Cancer Causes and Control **13**: 625–635, 2002.

High breast cancer incidence rates among California teachers: results from the California Teachers Study (United States)

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Received 23 October 2001; accepted in revised form 30 March 2002

Key words: breast cancer, cohort study, rate ratio, risk factors, teachers.

Abstract

Objective: To determine risk factor profiles and cancer incidence rates among participants in the California Teachers Study (CTS), a study designed to document high breast cancer incidence rates of California teachers and to investigate emergent hypotheses in the etiology of breast and other cancers.
Methods: The CTS is a prospective study of 133,479 California female teachers and administrators, established in 1995–1996 with members of the California State Teachers Retirement System completing a detailed mailed questionnaire regarding possible risk factors for breast and other cancers. Cancer outcomes were identified by linkage with the California Cancer Registry.
Results: CTS participants have a 51% higher age-standardized invasive breast cancer incidence rate and a 67% higher *in-situ* breast cancer incidence rate than would be expected based on race-specific statewide rates after three years of follow-up. CTS participants also have substantially elevated rates of endometrial cancer (rate ratio, RR = 1.72), ovarian cancer (RR = 1.28), melanoma (RR = 1.59), non-Hodgkin's lymphoma (RR = 1.53), and leukemia (RR = 1.28), but low rates of invasive cervix cancer (RR = 0.53) and lung cancer (RR = 0.66).
Conclusions: CTS members have high rates of several major cancers, particularly breast cancer, and low rates of lung and cervix cancer. Although late age at first birth can explain a portion of the observed excess risk of breast cancer in this cohort, the unique risk factor profile of CTS members may account for much of their higher risk of breast and selected other cancers. The CTS offers a rich resource for future studies of cancer risk and of women's health, in general.

Introduction

Teachers have long been suspected to be at high risk of breast cancer [1, 2]. In 1987 the California Department of Health Services noted a substantial excess mortality from breast cancer in California teachers despite a low overall mortality rate [1]. An excess incidence of breast and selected other cancers was later documented for women employed by the California school systems [2]. In 1995 we initiated a large cohort study to further document this excess risk and to study in greater detail the determinants of breast and other cancers in the cohort. We report here a description of the study's design and implementation to evaluate these questions, a comparison of incidence rates of breast and other cancers among teachers in this study to those of comparable California women, and a description of

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baseline characteristics of the study population including participants' profile of breast cancer risk factors.

Materials and methods

The California Teachers Study (CTS) is a prospective study of 133,479 current and former public school teachers or administrators who participate in the California State Teachers Retirement System (STRS). The initiation of the cohort was supported by the State of California through revenues generated by cigarette taxes for the purpose of supporting breast cancer research. The CTS was developed by a consortium of 11 investigators from the California Department of Health Services; the Northern California Cancer Center; the University of California, Irvine; and the University of Southern California. The CTS was approved by the institutional review board at each of the four participating centers in accord with assurances filed with and approved by the US Department of Health and Human Services.

Establishing the CTS cohort

The CTS cohort is composed of women who were active or retired California teachers or administrators at the time the cohort was established in 1995. STRS members are California public school employees, kindergarten through community college, who teach, are involved in the selection and preparation of instructional materials, or are supervising persons engaged in those activities. All public school employees must pay into and receive retirement benefits through STRS; STRS membership is in effect as long as retirement contributions remain on deposit with the program. STRS members have been employed in approximately 1160 public school districts, community college districts, county offices of education, and state reporting entities in California.

In Fall 1995 we sent a mailed, self-administered questionnaire to 329,684 women who had been professional public school employees and were active members of STRS in 1995 with at least one full year of service in California schools, had recently (within the past 72 months) left the school system, or were retired. STRS printed mailing labels for the recruitment effort so that only those women choosing to join the cohort were identified to the investigators. Two mailings were conducted with approximately 105,000 women responding to the first mailing and 28,000 responding to the second mailing. A total of 133,479 women (approximately 40% of those approached) chose to join the cohort, returning the completed questionnaire and providing identifying and contact information to the CTS investigators. The resulting cohort is well characterized, diverse, and even represents a range of socioeconomic levels, depending in part on spousal income. The cohort includes a broad age range of women who reside in both urban and rural areas and is multiethnic in composition (Table 1); as reflected in Table 2 (which is restricted to women with no personal history of breast cancer), the cohort has a wide range of lifestyle experiences.

