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Screening and surveillance for second malignant neoplasms in adult survivors of childhood cancer: A report from the Childhood Cancer Survivor Study (CCSS)

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Abstract

Background—Childhood cancer survivors may develop a second malignant neoplasm during adulthood and therefore require regular surveillance.

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Objective—To examine adherence to population cancer screening guidelines by survivors at average risk of developing a second malignant neoplasm, and to cancer surveillance guidelines by survivors at high risk of developing a second malignant neoplasm.

Design—Retrospective cohort study.

Setting—The Childhood Cancer Survivor Study (CCSS), a 26 center study of long-term survivors of childhood cancer who were diagnosed between 1970 and 1986.

Patients—4,329 male and 4,018 female survivors of childhood cancer who completed a CCSS questionnaire assessing screening and surveillance for new cancers.

Measurements—Patient-reported receipt and timing of mammography, Papanicolaou smear, colonoscopy, or skin examination was categorized as adherent to the United States Preventive Services Task Force guidelines for survivors at average risk for breast or cervical cancer, or the Children's Oncology Group guidelines for survivors at high risk for developing breast, colorectal or skin cancer as a result of their therapy.

Results—Among average risk female survivors, 2,743/3,392 (80.9%) reported a Papanicolaou smear within the recommended period, and 140/209 (67.0%) reported a mammogram within the recommended period. Among high risk survivors, rates of recommended mammography among females, and colonoscopy and complete skin exams among both genders were only 241/522 (46.2%), 91/794 (11.5%) and 1,290/4,850 (26.6%), respectively.

Limitations—Data were self report. CCSS participants are a select group of survivors and their compliance may not be representative of all childhood cancer survivors.

Conclusions—Female survivors at average risk for developing a second malignant neoplasm demonstrate reasonable rates of screening for cervical and breast cancer. However, surveillance for new cancers is very poor amongst survivors at highest risk for colon, breast or skin cancer, suggesting that survivors and their physicians need education about their risks and the recommended surveillance.

INTRODUCTION

There are over 325,000 survivors of childhood cancer alive in the United States (1), many of whom are at increased risk for the development of a second malignant neoplasm as a result of the therapy for their primary cancer (2-5). Almost 10% of survivors will develop a second malignant neoplasm by 30 years from their initial cancer diagnosis (2), and new malignancies are the most frequent cause of late mortality in patients who survive for more than 20 years after their childhood cancer diagnosis (6, 7). Among childhood cancer survivors who are not considered to be at an increased risk of developing a specific second malignant neoplasm (average risk survivors), adherence to cancer screening guidelines directed at the general population is of particular importance. These screening guidelines are published by organizations such as the United States Preventive Services Task Force (USPSTF), the Canadian Task Force on Preventive Health Care, and the American Cancer Society. Since many children with cancer receive intensive chemotherapy or radiation, their options for therapy may be limited if they develop a second malignant neoplasm later in life. For example, a female survivor who develops invasive node-positive breast cancer during adulthood may not be able to receive adjuvant doxorubicin if she received anthracycline chemotherapy as treatment for her childhood cancer (8). Adherence to recommended screening for breast or cervical cancer in adult survivors of childhood cancer at average risk may lead to earlier detection and reduced morbidity or mortality, and is therefore imperative.

The use of radiation therapy to treat some childhood malignancies has resulted in breast cancer (4, 5, 9, 10), colorectal cancer and other gastrointestinal malignancies (5, 11-13),

malignant melanoma (5, 14, 15) and non-melanoma skin cancer (2, 16) occurring at a younger age and with increased frequency in survivors of childhood cancer when compared to the general population. Studies of other population groups at increased risk for developing one of these neoplasms have demonstrated that more intense surveillance beginning at an earlier age than is recommended for the general population may lead to improved outcome in high-risk individuals (17-22). Consequently, the Children's Oncology Group (COG) (23, 24) and other national and international groups (25-27) have published consensus-based guidelines for lifelong surveillance for second malignant neoplasms in survivors of childhood cancer who are considered at increased risk of developing a therapy-related malignancy.

