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Comprehensive evaluation of the incidence of late effects in five-year survivors of breast cancer

Timothy L. Lash¹, Soe Soe Thwin², Marianne Ulcickas Yood³, Ann M. Geiger⁴, Jaclyn Bosco⁵, Virginia P. Quinn⁶, Terry S. Field⁷, Pamala A. Pawloski⁸, and Rebecca A. Silliman⁹

¹Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia

²Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), VA Healthcare System, Boston, Massachusetts

³Department of Epidemiology, Boston University School of Public Health, Boston, Massachusetts

⁴Health Services and Economics Branch, Applied Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, Rockville, MD

⁵Real-World & Late Phase Research division of Quintiles, Inc., Cambridge, MA

⁶Department of Research & Evaluation, Kaiser Permanente Southern California, Pasadena, California

⁷Meyers Primary Care Institute, Worcester, MA (a joint endeavor of the University of Massachusetts Medical School, Reliant Medical Group, and Fallon Community Health Plan)

⁸HealthPartners Institute for Education and Research, Minneapolis, Minnesota

⁹Section of Geriatrics, Boston University School of Medicine, Boston Medical Center, Boston, Massachusetts

Abstract

Purpose—Late effects of breast cancer affect the quality of survivorship. Using administrative data, we compared the occurrence of almost all ICD9 codes among older breast cancer survivors to that among a matched comparison cohort to generate new hypotheses.

Methods—Breast cancer patients sixty-five years or older diagnosed 1990–1994 in six integrated care settings and who survived at least five years were matched with a cohort of women without a history of breast cancer on care setting, age, and calendar time. We collected data on the occurrence of incident ICD9 codes beginning six years after the breast cancer diagnosis date and continuing to year fifteen, and comparable data for the matched woman. We calculated hazard ratios and 95% confidence intervals associating breast cancer survivorship with incidence of each ICD9 code. We used semi-Bayes methods to address multiple comparisons.

Correspondence: Timothy L. Lash, DSc, MPH, Rollins School of Public Health, 1518 Clifton Rd, Atlanta, GA 30322, (t) 404.712.1270, tlash@emory.edu.

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Results—Older breast cancer survivors had about the same occurrence of diseases and conditions six to fifteen years after breast cancer diagnosis as comparable women. The median of 564 adjusted hazard ratios equaled 1.06, with interquartile range 0.92 to 1.3. The distribution of hazard ratios pertaining to cancer-related ICD codes was shifted towards positive associations, and the distribution pertaining to cardiovascular-related ICD codes was shifted towards negative associations.

Conclusions—In this hypothesis scanning study, we observed little difference in the occurrence of non-breast cancer-related diseases and conditions among older, long-term breast cancer survivors and comparable women without a history of breast cancer.

Keywords

Breast neoplasms, complications; breast neoplasms, quality of life; breast neoplasms, late effects; breast neoplasms, survivorship

Introduction

With improving survival of breast cancer patients, patient and provider attention has shifted to the relative occurrence of diseases, conditions, symptoms and complications long after the breast cancer diagnosis [1,2]. These adverse events, sometimes called “late effects,” affect the quality of survivorship and may be avoidable or manageable if they are treated prophylactically or detected and successfully treated before they fully develop [2,1].

Research on the late effects of breast cancer has focused on pre-specified hypotheses pertaining to particular organ systems—such as the cardiovascular system [3], reproductive system [4], and bone health [5]—or pertaining to particular functional consequences, such as loss of shoulder function [6,7] or quality of life [8]. Alternatively, research has been organized according to the adverse effects potentially related to radiation therapy [9], chemotherapy [10], or adjuvant endocrine therapies [11]. Rare, unusual, or late effects not routinely hypothesized to be associated with breast cancer or its therapies are often investigated only as case reports or case series [12-14].

The Long-term Survivorship in Older Women with Early Stage Breast Cancer study has constructed a cohort of older breast cancer patients treated in integrated health care systems [15], and a matched cohort of women free of breast cancer [16]. We have investigated whether the breast cancer survivors are at risk for heart disease [17], fractures [18], cancer [16], and the diseases included in the Charlson index (Jordan *et al.*, submitted). Given our access to administrative databases containing healthcare information for all members of both cohorts, we recognized the potential to investigate the association between breast cancer survivorship and a comprehensive set of late events. We therefore implemented a hypothesis scanning investigation to identify potential new associations for late effects of breast cancer by determining whether the distribution of these new associations was centered on the null overall and within disease categories, and whether any individual associations merit further investigation. The resulting data achieved these aims, and provide a pilot data resource for other investigations of late events among breast cancer survivors.

Methods

Setting, design, and subjects

We identified a breast cancer survivor cohort which consisted of 1361 Medicare-eligible women 65 years or older, diagnosed with TNM stage I, IIA, or IIB breast cancer between 1 January 1990 and 31 December 1994, who survived five years after diagnosis, and who were cared for in one of six integrated health care systems: Group Health Cooperative, Seattle, Washington; Kaiser Permanente, Southern California, Pasadena, California; Lovelace Health System, New Mexico; Henry Ford Hospital and Health System, Detroit, MI; HealthPartners, Minnesota; and Reliant Medical Group (formerly Fallon Clinic), Massachusetts [15]. These sites, which are members of the HMO Cancer Research Network (CRN), were chosen to achieve diversity in geography, system size, and patient populations while optimizing study feasibility. At the time the study began, the CRN consisted of the research programs and enrollee populations of 14 integrated health systems with over 11 million enrollees. The overall goal of the CRN is to improve the effectiveness of preventive, curative, and supportive interventions for both major cancers and rare tumors [19].