The 1995 baseline questionnaire was developed as a collaborative effort among the investigators with each investigator providing candidate questions. Where feasible, phrasing of questions was drawn from established and validated instruments. Questions were reviewed and revised at a series of CTS investigators' meetings. Pilot versions of the instrument were evaluated by selected California epidemiologists, randomly selected teachers at schools in Los Angeles, residents of a retired teachers facility, and staff and other teachers who offered to help with the critiquing process. The resulting 16-page optically-scannable questionnaire included an assessment of a wide variety of experiences and exposures: menstrual and reproductive events, use of hormone replacement therapy (HRT) and oral contraceptives, usual diet during the previous year [3], vitamin supplement and alcohol use, height and weight, family and personal history of cancer and other diseases, smoking and alcohol use, history of physical exercise activity, selected environmental exposures, and history of cancer screening (mammography, breast self-examination and PAP). A validation/calibration study of the baseline dietary assessment and a validation study of self-reported family history of cancer are ongoing; the physical activity section of the questionnaire is being evaluated in a study of women who had previously completed an interview with visual aids where a lifetime history of exercise activities was collected.

The CTS Steering Committee, a collaborative partnership of the 11 investigators from the four participating institutions, manages the CTS. This committee is responsible for the scientific integrity and overall development, direction, management, and analysis of the CTS. The CTS Steering Committee has formed an External Advisory Committee to guide some of its activities. The 12 members who comprise the advisory committee include five internationally recognized experts in cancer epidemiology, three representatives from cancer advocacy groups within California, an oncologist, a breast surgeon, and one representative each from STRS and from the California Teachers Association.

A strong infrastructure for the cohort is maintained through questionnaires mailed approximately biennial-

Table 1. Demographic and other characteristics of 133,479 members of the California Teachers Study cohort at study entry

Characteristic	Frequency (%)
Age at entry (years)	
20–29	5,583 (4.2)
30–39	16,547 (12.4)
40–49	33,494 (25.1)
50–59	31,802 (23.8)
60–69	23,063 (17.3)
70–79	15,948 (11.9)
≥80	7,042 (5.3)
Mean age ± standard deviation	54.1 ± 14.8
Race	
White	115,788 (86.7)
African-American	3,548 (2.7)
Hispanic	5,405 (4.0)
Asian/Pacific Islander	4,563 (3.4)
Other/mixed/not specified	4,175 (3.1)
Current California resident	
No, reside elsewhere in US	8,851 (6.6)
Yes	124,628 (93.4)
Region of residence within California[a]	
Bay Area	15,660 (12.6)
Central	11,806 (9.5)
Desert Sierra	11,229 (9.0)
Los Angeles County	26,207 (21.0)
North	7,920 (6.4)
Orange County	11,689 (9.4)
Sacramento	12,749 (10.2)
San Diego	11,365 (9.1)
Santa Clara	9,510 (7.6)
Tri-County	6,493 (5.2)
Birth place	
California	57,615 (43.2)
Other United States	67,246 (50.4)
Mexico, South and Central America, Caribbean	1,828 (1.4)
Asia/Pacific Islands	1,856 (1.4)
Europe	2,210 (1.7)
Africa/Middle East	316 (0.2)
Other/not specified	2,408 (1.8)
Type of teacher	
Preschool	2,359 (1.8)
Elementary school	68,166 (51.1)
Junior/senior high school	35,656 (26.7)
Pupil services	5,736 (4.3)
Administrative	3,779 (2.8)
Other/multiple roles/not specified	17,783 (13.3)
Years worked in school	
<5	12,642 (9.5)
5–9	22,664 (17.0)
10–14	19,604 (14.7)
15–19	20,815 (15.6)
≥20	56,809 (42.6)
Unknown	945 (0.7)

[a] See Figure 1.

ly, annual newsletters, and annual record linkages for follow-up, including linkage with the statewide, population-based California Cancer Registry.

Cohort follow-up

In addition to the baseline questionnaire two additional questionnaires have been sent to participants. The first biennial questionnaire (Wave II, four pages) was sent in 1997–1998, focusing on exposure to secondhand smoke and medical radiation. It also included self-measurement of waist and hip circumferences and collected additional information on pregnancy history. The questionnaire return rate was 77%. The second biennial questionnaire (Wave III) was mailed in 2000–2001. This 8-page questionnaire focused on perception of stress, social support, and cognition, and also provided updated information on the use of oral contraceptives, hormone replacement therapy, and other medications. The response rate for Wave III is not finalized since the questionnaire collection process is ongoing. Nevertheless, thus far 9091 cohort members who did not reply to the Wave II questionnaire, have replied to the Wave III questionnaire, resulting in an 83.4% response rate to a follow-up questionnaire (either Wave II or Wave III) after consideration of deaths among cohort members.

We mail annual newsletters to CTS members as an integral part of the long-term study plan to help maintain interest and motivation of the study participants, to provide an opportunity to communicate study progress and results, and to maintain a channel of communication between study participants and the research team. The newsletters simultaneously serve as a follow-up tool, both by receipt of address corrections from the post office and by direct notification of name, address, and vital status changes by study participants and their families *via* a detachable postcard. Prior to each newsletter mailing, linkages with the national change of address database and with the California Department of Motor Vehicles database provide useful information for locating cohort members. Linkages with state and national mortality files identify deceased cohort members. Linkages with other files, such as California hospital discharge summaries, provide information on updated addresses, health status, and surgical procedures such as hysterectomy and oophorectomy, and non-cancer outcomes such as hip fractures.