In order to evaluate adherence to recommended screening and surveillance in childhood cancer survivors at average or high risk for developing a second malignant neoplasm during adulthood, we assessed these health practices in the Childhood Cancer Survivor Study (CCSS) cohort. We evaluated adherence to population screening guidelines in female survivors at average risk of developing breast or cervical cancer. Additionally, we examined adherence to cancer surveillance guidelines in survivors at high risk for developing breast, colorectal or skin cancer as a result of their cancer therapy.

METHODS

Childhood Cancer Survivor Study (CCSS)

The CCSS methodology and a description of the participants have been published previously (28-30). Briefly, the cohort includes individuals diagnosed with cancer before age 21 years at one of 26 centers (25 US, 1 Canada) from 1970-1986, who were alive at least five years from their original diagnosis. The eligible cohort consisted of 20,626 participants, of whom 17,568 (85.2%) were successfully contacted and 14,357 (69.6%) enrolled in the study. There were no statistically significant differences between participants and non-participants by gender, age at diagnosis, cancer type or treatment (28, 31). Detailed diagnosis and treatment information were systematically abstracted from participants' hospital records. Participants completed a comprehensive baseline questionnaire and several subsequent questionnaires. Eligibility for this analysis was limited to participants (n=8,347) who completed a questionnaire in 2002-2003 (hereafter referred to as the CCSS 2003 Questionnaire) that addressed cancer screening and surveillance practices, and who had not developed a new neoplasm prior to completing the questionnaire (Online appendix 1). Study instruments are available at <http://ccss.stjude.org>. The study was approved by Institutional Review Boards at each participating institution and informed consent was obtained from each participant.

Cancer screening in average risk female survivors

We examined female survivors' adherence to the cervical and breast cancer screening recommendations for the general (average risk) population published by the USPSTF (available at <http://www.ahrq.gov/CLINIC/uspstfix.htm>; summarized in Online appendix 2) (32). We used the guidelines current at the time of the survey (i.e. the 2002 breast cancer guidelines and the 2003 cervical cancer guidelines). The survey questions were designed to mirror those used on the 2003 National Health Interview Survey (33). The USPSTF recommends screening for cervical cancer with a periodic Papanicolaou smear every three years starting at the time of first sexual intercourse or age 21 years, whichever is earlier. Since time of first intercourse was not captured by the study questionnaire, we used age 21 years as the expected time of commencement of screening. The USPSTF recommends a mammogram every one to two years in all women aged 40 years or older. For each screening test, we classified survivors as (i) completing the test within the recommended

period; (ii) completing the test, but not within the recommended period; or (iii) never having completed the test. Only those survivors who completed the test within the recommended period were considered to be “adherent” to the guidelines. For example, to assess compliance with mammography screening recommendations, females respondents were asked, “*When was the last time you had a mammogram?*” and were presented with 6 response options: (i) *Never*; (ii) *Less than 1 year ago*; (iii) *1-2 years ago*; (iv) *More than 2 years but less than 5 years ago*; (v) *5 or more years ago*; or (vi) *Don’t know*. Women aged 42 or older (allowing for 2 years from their 40th birthday) who reported a mammogram “*less than 1 year ago*” or “*1-2 years ago*” were considered adherent to the guidelines. Canadian survivors were excluded from the breast cancer screening analysis since that country’s guidelines suggest mammography starting at age 50 years (34), rather than age 40 years as was suggested by the USPSTF at the time of the questionnaire. Additionally, survivors who were classified as being at high risk for developing breast cancer were excluded from this analysis of breast cancer screening in average risk individuals, and are included in the analysis of breast cancer surveillance among high risk individuals described below.

Cancer surveillance among female survivors at high risk for breast cancer, and male and female survivors at high risk for colorectal cancer, malignant melanoma or non-melanoma skin cancer

We assessed adherence to the COG Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers (COG LTFU Guidelines; available at www.survivorshipguidelines.org) (23) in all survivors considered to be at increased risk for developing breast cancer, colorectal cancer or skin cancer (malignant melanoma or non-melanoma skin cancer) as a result of their cancer therapy (Online appendix 2). COG defines females at high risk for developing breast cancer as those who received greater or equal to 20 Gray of radiation therapy to the chest, and recommends an annual mammogram beginning eight years after radiation or at age 25 years, whichever occurs last. Survivors are considered at high risk for colorectal cancer if they received greater or equal to 30 Gray of radiation therapy to the abdomen, pelvis or spine. COG recommends a colonoscopy every five years starting at age 35 years for these survivors. Finally, survivors are considered at high risk for skin cancer if they received any radiation therapy, and an annual dermatologic exam of all irradiated areas is recommended.