We matched members of a breast cancer free comparison cohort to the members of the breast cancer survivor cohort [16]. Comparison members were selected from women enrolled in the health plan at least one year before the matched breast cancer patient's diagnosis date, to satisfy the same enrollment criterion as applied to breast cancer patients. Comparison cohort members were further matched one to one on the breast cancer cases' age at diagnosis date. The index date for breast cancer patients was the date of their breast cancer diagnosis. The index date for members of the comparison cohort was the date of breast cancer diagnosis for their matched member of the breast cancer cohort. The protocol for this study was reviewed and approved by the Institutional Review Boards for each participating institution. The study was conducted in compliance with U.S. regulations governing the protection and privacy of human subjects.

Data collection

We collected demographic and comorbidity data for members of both cohorts. Data were collected from electronic sources when available and were supplemented and/or collected from the women's medical records. Standardized medical record reviews were conducted at each site by trained medical record abstractors, and the data were entered directly into a computer-based, menu-driven data collection system [20].

We gathered information on each woman's date of birth, race, and ethnicity for members of the breast cancer cohort from cancer registry databases for sites with cancer registries, from the women's medical records at the sites without cancer registries, and for comparison subjects from medical records. We classified race and ethnicity at all sites using the National Cancer Institute Surveillance, Epidemiology and End Results (SEER) coding instructions for consistency. We identified women of Hispanic ethnicity and grouped the women into the following SEER race categories: white, African-American, American Indian or Alaskan Native, Asian, and native Hawaiian or Pacific Islander.

For members of the breast cancer and comparison cohorts, we collected information on prevalent comorbid conditions one year before and five years after the index date, and incident comorbid conditions over ten years of follow-up beginning on the first day of the sixth year after the index date. We used the prevalent comorbidity data to calculate the Charlson Comorbidity Index (CCI) [21], previously validated in a breast cancer cohort. Data on incident diseases, conditions, and events were collected by harvesting all ICD9 codes that appeared during the ten years of follow-up from the electronic administrative data maintained by the study health plans. These ICD codes were recorded electronically for each patient encounter, including inpatient, outpatient, pharmacy, laboratory, and out-of-plan claims data.

We obtained date of death by matching identifying information with the records of the National Death Index.

Statistical analyses

We computed the frequency and proportion of the breast cancer and comparison cohorts within categories of the demographic variables. We restricted the analysis to ICD codes that had no V prefix (indicating an encounter with a disease or injury, but not a current illness) or E prefix (indicating the source of an external injury) and that were present in at least two members of each cohort. For all incident ICD codes included in the analyses, we computed the follow-up time as the time from the first day of the sixth year after index date to the first recording of that ICD code or end of follow up due to death, disenrollment, or completion of ten years of follow-up (year 6 through 15 after index date). Treating each ICD code as an independent event, we computed the hazard ratio (HR) comparing the incidence rate in the breast cancer cohort with the incidence rate in the comparison cohort.

Comorbidities known to have an association with breast cancer were excluded from this analysis. One of us (TLL) examined the ICD codes and their hazard ratios and prepared a list of those that were candidates for exclusion because their occurrence was clearly expected to be elevated given their close relation to breast cancer and its sequelae. Another of us (RAS) examined this list of candidates for exclusion, blinded to the hazard ratio, and determined a final list of ICD codes for exclusion. This list, and the initial hazard ratio with its 95% confidence interval (CI), included: (a) ICD9 174 malignant neoplasm of female breast (HR=25, 95% CI=20, 33), (b) ICD9 196 secondary and unspecified malignant neoplasm of lymph nodes (HR= 2.4, 95% CI=1.6, 3.8), (c) ICD9 197 secondary malignant neoplasm of respiratory and digestive systems (HR=2.9, 95% CI=2.1, 4.0), (d) ICD9 198 secondary malignant neoplasm of other specified sites (HR=6.6, 95% CI=4.7, 9.2), (e) ICD9 217 benign neoplasm of breast (HR=1.3, 95% CI=0.80, 2.0), (f) ICD9 233 carcinoma *in situ* of breast and genitourinary system (HR=4.3, 95% CI=2.7, 6.8), (g) ICD9 611 other disorders of breast (HR=1.9, 95% CI=1.6, 2.3).

After excluding the above associations that we expected *a priori*, we applied semi-Bayes shrinkage methods to the distribution of remaining hazard ratios [22,23]. Semi-Bayes shrinkage narrows the distribution of observed (conventional) hazard ratios and improves their precision by applying a shrinkage estimator derived from regression methods. Associations well above or below the null, but imprecisely measured, are drawn towards the

center of the distribution to reduce the potential to take notice of what are likely to be overestimates of the true association. To implement the semi-Bayes shrinkage method, we assumed that 95% of true hazard ratios would fall between 0.25 and 4.