Cancer outcomes are identified through annual linkage with the California Cancer Registry (CCR). The CCR is a population-based, statewide cancer registration system modeled after the National Cancer Institute's Surveillance, Epidemiology, and End Results program. Cancer reporting has been legally mandated in California since 1985; statewide population-based reporting was fully implemented in 1988 with standardized data collection and quality control procedures [4]. The CCR has consistently met the highest standards for

Table 2. Cancer risk factor profile of participants in the California Teachers Study (among 116,927 women with no prior history of breast cancer at baseline who were living in California at cohort entry[a])

Risk factor	No.	Percentage	California women[b]
Family history of breast cancer (first-degree relative)			
No	101,393	86.7	
Yes	13,789	11.8	
Adopted	1,745	1.5	
History of biopsy for benign breast disease			
No	98,798	84.5	
Yes	18,126	15.5	
Age at menarche (years)			
≤10	8,155	7.1	
11	17,714	15.4	
12	31,506	27.4	
13	33,882	29.4	
14	14,498	12.6	
≥15	9,359	8.1	
Mean age ± standard deviation (SD)	12.5 ± 1.5		12.9
Number of term pregnancies			
Never pregnant	23,768	20.7	13.7%
No term pregnancy	6,990	6.1	2.8%
1	18,139	15.8	83.5%
2	37,524	32.7	
3	18,449	16.1	
4	6,646	5.8	
≥5	3,120	2.7	
Mean ± SD (among women with a term pregnancy)	2.3 ± 1.1		2.7
Age at first term pregnancy (years)			
<20	4,318	5.1	
20–24	25,783	30.7	
25–29	34,066	40.6	
30–34	14,989	17.9	
>35	4,722	5.6	
Mean age ± SD (among women with a term pregnancy)	26.4 ± 4.7		23.7
Months of breast-feeding (parous women only)			
0	18,953	22.7	
<6	20,347	24.3	
6–11	15,750	18.8	
12–23	16,570	19.8	
≥24	11,970	14.3	
Mean months ± SD (among women who ever breast-fed)	14.4 ± 13.0		
Duration of oral contraceptive use (years)			
Never used	36,352	33.0	
<5	33,905	30.8	
5–9	23,266	21.1	
10–14	11,188	10.2	
≥15	5,513	5.0	
Mean years ± SD (among women who ever used oral contraceptives)	6.4 ± 5.2		
Menopausal status			
Premenopausal	41,824	40.2	
Perimenopausal	2,804	2.7	
Postmenopausal	59,399	57.1	
Ever hysterectomy			
No	87,409	76.4	
Yes	26,931	23.6	28.9%
Ever oophorectomy			
No	95,936	82.7	
Yes	20,117	17.3	

Table 2. (Continued)

Risk factor	No.	Percentage	California women[b]
Use of hormone replacement therapy (HRT) by postmenopausal women			
Duration of estrogen replacement therapy (years)			
Never used	15,671	26.4	
Ever used	43,728	73.6	51.5%[c]
≤5	18,392	43.7	
>5	23,680	56.3	
Also used a progestin as part of HRT regimen			
No	35,845	60.3	
Yes	23,554	39.7	
Body mass index (weight (kg)/height (m^2))			
<20	12,041	11.1	53.3%
20–24.9	54,795	50.3	
25–27.4	16,088	14.8	46.7%
27.5–29.9	10,952	10.1	
≥30	15,066	13.8	
Mean ± SD	24.8 ± 5.0		25.7
Average hours per week of exercise in the past 3 years			
None	35,792	30.8	
<1	12,713	10.9	
1–3	35,254	30.4	
≥4	32,392	27.9	
Mean hours/week among those who exercise ± SD	4.2 ± 4.1		
Alcohol consumption in past year (g/day)			
None	35,061	33.3	
<10	38,442	36.5	
10–19	22,939	21.8	
≥20	8,846	8.4	
Mean g/day among consumers ± SD	11.4 ± 9.8		
Smoking status			
Never smoked	75,296	66.9	55.3%
Former smoker	31,539	28.0	28.9%
Current smoker	5,669	5.0	15.8%

[a] Totals vary because of missing values for some women.
[b] Selected data available for comparable California women: percentages and means adjusted to the race and age distribution of the California Teachers cohort.
[c] Age- and race-adjusted percentage of women aged 40 years or older in California.

data quality and completeness [5]. Extensive auditing procedures have demonstrated that cancer reporting in California is over 95% complete for all cancers combined, and even higher for those cancers for which patients nearly always receive hospital-based diagnosis or treatment. An extremely important design advantage to conducting this cohort study within California is that, as long as participants remain California residents, they can be considered in active follow-up for cancer outcomes due to the high-quality statewide coverage provided by the CCR, whether or not they fill out the biennial questionnaires. At baseline, 93% of the cohort resided in California (Table 1); of those still alive in December 1998, 91.4% were residents of California. Another important advantage of the study, in terms of follow-up potential, is the high degree of motivation for all participants to remain affiliated with STRS.