Predictors of screening and surveillance

Demographic data were obtained on the baseline questionnaire. Socio-demographic status (marital status, health insurance, education) was assessed in the CCSS 2003 Questionnaire. Disease and treatment variables were abstracted from medical records. In order to evaluate the association between health status, chronic medical conditions and surveillance/screening, the severity of chronic health conditions reported on the baseline questionnaire was classified as (0) none; (1) mild; (2) moderate; (3) severe; or (4) life-threatening or disabling using the National Cancer Institute’s Common Terminology Criteria for Adverse Events (version 3), as published previously (35). Health status was measured using a previously defined set of domains (emotional health, physical function, cancer-related pain, and cancer-related anxiety and fears) (36). Emotional health was assessed with the 18-item Brief Symptom Index, and was classified as poor in patients scoring greater than 63 on this instrument’s global status index (36, 37). Physical function was assessed with the role function-physical subscale of the 36-Item Short Form Health Survey (SF-36) (38) and was classified as poor in patients scoring below 40. Cancer-related pain and anxiety were assessed separately on a five-point Likert scale and were dichotomized into none or a small amount versus moderate, a lot or extreme (36). In order to evaluate survivors’ concern regarding their future health, they were asked whether the statement, “*I expect my health to*

get worse” was “*definitely true*,” “*mostly true*,” “*mostly false*” or “*definitely false*”, and their responses were dichotomized as “*true*” or “*false*”.

Statistical analysis

Descriptive statistics including frequencies, percentages, means and standard deviations (as appropriate) were calculated for demographic, disease and health status. The proportions of survivors in the average risk and high-risk categories for second malignant neoplasms who adhered to the appropriate screening/surveillance guidelines were calculated and are reported as percentages. The relative risks for adherence to the guidelines were calculated by demographic and health status variables and compared in multiple variable regression models using a log link and a Poisson distribution (39). Demographic, socioeconomic, health history, chronic disease and health status predictors of participation in surveillance were evaluated in multiple variable models if they were independently associated with the outcome ($p < 0.10$). Independent variable collinearity was evaluated by examining variance inflation factors and tolerance (40). Variables that were highly correlated were not included in the same models. Data analyses were completed with SAS statistical software version 9.2 (Cary, NC).

RESULTS

Characteristics of the study cohort

Of the 9,308 survivors who responded to the CCSS 2003 Questionnaire, 961 were not eligible for this analysis. One did not complete the baseline questionnaire and 960 had developed a second malignant neoplasm. Consequently, there were a total of 8,347 survivors (4,018 female, 4,329 male). The mean age at diagnosis among males was 8.1 years (standard deviation [SD] 5.7 years) and among females was 7.6 years (SD 5.7). The mean age at the time of questionnaire completion was 31.5 years (SD 7.3) and 30.8 years (SD 7.3) for males and females, respectively. Demographic, treatment and health status characteristics of the participants, stratified by gender, are presented in Table 1.

Cancer screening in survivors at average risk of developing cervical or breast cancer

The number of female survivors who were not at increased risk for cervical or breast cancer as a result of their prior cancer therapy and had reached the age where screening was recommended in the general population was 3,392 and 209 for Papanicolaou smear and mammography, respectively. Eighty-one percent (2,743/3,392) reported a Papanicolaou smear within the recommended period, and 67.0% (140/209) reported a mammogram within the recommended period (Figure 1, panels a and b). Six percent (200/3,392) and 12.4% (26/209) of survivors reported never having had a Papanicolaou smear or mammogram, respectively. Table 2 displays the univariate and multiple variable logistic regression models predicting adherence to mammography and Papanicolaou smear screening guidelines. The following variables were not statistically significant in the univariate analysis for mammography or Papanicolaou smear adherence and so are not shown in the table: concern about future health, poor physical function, cancer related pain, the survivor having a treatment summary, medical care at a cancer center in the preceding two years or a cancer related visit in the preceding two years. Being “married or living as married” (RR 1.15, 95% CI 1.06-1.24) was associated with an increased likelihood of Papanicolaou smear adherence, while having a high school education or less (RR 0.87, 95% CI 0.77-0.98) or being uninsured (RR 0.85, 95% CI 0.74-0.97) were associated with a decreased likelihood of adherence. No demographic, socioeconomic or health status factors predicted adherence to mammography screening recommendations.

