	0.80 (0.37 to 1.74)	3	0.21 (0.01 to 4.30)
Other malignant neoplasms	54	1.47 (0.96 to 2.26)	57	1.01 (0.64 to 1.58)	102	1.00 (0.73 to 1.38)	61	0.47 (0.28 to 0.80)†
All diagnoses combined	289	0.75 (0.62 to 0.92)†	263	0.93 (0.76 to 1.13)	352	0.76 (0.63 to 0.91) †	302	0.61 (0.49 to 0.76)‡

NOTE. Some patients had more than one cancer diagnosis, so numbers for all diagnoses cannot be summarized across individual rows. Em dash represents comparisons for which models were not possible because of small sample size and/or skewed distribution.
Abbreviation: HR, hazard ratio.
*Significant at $P < .05$.
†Significant at $P < .01$.
‡Significant at $P < .001$.

be dependent on the distribution of diagnostic groups. In this study, a higher proportion of adolescent men had been diagnosed with mesothelial and soft tissue tumors, which had low HRs for first live birth (0.07).

This study demonstrates large differences in HR for first live birth between groups with different diagnoses. Among the largest diagnostic groups, those with CNS tumors had a low HR among both male and female survivors (HR, 0.39 and 0.48, respectively), similar to previously reported data.[6,30] Treatment of CNS tumors often combines chemotherapy, radiotherapy, and/or surgery, all of which may have a negative impact on fertility. In addition, survivors of CNS tumors are at a higher risk for severe neurocognitive impairment, which is associated with lower educational level, higher unemployment, less independent living,[31] and a higher risk of never getting married[8,26]; these all are factors that may have affect the opportunities to build a family.

Diagnosis of leukemia also was associated with a low HR for first live birth among both male and female survivors (HR, 0.53 and 0.62, respectively). Interestingly, the probability of having children after being treated for leukemia decreased among male survivors and increased among female survivors when diagnostic era was explored; this finding also was reported previously among survivors diagnosed during adolescence or adulthood (age 16 to 45 years).[32] The same pattern was present in the total group of survivors, and it seems that changes in treatment regimens with time have benefitted female survivors more than male survivors. In contrast, an earlier Swedish study among female survivors (age < 44 years) found that pediatric cancer survivors diagnosed before 1980 were more likely to have children than those diagnosed between 1980 and 2001.[7] However, it is possible that the difference between results depended on the difference in the division of diagnostic eras.

This study showed that a shorter time period passed between diagnosis/referent date and first life birth among cancer survivors compared with controls. Also, female survivors were younger when their first live birth occurred. Research has shown that the desire to have children may increase among those who have been diagnosed with cancer[33] and childhood cancer survivors have described how they put greater value in family life than those without a cancer experience do.[24] Also, building a family has been described as a way to restore normality, as a way to connect with others, and as a way to form an identity.[24,33] An additional explanation of the age difference between female survivors and controls could be that the survivors had been informed about the risk of premature menopause and, therefore, decided to have children earlier. Earlier findings are inconsistent about the timing of childbirth among survivors. A study of female survivors ages 0 to 44 years at time of diagnosis[7] found that the probability of having a child increased substantially among childhood and adolescent cancer survivors after the age of 35 years, whereas a study of survivors younger than 21 years at time of diagnosis[5] showed that the probability of pregnancy or live birth was reduced after the age of 30 years among female survivors but not among male survivors.

The major strength of this study was the population-based design, in which a 5-year birth cohort was observed through register linkage. Pediatric cancer care in Sweden is centralized to university hospitals that overall report inpatient care to the NPR to a high degree. However, it is possible that some individuals who were diagnosed with cancer between 1973 and 1986 were not included, because some county councils did not report to the NPR

until 1987. By adjusting for the age of the mothers of participants at birth and for educational level, marital status, and birth characteristics, the analysis could be controlled for factors known to have an impact on reproductive patterns. However, information about other factors that may have an impact on childbirth after cancer, such as worries about genetic risks, pregnancy and childbirth, were lacking; these factors, if included, would have allowed for a deeper analysis of the observed reproduction pattern. The sample consisted of 1,206 cancer survivors, which allowed computation of statistically trustworthy estimates, but some of the diagnostic groups in the stratified models did not reach enough power. Therefore, caution is advised for interpretation of the results. Also, some caution is advised for interpretation of the results about the diagnostic era, because the analysis was confounded by age. The study included all individuals born between 1973 and 1977. The MBR started in 1973, so this determined the start date. To allow the participants to at least approach the end of their reproductive era, 1977 was selected as the end year. All participants were observed until the date of first childbirth or December 31, 2012, so the youngest participants included in this study were 35 years old. It is possible that some individuals who were childless at that point may have had children later, which in turn may have had an impact on the results.

In conclusion, our study demonstrates a reduced HR for first live birth among cancer survivors diagnosed during childhood or adolescence, especially among male survivors and among those diagnosed with CNS tumors. To improve the possibilities for building a family in the future, patients with newly diagnosed cancer and/or parents should be informed about the risk of infertility to make informed decisions about future family planning.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Reproductive Patterns Among Childhood and Adolescent Cancer Survivors in Sweden: A Population-Based Matched-Cohort Study

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