In the appendix, we present the frequency of each incident ICD9 code recorded in the breast cancer and comparison cohorts, along with the hazard ratio before and after semi-Bayes shrinkage. We plot histograms of the frequency of occurrence of hazard ratios of varying strength, and cumulative probability plots to show the distribution of the strength of associations overall and within disease categories.

Statistical analyses were conducted using SAS version 9.2 (Cary, NC) and Excel® 2010 (Redmond, WA).

Results

Table 1 shows the demographic characteristics of the breast cancer cohort and matched comparison cohort. The two cohorts were well-balanced with regard to the distribution of age categories, race and ethnicity, and prevalent comorbidities. There were 564 ICD9 codes that met our inclusion criteria for this analysis.

In the ten years of follow-up that began at the start of six years after the index date, the conventional hazard ratios (HR) ranged from 0.21 (95% CI=0.05, 0.96) for other congenital anomalies (ICD9 751) to 5.8 (95% CI=2.0 to 17) for malignant neoplasm of connective and other soft tissue (ICD9 171). After semi-Bayes adjustment, the adjusted hazard ratios (sbHR) ranged from 0.51 (95% CI=0.18, 1.47) for other congenital anomalies of digestive system (ICD9 751) to 3.2 (95% CI=1.89, 5.48) for noninfectious disorders of lymphatic channels (ICD9 457).

Figures 1 and 2 show the distribution of the 564 conventional and semi-Bayes adjusted hazard ratios. The median of the conventional hazard ratios equaled 1.06 (95% CI=0.72, 1.6) and the interquartile range was from a hazard ratio of 0.92 (95% CI=0.33, 2.5) to 1.3 (95% CI=1.1, 1.5). The 2.5th conventional hazard ratio equaled 0.53 (95% CI 0.18, 1.5) and the 97.5th conventional hazard ratio equaled 1.3 (95% CI 1.1, 1.5). As expected, all of the hazard ratios shifted towards the null after semi-Bayes adjustment. The median of the semi-Bayes adjusted hazard ratios equaled 1.06 (95% CI 0.46, 2.45), and the interquartile range was from an adjusted hazard of 0.94 (95% CI 0.72, 1.23) to 1.24 (95% CI 0.87, 1.77). The 2.5th semi-Bayes adjusted hazard ratio equaled 0.69 (95% CI 0.37, 1.26) and the 97.5th semi-Bayes adjusted hazard ratio equaled 1.89 (95% CI 0.99, 3.59).

We compared the distribution of conventional hazard ratios within four disease subgroups, encompassing all included ICD codes, to the overall distribution (Figure 3). The distributions in the infectious diseases subcategory (ICD9 0-139, 680-686, 711) and in the injury and poisoning subcategory (ICD9 800-999) overlapped nearly perfectly with the overall distribution. The distribution in the circulatory system subcategory (ICD9 390-459) was shifted slightly in the direction of negative associations, whereas the distribution in the neoplasms subcategory (ICD9 140-239) was shifted slightly in the direction of positive associations. In the circulatory diseases subcategory, we noted that members of the breast

cancer cohort were less likely to have codes for aortic aneurysms (ICD9 441) over the course of follow-up (n=32) than members of the matched comparison cohort (n=63), yielding a conventional hazard ratio of 0.53 (95% CI=0.34, 0.81) and semi-Bayes adjusted hazard ratio of 0.56 (95% CI=0.35, 0.89). In the positive direction, members of the five-year breast cancer survivor cohort were twice as likely (HR=2.1, 95% CI 1.1, 4.2) to have ICD9 code 338 for pain, not elsewhere classified (n=26) than members of the matched comparison cohort (n=13), with semi-Bayes adjusted hazard ratio of 1.89 (95% CI 0.99, 3.59).

Discussion

The median survival duration after breast cancer diagnosis has continuously improved over the past few decades [24], as a result of screening-related migration of the stage at diagnosis towards earlier stages and as a result of improving primary and adjuvant therapies [25]. With this improving survival, patient and provider attention has shifted toward late effects of breast cancer among long-term survivors [1,2]. Using the cohort of older breast cancer survivors, and their matched comparison cohort, we have previously reported on the relative incidence of heart disease [17], fractures [18], cancer [16], and the comorbid conditions included in the Charlson index (Jordan *et al.*, submitted). Given the administrative setting from which cohort members were identified, we recognized that we could evaluate the complete spectrum of ICD-coded diseases, conditions, and symptoms with marginal effort and cost. We expected this hypothesis scanning exercise to yield new ideas for hypothesis-directed studies of late effects of breast cancer and to provide a data resource of associations that patients and providers could use to evaluate whether incident health effects may have been a late effect related to an earlier diagnosis of breast cancer or its treatment.

Our results generated findings worthy of further consideration. For example, members of the breast cancer cohort were less likely to have ICD codes for aortic aneurysms than members of the matched comparison cohort. Breast cancer and its therapies have been associated with both higher [3,26] and lower [27] risks of heart disease, but we know of no previous report regarding the association between long-term survivorship and the occurrence of aortic aneurysm. As a second example, members of the five-year breast cancer cohort were twice as likely (HR=2.1, 95% CI 1.1, 4.2) to have ICD9 code 338 for pain, not elsewhere classified (n=26) than members of the matched comparison cohort (n=13). Although pain has been identified as a concern in long-term breast cancer survivors [28], and pain is more common in breast cancer survivors than in comparable women at five-years post-diagnosis [29], we know of no study that has compared the occurrence of pain in long-term survivors with a matched comparison group.