Cancer surveillance in survivors at high-risk for breast, colorectal or skin cancer

Among female survivors at increased risk for developing breast cancer and survivors of both genders at increased risk for developing colorectal cancer who required surveillance according to the COG LTFU Guidelines, only 241/522 (46.2%) and 91/794 (11.5%) reported undergoing a mammogram or colonoscopy within the recommended period (Figure 1, panels c and d). Only 1,290/4,850 (26.6%) survivors at increased risk for skin cancer reported ever having a complete examination of all irradiated areas. Table 3 displays the univariate and multiple variable logistic regression models predicting adherence to mammography, colonoscopy and skin examination surveillance guidelines. Older age at interview (RR 1.08, 95% CI 1.05-1.11) was associated with an increased likelihood of reporting a mammogram. Older age at interview (RR 1.07, 95% CI 1.02-1.12), the survivor having a copy of their cancer treatment summary (RR 1.66, 95% CI 1.06-2.61) and a medical visit related to their prior cancer within the preceding two years (RR 2.77, 95% CI 1.69-4.52) were associated with an increased likelihood of reporting a colonoscopy. Having a college education or higher (RR 1.24, 95% CI 1.08-1.42), medical care at a cancer center within the preceding two years (RR 1.43, 95% CI 1.21-1.68), and the survivor having a copy of the cancer treatment summary (RR 1.31, 95% CI 1.15-1.49) were associated with an increased likelihood of reporting a skin exam. Survivors that were non-white (RR 0.67, 95% CI 0.52-0.86), had moderate to extreme cancer-related pain (RR 0.77, 95% CI 0.62-0.95), or who had not had a medical visit related to their prior cancer within the preceding two years (RR 0.84, 95% CI 0.73-0.96) were less likely to report a skin exam.

DISCUSSION

We assessed the cancer screening and surveillance practices of 8,347 survivors of childhood cancer. Encouragingly, female survivors considered average risk for developing cervical or breast cancer demonstrated acceptable rates of adherence to Papanicolaou smear and mammography recommendations, with adherence rates of 81% and 67% for each test, respectively. This suggests that female childhood cancer survivors are generally health conscious and aware of screening guidelines published for the general population. Survivors of cancer in adulthood have been demonstrated to have better adherence to cancer screening recommendations than that observed in the general population (41), although actual screening rates are quite variable and often sub-optimal.

Despite the relatively high screening rates for survivors at average risk for another cancer, the rates of cancer surveillance for those at high risk for a therapy-related second malignant neoplasm were alarmingly low. Less than half of the survivors at increased risk of breast, colorectal or skin cancer reported compliance with recommended surveillance. Females who have received radiation therapy to the chest during childhood demonstrate a 13% to 20% cumulative incidence of breast cancer by 40 to 45 years of age (42), a risk similar to that observed in women with breast cancer susceptibility gene mutations (43-45). Several studies have recognized an emerging risk of colorectal cancer in patients who have received abdominal or pelvic radiation as part of their primary therapy, with a 3.9 to 4.7- fold increased risk when compared to the general population (13, 14, 46). Increased rates of other gastrointestinal malignancies such as gastric cancer have also been observed, suggesting that clinicians need to be aware of new symptoms in survivors who have received radiation to any portion of their gastrointestinal tract. Malignant melanoma occurs with increased frequency in childhood cancer survivors (5, 14, 15), and the cumulative incidence of non-melanoma skin cancer is almost 7% in 30-year survivors of childhood cancer (2). Thus, the low surveillance rates observed in our cohort suggest that opportunities to detect secondary breast, colorectal or skin cancers early in their course are being missed, placing some survivors at increased risk for both serious morbidity and mortality.