Cancer incidence rates and risk factors

Cancer incidence rates reported here are based on the first three years of follow-up from date of study entry through 31 December, 1998. Person-months of follow-up were accrued for each participant beginning in the month following receipt of her questionnaire. Women included in each of these analyses had no prior diagnosis of the cancer of interest and were California residents at the beginning of follow-up. Women who moved out of California during follow-up (and prior to any cancer diagnosis) were presumed to have lived in California for one-half of their follow-up duration. We report age-specific and age-standardized (to the 1970 US population) CTS cancer incidence rates and compare these rates to California statewide incidence rates for non-Hispanic white women, as non-Hispanic whites comprise 87% of the cohort. The cancers selected for

evaluation are those for which cohort members provided information on the baseline questionnaire, allowing us to exclude women with a personal history: invasive and *in-situ* breast cancer (overall and by stage); cancers of the endometrium, cervix, ovary, colon and rectum, thyroid, and lung, as well as melanoma, Hodgkin's disease, non-Hodgkin's lymphoma (NHL), and leukemia. In this personal history, lymphomas and leukemias were not further differentiated. We calculated CTS incidence rates for endometrial and cervical cancer among women truly at risk of these cancers (*i.e.*, those with an intact uterus) and among all women irrespective of hysterectomy status, for comparability to the California incidence rates which do not exclude women with hysterectomies from population counts as this information is not available. Similarly, we calculated ovarian cancer incidence rates among women with at least one intact ovary and among all women. Although the California incidence rates include women who may have had a prior diagnosis of the cancer of interest, we excluded such women from the analyses of CTS incidence rates because it is possible that women were more likely to participate in the CTS if they had a prior cancer diagnosis. We also calculated rates specific for non-Hispanic white women in the CTS. However, differences in the observed incidence rates for all CTS members *vs* non-Hispanic white CTS members were slight, and we present only the overall rates.

We have calculated rate ratios (RR) comparing the CTS incidence rates to those for California women, and have estimated 95% confidence limits for the $\log_e$RR. We also provide the distribution of certain breast cancer risk factors (age at menarche, age at and type of menopause, parity, age at first term pregnancy, use of HRT, body weight, and family history of breast cancer) among CTS members with no prior history of breast cancer. For some of these risk factors we present comparison data for California women during the same time period (1996–1998) based on the California Women's Health Survey, the Behavioral Risk Factor Survey, and the California Adult Tobacco Survey, which are ongoing, monthly random-digit-dial telephone surveys of the California adult population conducted by the Department of Health Services. Where survey data are presented they have been adjusted to the age and race distribution of the participants in the CTS.

Results

Table 1 provides a demographic profile of participants in the CTS. Although the cohort represents a broad age range the majority of participants were over age 50 years (58%) at enrollment into the study and 17% were over age 70 years. The cohort is primarily non-Hispanic white (87%), but substantial numbers of African-American, Hispanic, Asian, and Pacific Island women are also cohort members. Reflecting the high historical migration into California, a minority of the cohort (43%) is California-born with 50% born elsewhere in the US. Approximately 78% of the cohort members were elementary or high school teachers for the majority of their careers and over 50% have been employed in the school system more than 15 years. The cohort is distributed throughout California (93%, Figure 1, Table 1) with 43% of the out-of-state members (a total of 7% of the entire cohort) living in the states of Washington, Oregon, Arizona, and Nevada.

A total of 5.3% of the cohort had a personal history of a breast cancer diagnosis prior to responding to the questionnaire. In California the prevalence of breast cancer adjusted to the age and racial/ethnic distribution of the CTS members is slightly lower (4%). In Table 2 we present the distribution of risk factors for breast cancer and smoking status among cohort members who had not been diagnosed with breast cancer at entry into the CTS. Nearly 12% of these cohort members report a first-degree family history of breast cancer. The average age at menarche is 12.5 years; for comparable California women the average age at menarche is 12.9 years. Nearly 21% of the CTS cohort reported never having had a pregnancy; the comparable age- and race-adjusted prevalence for California women is 14%. The average number of live births for parous CTS members was 2.3 compared with 2.7 for comparable California women. On average, CTS members had their first term pregnancy at age 26.4 years; among comparable California women the average age at first term pregnancy is 23.7 years. Among CTS participants, those who had previously borne a child were likely to have breast-fed at some time (nearly 78%), and those who breast-fed averaged 14.4 months of breast-feeding over their lifetime. Thirty-three percent of CTS members have never used oral contraceptives, reflecting the high percentage of women in the upper age groups. Among women under 50 years of age, 85% reported having used oral contraceptives for an average duration of 6.1 years. Among older women, 52% had used oral contraceptives for an average duration of 6.8 years. Fifty-seven percent of the cohort was menopausal. A greater percentage of California women have had a hysterectomy (28.9%) than CTS members (23.6%). Among postmenopausal women, 74% reported using estrogen replacement therapy and among these women nearly 40% have also used a progestin as part of an HRT regimen. Comparable data are not available for California women by menopausal status; however, among