These are examples of new directions for further research suggested by our scanning of 564 hypotheses. Many others, with both negative and positive associations, may draw interest from researchers, physicians, and patients interested in late effects associated with breast cancer and its treatments. Those who use the results to investigate a specific late event should focus on the conventional hazard ratio, whereas those who scan the results to identify new avenues for research should focus on the semi-Bayes hazard ratios, since these are less likely to lead down a false-positive path in the hypothesis-generating setting [22,23].

While these two examples and other results may merit further investigation, many of the associations were centered near the null, with a median of the distribution of 564 conventional adjusted hazard ratios equal to 1.06 and with interquartile range from 0.92 to 1.3. Overall, these results suggest that the health of long-term breast cancer survivors may be very similar to comparable women without a history of breast cancer. If there truly is no difference, then a distribution of hazard ratios above and below the null would be expected, which is approximately what we observed. Alternatively, these results may suggest a slight excess in recording of ICD codes for diseases and conditions among five-year survivors of breast cancer than among their matched comparison cohort. Part of this excess may be attributable to codes for neoplasms, the distribution of which was somewhat shifted toward positive associations compared with the overall distribution. This shift persisted despite the fact that we excluded ICD codes for which we expected and observed elevated hazard ratios likely related to the original breast cancer diagnosis. We note that our earlier hypothesis-driven comparison of the risk of second primary neoplasms in the breast cancer survivors, compared with the matched cohort, showed no overall excess risk [16]. In the present investigation, some elevated hazard ratios in the neoplasms category may have resulted from miscoding of breast cancer recurrences or from coding of history of breast cancer, particularly in the ambulatory setting. For example, the conventional hazard ratio for malignant neoplasm of uncertain nature (ICD9 239) equaled 2.1 (95% CI 1.7, 2.5).

The slight shift toward positive associations for all disease categories cannot be entirely explained by the neoplasms categories, however, since the distributions of conventional hazard ratios for the infectious diseases category (median of 31 hazard ratios equaled 1.05) and for the injury and poisoning category (median of 109 hazard ratios equaled 1.06) were very similar to the overall distribution, and therefore similarly shifted toward positive associations. In contrast, the distribution of conventional hazard ratios for the circulatory system ICD codes was slightly shifted toward negative associations compared with the overall distribution (median of 52 hazard ratios equaled 0.97).

This hypothesis scanning investigation has both strengths and limitations. The comparison cohort was matched to breast cancer patients on health plan, enrollment year, and age. Prevalent comorbidities were well balanced in the two cohorts, and there was little loss-to-follow-up aside from that due to deaths. As a result, non-null hazard ratios are unlikely to result entirely from confounding or differential loss to follow-up. We recognized the potential for measurement of multiple associations to generate imprecisely measured, strong estimates of relative effect, and used semi-Bayes methods to address this potential for overestimation. The administrative data used to generate outcomes are not, however, ideally suited for identifying incident diseases and conditions. Some codes likely reflect rule-out diagnoses as opposed to incident conditions, some probably pertain to screening tests rather than to diagnoses, and some likely reflect coding errors. We note, for example, that three members of the all-female breast cancer cohort and five members of the all-female comparison cohort received an ICD code for hyperplasia of the prostate.

In conclusion, this study used administrative data to generate new hypotheses for the late effects among older breast cancer survivors. As the size, complexity, and completeness of administrative health databases has grown, opportunities for high-quality hypothesis-

directed research have expanded as well [30]. The marginal effort to harvest additional information, beyond that required for the original aims, is often low. Prudent analysis and interpretation of these hypothesis-scanning datasets can yield new directions for research, such as the potential to investigate previously poorly studied late effects among breast cancer survivors (e.g., aortic aneurysms or pain). However, the centering of the overall distribution of hazard ratios near the null suggests that, beyond the expected sequelae of the initial breast-cancer, there is little difference in the overall health of long-term breast cancer survivors and comparable women without a history of breast cancer.

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Appendix Table

Frequencies and hazard ratios for included ICD9 codes, sorted by ICD9 code

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
000	16	14	1.4	0.76	2.5	1.3	0.74	2.4
001 Cholera	2	7	0.81	0.3	2.2	0.9	0.39	2.1
008 Intestinal infections due to other organisms	51	53	1.1	0.72	1.6	1.1	0.69	1.6
009 Ill-defined intestinal infections	32	32	1.2	0.8	1.8	1.2	0.76	1.9
011 Pulmonary tuberculosis	4	3	1.4	0.49	4.1	1.3	0.54	3.1
031 Diseases due to other mycobacteria	2	4	0.53	0.1	2.9	0.82	0.27	2.5
034 Streptococcal sore throat and scarlet fever	7	2	3.8	0.78	18.1	1.9	0.65	5.4
038 Septicemia	99	102	1.0	0.78	1.4	1.0	0.72	1.5
041 Bacterial infection in conditions classified elsewhere and of unspecified site	179	185	0.98	0.8	1.2	0.98	0.72	1.3
042 Human immunodeficiency virus [HIV] disease	2	3	1.2	0.63	2.2	1.2	0.63	2.1
053 Herpes zoster	95	99	1.0	0.88	1.2	1.0	0.78	1.4
054 Herpes simplex	23	26	1.1	0.87	1.3	1.1	0.79	1.4
070 Viral hepatitis	7	11	1.0	0.94	1.2	1.0	0.81	1.3
078 Other diseases due to viruses and chlamydiae	58	69	1.1	0.76	1.4	1.1	0.71	1.5
079 Viral and chlamydial infection in conditions classified elsewhere and of unspecified site	108	91	1.3	0.95	1.7	1.2	0.87	1.8