The dichotomy of low rates of surveillance among the high risk survivors within the setting of high rates of cancer screening among average risk survivors suggests that the problem is not simply a lack of interest or compliance on the part of the survivors. Survivors were more likely to report an indicated mammogram or skin exam if they received their follow-up care at a cancer center or in a long-term follow-up program. However, only a minority of adult survivors (12.4% in this cohort) continues to receive regular care at a cancer center once they reach adulthood (47). Although many pediatric cancer centers offer specialized care to survivors during childhood and adolescence, few provide access to specialized clinics once survivors reach adulthood (48). Several adult cancer centers run survivorship clinics although these generally target survivors of adult malignancies such as breast or colon cancer, and are not routinely used by survivors of childhood cancer (49, 50). These data suggest that interventions to improve adherence to cancer surveillance should be directed at the primary care physicians who care for the majority of long-term childhood cancer survivors, as well as to the survivors themselves. Prior research has suggested that a physician recommendation is a statistically significant determinant of adherence to mammography guidelines (51). However, since the guidelines for high risk patients recommend that breast and colorectal cancer surveillance commence many years before screening in the general population, many primary care physicians are likely unaware of the surveillance guidelines for these high risk patients (52). In fact, primary care physicians' lack of familiarity with the health problems faced by survivors has been identified as a substantial barrier to their provision of adequate survivor care (52, 53). Targeted education of physicians, open access to guidelines (such as the COG LTFU Guidelines available at www.survivorshipguidelines.org) and the availability of the pediatric cancer centers as a resource for primary care providers may improve survivor care. Perhaps most importantly, survivors must be provided with the knowledge and tools to advocate for their own care. Survivors are often unaware of the details of their cancer therapy, preventing them from seeking care focused on specific risks (54). Efforts to empower survivors have included provision of treatment summaries and survivor care plans at the conclusion of cancer therapy. Indeed, in the present study, survivors who had a summary of their cancer treatment were more likely to report a recommended colonoscopy or skin exam. The feasibility of providing survivors with a portable electronic record of their cancer history and recommended care that can be shared with their health care provider is being assessed currently.

Several methodological limitations must be considered when interpreting the results of this study. First, we relied on self report data about the completion of screening tests. Although self report of imaging or diagnostic tests such as mammography or Papanicolaou smear has been demonstrated to be generally reliable (55), there is no evidence to suggest that patients accurately report skin exams. Second, CCSS participants are a select group of survivors, and their compliance with surveillance recommendations may not be representative of all childhood cancer survivors. Third, this cohort of survivors received their therapy between 1970 and 1986. Caution should be exercised in generalizing these findings to patients treated more recently. It is plausible that patients treated in the current era are better informed about their need for routine surveillance. The CCSS is currently recruiting a cohort of survivors treated between 1987 and 1999 to examine such questions. Finally, assessment of screening compliance among survivors at average risk of developing a second malignant neoplasm focused only on females. There were too few survivors who had reached the age where colorectal cancer screening is recommended to assess compliance with these screening guidelines. Thus, the findings of good compliance among female survivors should not be generalized to male survivors.

In summary, survivors of childhood cancer who are not considered to be at increased risk for developing a second malignant neoplasm demonstrate reasonable adherence to Papanicolaou

smear and mammography guidelines. However, survivors at increased risk for developing a new cancer during adulthood demonstrate very poor adherence to recommended surveillance for breast, colorectal and skin cancer. Clinicians who care for survivors of childhood cancers must implement and evaluate methods for ensuring better adherence with recommended cancer surveillance and for improving awareness among both the survivors and the primary care clinicians who provide care for the majority of these survivors as they age. This should include provision of a treatment summary and care plan to all childhood cancer survivors prior to their transition out of a pediatric cancer center.

Acknowledgments

The **Childhood Cancer Survivor Study (CCSS)** is a collaborative, multi-institutional project, funded as a resource by the National Cancer Institute, of individuals who survived five or more years after diagnosis of childhood cancer. CCSS is a retrospectively ascertained cohort of 20,626 childhood cancer survivors diagnosed before age 21 between 1970 and 1986, and 3,899 siblings of survivors who serve as a control group. The cohort was assembled through the efforts of 26 participating clinical research centers in the United States and Canada. The study is currently funded by a U24 resource grant (NCI grant # U24 CA55727, Principal Investigator: LL Robison) awarded to St. Jude Children’s Research Hospital. Currently, we are in the process of expanding the cohort to include an additional 14,000 childhood cancer survivors diagnosed before age 21 between 1987 and 1999. For information on how to access and utilize the CCSS resource, visit <http://ccss.stjude.org>.