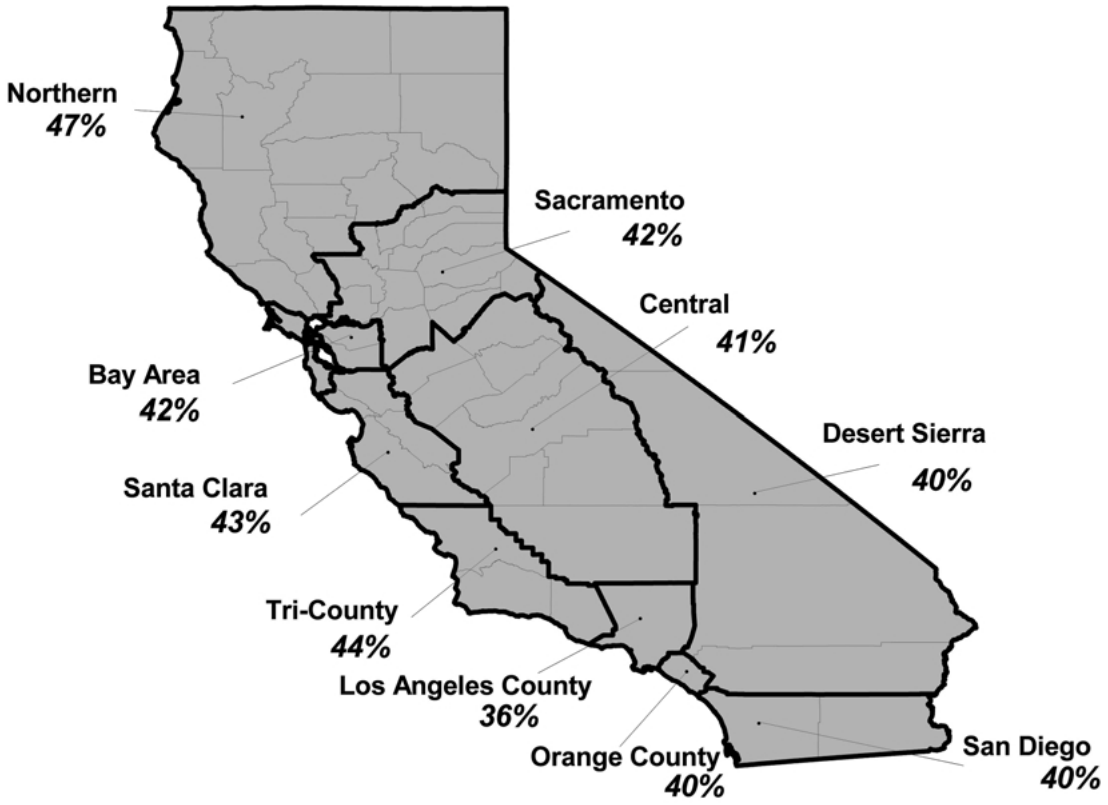

Fig. 1. Proportion of cohort participants living in California who responded by cancer reporting region.

California women who are at least 40 years of age, 51% have used menopausal estrogen replacement therapy. Sixty-one percent of the CTS cohort has a body mass index (weight (kg) divided by height in meters squared) that is less than 25.0 compared with 53% of comparable California women. The mean body mass index of CTS participants is 24.8 kg/m^2, whereas the mean is 25.7 kg/m^2 for comparable women in California. Women in the cohort are fairly active, with 69% participating in regular exercise activity over the past three years. Women who exercise average 4 h of exercise per week. One-third of the cohort reports no alcohol consumption over the past year. Among those who consume alcohol, the average daily consumption is about one drink (11 g of alcohol). Nearly 67% of the CTS cohort have never smoked cigarettes compared with 55% of comparable California women. Only 5% of the cohort reports being a current cigarette smoker; among comparable California women the prevalence of current smokers is nearly 16%.