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
110 Dermatophytosis	303	284	1.1	0.97	1.3	1.1	0.86	1.5
111 Dermatomycosis other and unspecified	29	36	0.85	0.52	1.4	0.88	0.52	1.5
112 Candidiasis	79	99	0.83	0.62	1.1	0.84	0.58	1.2
117 Other mycoses	9	11	0.87	0.36	2.1	0.93	0.43	2
133 Acariasis	8	9	0.95	0.37	2.5	0.99	0.44	2.2
134 Other infestation	4	4	1.1	0.27	4.3	1.1	0.4	3.0
136 Other and unspecified infectious and parasitic diseases	12	6	2.1	0.78	5.5	1.7	0.73	3.9
	5	5	1.1	0.31	3.7	1.1	0.42	2.8
	8	2	4.1	0.87	19.4	2.0	0.68	5.7
149 Malignant neoplasm of other and ill-defined sites within the lip oral cavity and pharynx	2	2	1.1	0.15	7.5	1.1	0.34	3.4
150 Malignant neoplasm of esophagus	5	2	2.6	0.51	13.4	1.6	0.53	4.6
151 Malignant neoplasm of stomach	7	8	0.9	0.33	2.5	0.96	0.41	2.3
153 Malignant neoplasm of colon	37	46	0.84	0.55	1.3	0.86	0.54	1.4
154 Malignant neoplasm of rectum rectosigmoid junction and anus	22	20	1.2	0.63	2.1	1.1	0.63	2.1
155 Malignant neoplasm of liver and intrahepatic bile ducts	15	10	1.6	0.71	3.5	1.4	0.7	3.0
157 Malignant neoplasm of pancreas	6	11	0.57	0.21	1.5	0.71	0.31	1.6
158 Malignant neoplasm of retroperitoneum and peritoneum	6	7	0.89	0.3	2.7	0.96	0.4	2.3
159 Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	3	2	1.6	0.27	9.5	1.3	0.41	3.8
160 Malignant neoplasm of nasal cavities middle ear and accessory sinuses	2	2	1.0	0.15	7.4	1.1	0.34	3.4
161 Malignant neoplasm of larynx	2	3	0.69	0.12	4.1	0.92	0.3	2.8
162 Malignant neoplasm of trachea bronchus and lung	77	44	1.8	1.3	2.7	1.8	1.2	2.7
164 Malignant neoplasm of thymus heart and mediastinum	20	10	2.1	0.99	4.5	1.8	0.9	3.7
170 Malignant neoplasm of bone and articular cartilage	20	5	4.2	1.6	11.2	2.7	1.2	6.2

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
171 Malignant neoplasm of connective and other soft tissue	22	4	5.8	2.0	16.8	3.1	1.3	7.5
172 Malignant melanoma of skin	17	11	1.6	0.76	3.5	1.5	0.73	3.0
173 Oth and unspec malignant neoplasm of skin	159	141	1.2	0.96	1.5	1.2	0.87	1.7
179 Malignant neoplasm of uterus, part unspecified	14	6	2.5	0.94	6.4	1.9	0.83	4.3
180 Malignant neoplasm of cervix uteri	7	3	2.4	0.63	9.4	1.6	0.61	4.5
182 Malignant neoplasm of body of uterus	16	13	1.3	0.62	2.7	1.2	0.63	2.5
183 Malignant neoplasm of ovary and other uterine adnexa	20	9	2.3	1.1	5.1	1.9	0.94	4.0
184 Malignant neoplasm of other and unspecified female genital organs	8	3	2.8	0.73	10.4	1.8	0.66	4.8
185 Malignant neoplasm of prostate	3	4	0.78	0.18	3.5	0.94	0.33	2.7
188 Malignant neoplasm of bladder	18	8	2.3	1.0	5.4	1.9	0.9	4.0
189 Malignant neoplasm of kidney and other and unspecified urinary organs	11	10	1.1	0.48	2.7	1.1	0.52	2.4
190 Malignant neoplasm of eye	5	5	1	0.3	3.6	1.1	0.41	2.8
191 Malignant neoplasm of brain	23	13	1.8	0.94	3.7	1.7	0.87	3.2
192 Malignant neoplasm of other and unspecified parts of nervous system	3	2	1.6	0.26	9.4	1.3	0.41	3.8
193 Malignant neoplasm of thyroid gland	8	3	2.8	0.75	10.7	1.8	0.67	4.8
195 Malignant neoplasm of other and ill-defined sites	25	8	3.3	1.5	7.3	2.5	1.2	5.2
199 Malignant neoplasm without specification of site	89	30	3.1	2.1	4.8	2.9	1.8	4.6
200 Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue	5	6	0.88	0.27	2.9	0.96	0.38	2.4
201 Hodgkin's disease	4	2	2.1	0.38	11.3	1.4	0.47	4.2
202 Other malignant neoplasms of lymphoid and histiocytic tissue	28	18	1.6	0.9	2.9	1.5	0.85	2.8
203 Multiple myeloma and immunoproliferative neoplasms	11	9	1.3	0.53	3.1	1.2	0.56	2.6
204 Lymphoid leukemia	9	7	1.3	0.5	3.6	1.3	0.54	2.9
205 Myeloid leukemia	8	2	4.2	0.89	19.8	2	0.69	5.7