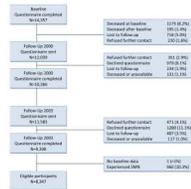
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Appendix 1

CCSS participants eligible for study of screening and surveillance practices



Appendix 2

Recommended screening (USPSTF) (32) and surveillance (COG) (23) for survivors at average or high risk of developing a second malignant neoplasm

Screening in survivors at AVERAGE risk of a second malignant neoplasm				
	Breast	Cervix	Colorectal	Skin
USPSTF recommended screening for the general (average risk) population	Mammogram every 1 to 2 years for women aged 40 years or older	Papanicolaou smear every 3 years commencing at age 21 years	**	Not applicable

Surveillance in survivors at HIGH risk of a second malignant neoplasm				
	Breast	Cervix	Colorectal	Skin
Definition (COG) of high risk group	Female, ≥ 20 Gy radiation therapy to the chest	Not applicable	≥ 30 Gy radiation therapy to the abdomen, pelvis or spine	Any radiation therapy
COG recommended surveillance for survivors at high risk	Annual mammogram beginning 8 years after radiation or age 25 years, whichever occurs last***	Not applicable	Colonoscopy every 5 years beginning at age 35 years	Annual dermatologic exam of irradiated areas

MRI is not assessed in this analysis.

* Guideline recommends Papanicolaou smear screening to start at time of first sexual intercourse or age 21 years, whichever is earlier (<http://www.ahrq.gov/clinic/3rduspstf/cervcan/cervcanrr.htm>). Since time of first intercourse was not captured by the study questionnaire, we used age 21 years as the expected time of the commencement of screening.

** Since few survivors in the cohort have reached the age at which colorectal cancer screening in the general population is recommended, this outcome is not presented in this analysis

*** Breast MRI was identified as an adjunct to mammography in a revised version of the COG surveillance guidelines published in 2008 after the completion of the study surveys.

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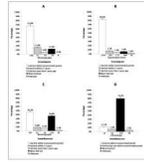


Figure 1. Adherence to screening guidelines for (A) mammography and (B) Papanicolaou smears by female survivors at average risk of breast or cervical cancer, and to surveillance guidelines for (C) mammography (females only) and (D) colonoscopy (both genders) for survivors at increased risk of breast cancer or colorectal cancer

Table 1

Demographic, disease and health status data

Characteristics	Survivors Male (n=4,329)		Survivors Female (n=4,018)	
	N	%	N	%
Race/Ethnicity				
White, Non-Hispanic	3,842	88.7	3,536	88.0
Non-white	472	10.9	468	11.6
Not reported	15	0.4	14	0.4
Cancer diagnosis				
Leukemia	1,441	33.3	1,447	36.0
CNS tumor	562	13.0	502	12.5
Hodgkin lymphoma	495	11.4	380	9.4
Non-Hodgkin lymphoma	452	10.4	199	5.0
Wilms tumor	371	8.5	465	11.6
Neuroblastoma	263	6.1	336	8.4
Soft tissue sarcoma	393	9.1	346	8.6
Bone cancer	350	8.1	343	8.5
Unknown	2	0.1	-	-
Age group				
<18 years	10	0.2	8	0.2
18-24 years	959	22.2	1,033	25.7
25-34 years	1,971	45.5	1,827	45.5
35+ years	1,389	32.1	1,150	28.6
Marital status				
Single/widowed/divorced or separated	2,421	55.9	2,120	52.7
Married or living as married	1,873	43.3	1,859	46.3
Unknown	35	0.8	39	1.0
Education				
Post high school or some college	1,597	36.9	1,469	36.6
High school or less	1,015	23.4	806	20.0
College or higher	1,674	38.7	1,701	42.3
Unknown	43	1.0	42	1.1
Insurance status				
US Insured or Canadian	3,683	85.1	3,520	87.6
US not insured	603	13.9	470	11.7
Unknown	43	1.0	28	0.7
Concern about future health (Expect worse)				
False	3,153	72.8	3,048	75.8
True	1,145	26.5	959	23.9
Unknown	31	0.7	11	0.3
Chronic disease status *				
Grade 0, 1, 2	3,449	79.7	3,027	75.3