Table 3 shows average annual age-adjusted incidence rates (standardized to the 1970 US population) for the major cancer sites in CTS participants. The maximum length of follow-up since study entry is 39 months. These incidence rates are compared to those for non-Hispanic white women aged 20 years or older in California for the years 1996 through 1998. The results confirm the anticipated high rates of invasive breast cancer in teachers, with the CTS breast cancer incidence rate 51% higher than the incidence rate for California non-Hispanic white women. Restricting the analysis to non-Hispanic white CTS members, we find that the CTS incidence rate is 53% higher than that of comparable California women. The relative excess incidences are even greater for *in-situ* breast cancer (67%) and localized invasive breast cancer (65%), and less for non-local disease (25%). Figure 2 shows that, for invasive breast cancer, the relative excess breast cancer risk among CTS participants compared to California non-Hispanic whites is apparent across all age groups, in both the "premenopausal" ($\leq$age 50) and "postmenopausal" ($>$age 50) age ranges.

CTS participants show a similarly large relative excess of endometrial cancer (72%) compared to California non-Hispanic white women and a lesser but still substantial relative excess of ovarian cancer (28%) (Table 3). Risk of cervix cancer, on the other hand, is only roughly one-half that expected based on rates in California's non-Hispanic white population (Table 3). Among CTS members with an intact uterus the rates of

Table 3. Average annual age-adjusted cancer incidence rates per 100,000 person-years among members of the California Teachers Study cohort living in California and among non-Hispanic white women in California, 1996–1998. (Rates standardized to the 1970 United States population)

Cancer[a]	Teachers (No. of cases)	California non-Hispanic white women	Rate ratio (95% confidence interval)
Breast			
In-situ	28.4 (223)	17.1	1.67 (1.59–1.75)
Invasive	150.7 (1151)	99.7	1.51 (1.48–1.54)
Localized	106.2 (815)	64.1	1.65 (1.62–1.70)
Nonlocalized	44.7 (336)	35.5	1.25 (1.21–1.30)
Uterine corpus	31.3 (256)	18.2	1.72 (1.65–1.80)
Ovary	15.5 (124)	12.1	1.28 (1.20–1.36)
Uterine cervix	3.2 (22)	5.9	0.53 (0.46–0.62)
Lung	25.3 (212)	38.2	0.66 (0.63–0.69)
Melanoma	19.0 (134)	11.9	1.59 (1.50–1.70)
Lymphoma[b]	17.6 (140)	12.0	1.47 (1.39–1.56)
Hodgkin's disease	2.2 (14)	1.9	1.18 (0.98–1.42)
Non-Hodgkin's lymphoma	15.4 (126)	10.1	1.53 (1.44–1.63)
Leukemia	6.7 (55)	5.3	1.28 (1.17–1.40)
Thyroid	7.7 (52)	6.6	1.16 (1.05–1.28)
Colon/rectum	28.1 (233)	26.4	1.07 (1.02–1.11)

[a] With the exception of *in-situ* breast cancer, all rates are for invasive cancers only.
[b] Combines Hodgkin's disease and non-Hodgkin's lymphoma.

endometrial cancer and cervix cancer are 47.5 and 18.1 per 100,000 woman-years, respectively. Restricting the CTS cohort to women with at least one intact ovary, the age-adjusted incidence rate for ovarian cancer is 18.1 per 100,000 woman-years.

Lung cancer incidence rates are 34% lower among CTS cohort members than among women in California, whereas rates of melanoma are 59% higher. Overall, CTS members have substantially higher risk of lymphoma, with the majority of lymphoma patients diagnosed with non-Hodgkin's lymphoma (NHL). The age-adjusted NHL incidence rate, 15.4 per 100,000 woman-years, is 53% higher than that of California non-Hispanic white women. The leukemia incidence rate for CTS members is 28% greater than that of California women. The majority of the 55 leukemias diagnosed among cohort members are chronic leukemias (20 chronic lymphocytic leukemias and 22 chronic myeloid leukemias *vs* three acute monocytic leukemias, two other acute leukemias, and four of other types). The rate of thyroid cancer is only modestly elevated (RR = 1.16) for CTS members relative to non-Hispanic white women in California, and that of colorectal cancer does not differ substantially between CTS members and California women (RR = 1.07).

Discussion

Based on results from this prospective analysis of cancer incidence in the CTS cohort, California teachers have not only a substantially higher than expected incidence of breast cancer, as hypothesized, but also substantial excess risks of both ovarian and endometrial cancer. This clustering of excess risk for these three sites is not entirely unexpected, as these cancers share important risk factors. The risk of both ovarian cancer and breast cancer has been related directly to a woman's cumulative lifetime number of ovulatory menstrual cycles [6, 7]. As such, low parity and low frequency of lactation are risk factors for both cancers [8, 9]. Endometrial cancer also shares risk factors with breast cancer, particularly postmenopausal obesity and low parity [10]. Endometrial cancer is also related to use of estrogen replacement therapy [10] and breast cancer risk is also increased by use of postmenopausal hormones, particularly combined estrogen and progestin regimens [11, 12]. On the other hand, cervix cancer, for which CTS members have an especially low rate, is a disease in which early intercourse and multiple sex partners constitute the major risk factors [13], in sharp contrast to breast cancer risk factor profiles. It is also a cancer that can be prevented by screening with the PAP test; 91% of CTS cohort members reported a PAP test within the past two years and 99% had been screened at some time in their lives.