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
208 Leukemia of unspecified cell type	5	5	1.1	0.31	3.6	1.1	0.41	2.8
210 Benign neoplasm of lip oral cavity and pharynx	11	10	1.2	0.49	2.7	1.1	0.53	2.4
211 Benign neoplasm of other parts of digestive system	134	144	0.98	0.77	1.2	0.98	0.71	1.4
212 Benign neoplasm of respiratory and intrathoracic organs	6	5	1.2	0.38	4.1	1.2	0.47	3.0
213 Benign neoplasm of bone and articular cartilage	10	7	1.5	0.57	3.9	1.4	0.59	3.1
214 Lipoma	33	34	1.0	0.63	1.6	1	0.62	1.7
215 Other benign neoplasm of connective and other soft tissue	19	14	1.4	0.72	2.9	1.4	0.7	2.6
216 Benign neoplasm of skin	149	140	1.1	0.9	1.4	1.1	0.82	1.6
218 Uterine leiomyoma	24	20	1.3	0.7	2.3	1.2	0.68	2.2
220 Benign neoplasm of ovary	9	11	0.85	0.35	2.1	0.91	0.42	2.0
221 Benign neoplasm of other female genital organs	7	4	1.9	0.55	6.4	1.5	0.57	3.8
224 Benign neoplasm of eye	19	19	1.0	0.55	2.0	1.0	0.56	2.0
225 Benign neoplasm of brain and other parts of nervous system	22	13	1.8	0.89	3.5	1.6	0.83	3.1
227 Benign neoplasm of other endocrine glands and related structures	7	3	2.5	0.65	9.7	1.7	0.62	4.5
228 Hemangioma and lymphangioma any site	29	16	1.9	1.0	3.6	1.8	0.96	3.2
229 Benign neoplasm of other and unspecified sites	8	9	0.94	0.36	2.4	0.98	0.43	2.2
230 Carcinoma in situ of digestive organs	10	5	2.1	0.71	6.1	1.6	0.68	3.9
231 Carcinoma in situ of respiratory system	4	2	2.1	0.39	11.5	1.4	0.47	4.3
232 Carcinoma in situ of skin	32	21	1.6	0.93	2.8	1.5	0.87	2.7
235 Neoplasm of uncertain behavior of digestive and respiratory systems	13	10	1.4	0.6	3.1	1.3	0.61	2.7
236 Neoplasm of uncertain behavior of genitourinary organs	7	5	1.5	0.46	4.6	1.3	0.52	3.2
237 Neoplasm of uncertain behavior of endocrine glands and nervous system	9	3	3.2	0.86	11.7	1.9	0.72	5.1
238 Neoplasm of uncertain behavior of other and unspecified sites and tissues	129	86	1.6	1.2	2.1	1.6	1.1	2.3

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
239 Neoplasms of unspecified nature	246	137	2.0	1.7	2.5	2.0	1.5	2.7
240 Simple and unspecified goiter	17	18	1.0	0.51	1.9	1.0	0.53	1.9
241 Nontoxic nodular goiter	36	25	1.5	0.91	2.5	1.5	0.86	2.5
242 Thyrotoxicosis with or without goiter	51	65	0.82	0.57	1.2	0.84	0.55	1.3
244 Acquired hypothyroidism	335	357	0.96	0.83	1.1	0.96	0.73	1.3
245 Thyroiditis	8	7	1.2	0.44	3.3	1.2	0.5	2.7
246 Other disorders of thyroid	50	40	1.3	0.87	2.0	1.3	0.82	2.1
250 Diabetes mellitus	393	351	1.2	1.0	1.4	1.2	0.91	1.6
251 Other disorders of pancreatic internal secretion	56	44	1.3	0.9	2.0	1.3	0.85	2.1
252 Disorders of parathyroid gland	29	22	1.4	0.81	2.4	1.4	0.77	2.4
253 Disorders of the pituitary gland and its hypothalamic control	15	19	0.83	0.42	1.6	0.87	0.46	1.7
255 Disorders of adrenal glands	21	16	1.4	0.73	2.7	1.3	0.71	2.5
256 Ovarian dysfunction	10	6	1.7	0.62	4.7	1.5	0.63	3.4
258 Polyglandular dysfunction and related disorders	3	6	0.53	0.13	2.1	0.76	0.28	2.1
260 Kwashiorkor	2	7	0.31	0.06	1.5	0.63	0.22	1.8
261 Nutritional marasmus	3	2	1.6	0.27	9.5	1.3	0.41	3.8
263 Other and unspecified protein-calorie malnutrition	66	70	1.0	0.72	1.4	1.0	0.68	1.5
266 Deficiency of b-complex components	30	36	0.87	0.54	1.4	0.89	0.53	1.5
268 Vitamin d deficiency	8	15	0.57	0.24	1.3	0.68	0.32	1.5
269 Other nutritional deficiencies	10	7	1.5	0.58	4.0	1.4	0.6	3.1
270 Disorders of amino-acid transport and metabolism	5	2	2.6	0.51	13.6	1.6	0.53	4.7
271 Disorders of carbohydrate transport and metabolism	11	16	0.74	0.34	1.6	0.81	0.4	1.6
272 Disorders of lipid metabolism	524	604	0.88	0.78	0.99	0.88	0.68	1.1
273 Disorders of plasma protein metabolism	25	33	0.8	0.48	1.4	0.84	0.49	1.4
274 Gout	77	88	0.92	0.68	1.2	0.93	0.64	1.3
275 Disorders of mineral metabolism	113	94	1.3	0.98	1.7	1.3	0.9	1.8
276 Disorders of fluid electrolyte and acid-base balance	589	589	1.1	0.94	1.2	1.1	0.82	1.4