Characteristics	Survivors Male (n=4,329)		Survivors Female (n=4,018)	
	N	%	N	%
Grade 3, 4	880	20.3	991	24.7
Poor emotional health				
No	3,586	82.8	3,367	83.8
Yes	386	8.9	397	9.9
Unknown	357	8.3	254	6.3
Poor physical function				
No	3,942	91.1	3,492	86.9
Yes	369	8.5	505	12.6
Unknown	18	0.4	21	0.5
Cancer-related pain				
None, a small amount	3,916	90.5	3,564	88.7
Moderate, a lot, extreme	381	8.8	439	10.9
Unknown	32	0.7	15	0.4
Survivor has cancer treatment summary				
No	2,711	62.6	2,464	61.3
Yes	996	23.0	1,058	26.3
Unknown	622	14.4	496	12.4
Medical care in last 2 years at cancer center				
No	3,827	88.4	3,483	86.7
Yes	502	11.6	535	13.3
Cancer related visit in last 2 years				
Yes	1,170	27.0	1,244	31.0
No	3,049	70.4	2,675	66.6
Unknown	110	2.6	99	2.5

* National Cancer Institute's Common Terminology Criteria for Adverse Events (version 3) grading = none (0), mild (1), moderate (2), severe (3), life threatening/disabling (4)

Table 2

Predictors of adherence to mammography and Papanicolaou smear guidelines in female survivors at average risk of breast or cervical cancer*

	Mammography (N=209 females; Adherent=140)				Papanicolaou smear (N=3,392 females; Adherent=2,743)			
	Univariate		Multivariate**		Univariate		Multivariate**	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Race								
White (referent)	1.00		1.00		1.00		1.00	
Non-white	1.00	0.55-1.80	0.99	0.54-1.81	1.02	0.91-1.15	1.05	0.94-1.19
Age at interview, years								
	1.02	0.95-1.10	1.03	0.95-1.11	1.00	1.00-1.01	1.00	0.99-1.01
Marital status								
Single/widowed/divorced or separated (referent)	1.00				1.00		1.00	
Married or living as married	1.14	0.79-1.66			1.17	1.08-1.26	1.15	1.06-1.24
Education								
Post high school or some college (referent)	1.00		1.00		1.00		1.00	
High school or less	1.06	0.64-1.75	1.04	0.63-1.74	0.84	0.75-0.95	0.87	0.77-0.98
College or higher	1.37	0.92-2.02	1.37	0.92-2.03	1.05	0.97-1.14	1.03	0.95-1.12
Insurance status								
US Insured or Canadian (referent)					1.00		1.00	
US not insured					0.81	0.71-0.92	0.85	0.74-0.97
Chronic disease status								
Grade 0, 1, 2 (referent)	1.00				1.00			
Grade 3, 4	1.06	0.76-1.49			0.97	0.89-1.05		
Poor emotional health								
No (referent)	1.00				1.00		1.00	
Yes	0.76	0.46-1.26			0.93	0.81-1.06	0.95	0.85-1.08

* A relative risk (RR)>1 indicates increased compliance with the recommended screening test; a RR<1 indicates decreased compliance

** Univariate analysis was performed and all the variables with p-value less than 0.10 were included in the multivariate model. Independent variable collinearity was evaluated by examining variance inflation factors and tolerance. Variables that were highly correlated were not included in the same models. The multivariate analysis of mammogram and Papanicolaou smear are adjusted for race, age at questionnaire and age at diagnosis.

Table 3

Predictors of adherence to mammography, colonoscopy and skin exam guidelines in survivors at high risk of breast, colorectal or skin cancer*