The high rates of *in-situ* and localized breast cancer are not unexpected in this population considering that the mammography screening rates are quite high; 94% of women between the ages of 40 and 49 years reported having had at least one screening mammogram, as did 97% of those women who were 50 years or older at the

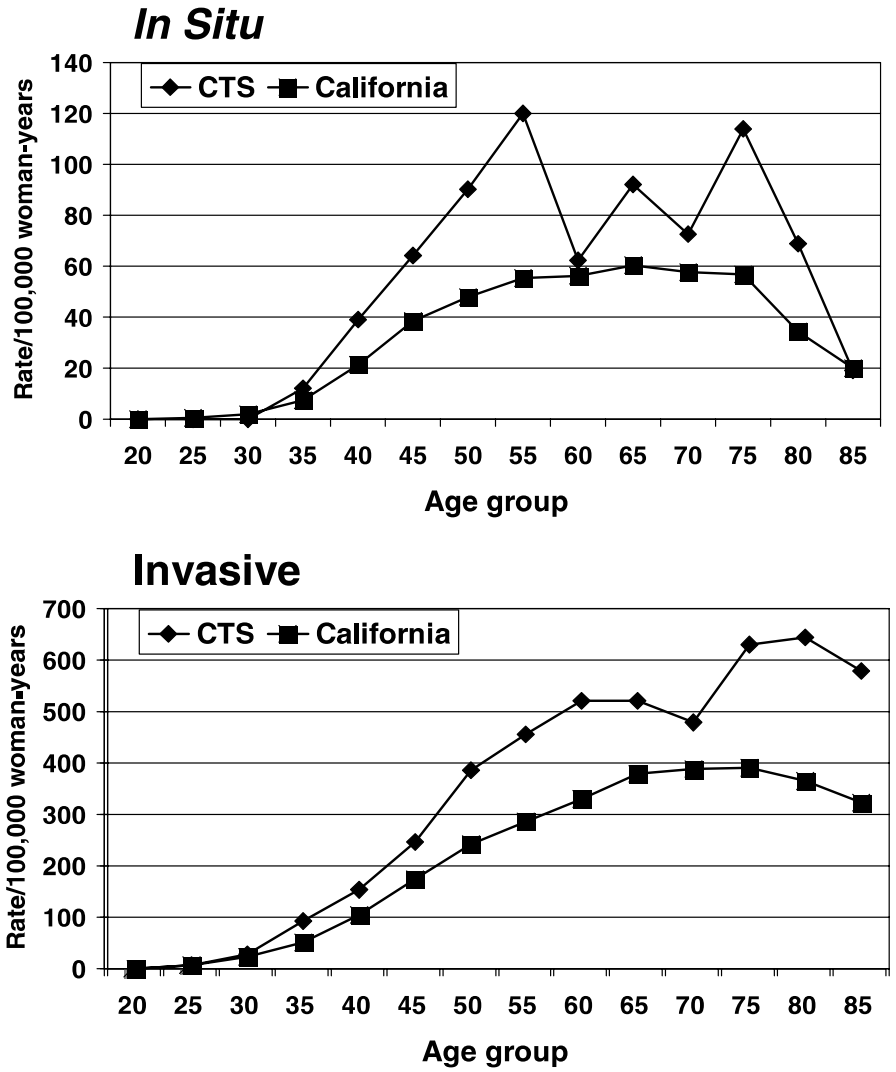

Fig. 2. Age-specific incidence rates of *in-situ* (upper graph) and invasive (lower graph) breast cancer in the California Teachers Study (CTS) and among non-Hispanic white women in California during the years 1996 through 1998.

time of cohort entry. Furthermore, the majority of these women had had a recent mammogram (that is, within the two years prior to cohort entry, 82% of women aged 40–49 years at baseline and 91% of women aged 50 years or older at baseline had had a mammogram). Nevertheless, despite the high frequency of mammography in this population, we also observe an excess incidence of non-local disease relative to non-Hispanic white women in California.

We have considered the possibility that the high breast cancer rates observed in the CTS may be due to a lack of representativeness of CTS participants in comparison to all California female educators and may, therefore, not represent the true risk among teachers overall. We note a high participation rate among women previously diagnosed with breast cancer. Our ability to assess representativeness of our cohort members is somewhat limited. We have compared those STRS members who chose to participate in the CTS with those STRS members who did not, in terms of age or geographic location in California and find similar distributions (see Table 1). Furthermore, STRS membership overall would be expected to represent well all California public school teachers demographically, since retirement benefits provide a strong incentive for all teachers to participate in this system.