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
277 Other and unspecified disorders of metabolism	11	8	1.5	0.58	3.6	1.3	0.6	2.9
278 Overweight, obesity and other hyperalimentation	168	172	1.0	0.84	1.3	1.0	0.76	1.4
279 Disorders involving the immune mechanism	5	6	0.89	0.27	2.9	0.97	0.38	2.5
280 Iron deficiency anemias	194	191	1.1	0.88	1.3	1.1	0.8	1.5
281 Other deficiency anemias	68	68	1.1	0.75	1.5	1.1	0.71	1.6
282 Hereditary hemolytic anemias	10	10	1.1	0.44	2.5	1.1	0.49	2.3
283 Acquired hemolytic anemias	7	7	1.0	0.37	3.0	1.1	0.45	2.5
284 Aplastic anemia and other bone marrow failure syndromes	25	16	1.6	0.87	3.1	1.5	0.82	2.8
285 Other and unspecified anemias	512	523	1.1	0.93	1.2	1.1	0.81	1.4
286 Coagulation defects	60	48	1.3	0.91	1.9	1.3	0.85	2.0
287 Purpura and other hemorrhagic conditions	60	61	1.0	0.73	1.5	1.0	0.69	1.6
288 Diseases of white blood cells	90	85	1.1	0.83	1.5	1.1	0.77	1.6
289 Other diseases of blood and blood-forming organs	41	33	1.3	0.83	2.1	1.3	0.79	2.1
290 Dementias	200	220	0.95	0.79	1.2	0.95	0.71	1.3
292 Drug-induced mental disorders	18	21	0.91	0.48	1.7	0.94	0.51	1.7
293 Transient mental disorders due to conditions classified elsewhere	89	92	1.0	0.76	1.4	1.0	0.71	1.5
294 Persistent mental disorders due to conditions classified elsewhere	303	292	1.1	0.94	1.3	1.1	0.84	1.5
295 Schizophrenic disorders	8	5	1.7	0.55	5.1	1.4	0.58	3.5
296 Episodic mood disorders	138	145	1.0	0.79	1.3	1.0	0.73	1.4
297 Delusional disorders	13	17	0.81	0.39	1.7	0.86	0.44	1.7
298 Other nonorganic psychoses	110	121	0.96	0.74	1.2	0.96	0.69	1.4
299 Pervasive developmental disorders	2	2	1.1	0.15	7.6	1.1	0.34	3.4
300 Anxiety, dissociative and somatoform disorders	282	279	1.1	0.91	1.3	1.1	0.81	1.4
301 Personality disorders	6	8	0.78	0.27	2.3	0.88	0.37	2.1
303 Alcohol dependence syndrome	16	12	1.4	0.66	3	1.3	0.66	2.7
304 Drug dependence	6	6	1.1	0.34	3.3	1.1	0.43	2.7
305 Nondependent abuse of drugs	93	89	1.1	0.81	1.5	1.1	0.75	1.6