	Mammography (N=522 females; Adherent=241)				Colonoscopy (N=794 males and females; Adherent=91)				Skin exam (N=4,850 males and females; Adherent=1,290)			
	Univariate		Multivariate**		Univariate		Multivariate**		Univariate		Multivariate**	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Sex												
Female (referent)					1.00		1.00		1.00		1.00	
Male	N/A				1.00	1.56	0.79	1.23	1.14	1.27	1.08	0.97-1.22
Race												
White (referent)	1.00		1.00		1.00		1.00		1.00		1.00	
Non-white	1.12	0.73-1.72	1.29	0.81-2.04	1.25	0.63-2.46	1.48	0.78-2.80	0.68	0.55-0.84	0.67	0.52-0.86
Age at interview, years												
	1.08	1.06-1.10	1.08	1.05-1.11	1.06	1.03-1.10	1.07	1.02-1.12	1.01	1.00-1.02	1.01	1.00-1.03
Marital status												
Single/widowed/divorced or separated (referent)	1.00		1.00		1.00				1.00			
Married or living as married	1.63	1.23-2.16	1.24	0.92-1.66	1.12	0.72-1.74			1.09	0.98-1.22		
Education												
Post high school or some college (referent)	1.00		1.00		1.00				1.00		1.00	
High school or less	0.70	0.46-1.07	0.75	0.48-1.15	1.00	0.53-1.90			0.88	0.75-1.03	0.93	0.77-1.12
College or higher	1.00	0.76-1.33	0.98	0.73-1.30	1.04	0.64-1.71			1.28	1.13-1.45	1.24	1.08-1.42
Insurance status												
US Insured or Canadian	1.00		1.00		1.00				1.00		1.00	

	Mammography (N=522 females; Adherent=241)				Colonoscopy (N=794 males and females; Adherent=91)				Skin exam (N=4,850 males and females; Adherent=1,290)			
	Univariate		Multivariate **		Univariate		Multivariate **		Univariate		Multivariate **	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
(referent)												
US not insured	0.63	0.35-1.16	0.88	0.47-1.64	0.97	0.47-2.01			0.67	0.56-0.82	0.85	0.69-1.06
Concern about future health (Expect worse)												
False (referent)	1.00				1.00		1.00		1.00		1.00	
True	1.18	0.89-1.57			1.78	1.13-2.80	1.15	0.72-1.83	1.15	1.02-1.30	1.07	0.92-1.23
Chronic disease status												
Grade 0, 1, 2 (referent)	1.00				1.00		1.00		1.00			
Grade 3, 4	1.10	0.85-1.44			1.63	1.04-2.55	1.28	0.82-2.01	1.09	0.96-1.24		
Poor emotional health												
No (referent)	1.00				1.00		1.00		1.00			
Yes	0.91	0.60-1.38			1.15	1.07-1.24	1.63	0.91-2.92	0.88	0.72-1.08		
Poor physical function												
No (referent)	1.00				1.00		1.00		1.00			
Yes	0.83	0.56-1.23			1.07	1.01-1.14	0.95	0.53-1.69	0.90	0.75-1.08		
Cancer-related pain												
None, a small amount (referent)	1.00				1.00				1.00		1.00	
Moderate, a lot, extreme	0.79	0.51-1.22			1.40	0.79-2.48			0.85	0.70-1.03	0.77	0.62-0.95
Survivor has cancer treatment summary												
No (referent)	1.00				1.00		1.00		1.00		1.00	
Yes	1.04	0.78-1.38			1.84	1.15-2.94	1.66	1.06-2.61	1.40	1.25-1.57	1.31	1.15-1.49

	Mammography (N=522 females; Adherent=241)				Colonoscopy (N=794 males and females; Adherent=91)				Skin exam (N=4,850 males and females; Adherent=1,290)			
	Univariate		Multivariate**		Univariate		Multivariate**		Univariate		Multivariate**	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Medical care in last 2 years at cancer center												
No (referent)	1.00		1.00		1.00		1.00		1.00		1.00	
Yes	1.51	1.12-2.02	1.35	0.97-1.87	1.68	0.98-2.88	1.08	0.63-1.84	1.64	1.43-1.87	1.43	1.21-1.68
Cancer related visit in last 2 years												
Yes (referent)	1.00		1.00		1.00		1.00		1.00		1.00	
No	0.72	0.56-0.93	0.79	0.60-1.05	0.33	0.21-0.53	0.37	0.22-0.62	0.70	0.63-0.78	0.84	0.73-0.96

* Relative risks (RR)>1 indicates increased compliance with the recommended surveillance test; a RR<1 indicates decreased compliance

** Univariate analysis was performed and all the variables with p-value less than 0.10 were included in the multivariate model. Independent variable collinearity was evaluated by examining variance inflation factors and tolerance. Variables that were highly correlated were not included in the same models. The multivariate analysis of colonoscopy and skin exam is adjusted for sex, race, age at questionnaire and age at diagnosis. The multivariate analysis of mammography (which is restricted to females) is adjusted for race, age at questionnaire and age at diagnosis.