Results from the prior statewide study linking California school employees to the California Cancer Registry provide additional evidence that our cohort is representative of women who are employed in the school

system [2]. In that study, which was based on *all* women who were administrators, teachers, or other professional support staff in the California school system during a time period spanning 1987 through 1992, we observed the same general pattern of cancer risk, with higher standardized incidence ratios (SIR) of invasive breast, *in-situ* breast, uterine corpus, and ovarian cancer (SIRs respectively of 1.21, 1.58, 1.17, and 1.21) and lower SIRs for cervical cancer (SIR = 0.49) and lung cancer (SIR = 0.40). The risks of melanoma (SIR = 1.23) and thyroid cancer (SIR = 1.28) were also elevated, as they are in our cohort. Our prior study reported a lower risk for colorectal cancer (SIR = 0.78); however, we do not observe any decrease in risk among CTS members. Although we observe an increase in incidence for all lymphomas, the distribution differs from what we observed previously where the SIR for Hodgkin's disease (SIR = 1.55), but not for NHL (SIR = 1.05) was substantially elevated. The difference between our prior observation of reduced leukemia risk (SIR = 0.74) and the elevated risk in the CTS, as well as the reversal in risk for Hodgkin's disease *vs* NHL, can be explained by the difference in the age distributions of the two studies as our previous study considered only active employees and the CTS includes both active, or recently active, and older, retired STRS members.

We attempted to determine how much of the excess breast cancer risk in the CTS might be explained by a standard set of breast cancer risk factors used in the Gail risk prediction model [13]. This model estimates the absolute probability that a woman with a particular risk profile who is regularly screened will develop invasive or *in-situ* breast cancer over a defined interval. For our typical CTS participant we predicted breast cancer risk at age 53 years (as this is the average age of women with no prior *in-situ* or invasive breast cancer diagnosis), and assumed that this woman was white, had menarche at age 12, a first live birth at age 26, no family history of breast cancer, and no prior biopsy. The predicted risk for our cohort member was 1.2% over the next five years (relative to 0.7% for a low-risk woman in the Gail model who would have menarche at age 14 years and first birth at age 19 years) and 9.4% over her remaining lifetime (relative to 5.7% for the low-risk woman). Using the data for comparable California women (menarche at 12 years and first birth at 23 years), the Gail model predicts a breast cancer risk of 1.0% over the next five years and a lifetime risk of 7.7%. Age at first live birth of CTS participants explains only part of the extraordinarily high risk of breast cancer experienced by California teachers, based on the Gail model. It is clear that California teachers also have an exceptional profile of other acknowledged breast cancer risk factors not included in this model. Thus, the high rate of use of HRT (particularly in combination with a progestin) and overall low parity would be expected to be driving rates higher, while the low average body mass index, the rather high levels of physical activity, and the relatively low use of alcohol should tend to moderate breast cancer rates in cohort members, the majority of whom continue to participate with high frequency in mammographic screening programs.

The CTS provides an extraordinary resource for future studies of risk relationships for breast and other cancers and for women's health, in general. The CTS research methods are designed to maximize data quality at minimum costs, to address important public health questions in a timely manner, and to maintain a strong working relationship with cohort members so that new exposure and outcome data can be collected with maximum quality and efficiency. This cohort, even in these early stages, serves as the basis for ongoing (and separately funded) studies pursuing the influences of dietary and hormonal factors in combination with low-penetrance genetic factors in the etiology of breast and endometrial cancer risk, detailed examination of environmental tobacco exposure and cancer risks, and evaluation of risk factor profiles that may help to explain the broad regional variations in breast cancer incidence within the state of California.

Acknowledgements

We express our appreciation to all of the participants in the California Teachers Study and to the analysts and staff who have contributed so much to the success of this research project: Public Health Institute: Gretchen Agha, Susan Hurley, Debbie Goldberg, and Rachna Nivas; Northern California Cancer Center: Susan L. Stewart, PhD, Melissa R. Krone, Katherine J. Hoggatt, and Alison Canchola; University of California, Irvine: Tom Tjoa and Catherine Christie; University of Southern California: Jan Schaeffer, Sarah Marshall, Frank Stasio, Myles Cockburn, PhD, Doojduen Villaluna, and LaCreachia Carraway; Impact Assessment, Inc.: Hilary Rosen. This research is supported by the California Breast Cancer Act of 1993, the California Department of Health Services, and grant CA77398 from the National Cancer Institute, US National Institutes of Health. The ideas and opinions expressed are those of the authors and no endorsement by the California Department of Health Services or the California Public Health Institute should be inferred.

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