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
306 Physiological malfunction arising from mental factors	5	8	0.66	0.21	2	0.8	0.33	2.0
307 Special symptoms or syndromes not elsewhere classified	74	71	1.1	0.8	1.5	1.1	0.75	1.6
308 Acute reaction to stress	65	53	1.3	0.9	1.9	1.3	0.84	1.9
309 Adjustment reaction	70	88	0.83	0.61	1.1	0.84	0.57	1.2
310 Specific nonpsychotic mental disorders due to brain damage	24	44	0.57	0.35	0.94	0.62	0.37	1.0
311 Depressive disorder, not elsewhere classified	359	333	1.2	1.0	1.4	1.2	0.89	1.5
316 Psychic factors associated with diseases classified elsewhere	4	3	1.4	0.31	6.2	1.2	0.43	3.5
322 Meningitis of unspecified cause	6	7	0.9	0.3	2.7	0.97	0.4	2.3
327 Organic sleep disorders	6	6	1.1	0.35	3.3	1.1	0.44	2.7
330 Cerebral degenerations usually manifest in childhood	3	3	1.0	0.21	5.1	1.1	0.37	3.1
331 Other cerebral degenerations	217	264	0.86	0.72	1.0	0.86	0.64	1.1
332 Parkinson's disease	42	50	0.87	0.58	1.3	0.89	0.56	1.4
333 Other extrapyramidal disease and abnormal movement disorders	68	74	0.97	0.7	1.3	0.98	0.66	1.4
334 Spinocerebellar disease	2	5	0.42	0.08	2.2	0.73	0.25	2.2
336 Other diseases of spinal cord	12	13	0.97	0.44	2.1	1.0	0.48	2.0
337 Disorders of the autonomic nervous system	19	35	0.57	0.33	0.99	0.62	0.35	1.1
338 Pain, not elsewhere classified	26	13	2.1	1.1	4.2	1.9	0.99	3.6
340 Multiple sclerosis	8	3	2.7	0.72	10.3	1.8	0.66	4.7
341 Other demyelinating diseases of central nervous system	3	2	1.5	0.26	9.2	1.2	0.41	3.8
342 Hemiplegia and hemiparesis	71	86	0.86	0.63	1.2	0.87	0.6	1.3
343 Infantile cerebral palsy	5	5	1.0	0.29	3.5	1.0	0.41	2.7
344 Other paralytic syndromes	20	21	1.0	0.54	1.9	1.0	0.56	1.9
345 Epilepsy and recurrent seizures	26	30	0.92	0.54	1.5	0.94	0.55	1.6
346 Migraine	25	34	0.77	0.46	1.3	0.8	0.47	1.4
348 Other conditions of brain	74	72	1.1	0.78	1.5	1.1	0.73	1.6
349 Other and unspecified disorders of the nervous system	6	4	1.6	0.44	5.5	1.3	0.51	3.5

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
350 Trigeminal nerve disorders	16	7	2.4	1.0	5.9	1.9	0.88	4.2
351 Facial nerve disorders	22	15	1.5	0.8	3	1.4	0.77	2.7
352 Disorders of other cranial nerves	4	6	0.69	0.2	2.5	0.85	0.33	2.2
353 Nerve root and plexus disorders	11	5	2.3	0.81	6.7	1.8	0.74	4.2
354 Mononeuritis of upper limb and mononeuritis multiplex	86	70	1.3	0.95	1.8	1.3	0.88	1.9
355 Mononeuritis of lower limb and unspecified site	67	76	0.91	0.66	1.3	0.92	0.62	1.4
356 Hereditary and idiopathic peripheral neuropathy	115	98	1.3	0.96	1.6	1.2	0.88	1.8
357 Inflammatory and toxic neuropathy	94	70	1.4	1.0	1.9	1.4	0.96	2.1
358 Myoneural disorders	5	4	1.3	0.35	4.9	1.2	0.45	3.2
359 Muscular dystrophies and other myopathies	11	7	1.7	0.64	4.3	1.4	0.64	3.3
360 Disorders of the globe	15	16	0.99	0.49	2.0	1.0	0.52	2.0
361 Retinal detachments and defects	28	30	0.97	0.58	1.6	0.99	0.58	1.7
362 Other retinal disorders	456	424	1.1	1.0	1.3	1.1	0.87	1.5
363 Chorioretinal inflammations scars and other disorders of choroid	13	19	0.72	0.35	1.4	0.78	0.4	1.5
364 Disorders of iris and ciliary body	39	45	0.91	0.59	1.4	0.92	0.58	1.5
365 Glaucoma	317	318	1.0	0.89	1.2	1.0	0.79	1.4
366 Cataract	805	843	1.0	0.91	1.1	1.0	0.78	1.3
367 Disorders of refraction and accommodation	711	773	0.97	0.87	1.1	0.97	0.75	1.2
368 Visual disturbances	200	222	0.93	0.77	1.1	0.93	0.7	1.3
369 Blindness and low vision	52	63	0.87	0.6	1.3	0.89	0.58	1.3
370 Keratitis	56	54	1.1	0.75	1.6	1.1	0.71	1.7
371 Corneal opacity and other disorders of cornea	81	85	1.0	0.74	1.4	1.0	0.69	1.5
372 Disorders of conjunctiva	174	210	0.87	0.71	1.1	0.87	0.64	1.2
373 Inflammation of eyelids	204	208	1.0	0.86	1.3	1.0	0.78	1.4
374 Other disorders of eyelids	122	126	1.0	0.79	1.3	1.0	0.73	1.4
375 Disorders of lacrimal system	237	226	1.1	0.92	1.3	1.1	0.83	1.5
376 Disorders of the orbit	10	5	2.1	0.72	6.1	1.6	0.68	4.0
377 Disorders of optic nerve and visual pathways	24	37	0.68	0.41	1.1	0.72	0.42	1.2

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
378 Strabismus and other disorders of binocular eye movements	50	50	1.1	0.71	1.6	1.1	0.68	1.6
379 Other disorders of eye	231	225	1.1	0.9	1.3	1.1	0.81	1.4
380 Disorders of external ear	267	319	0.86	0.73	1.0	0.86	0.65	1.1
381 Nonsuppurative otitis media and	66	80	0.86	0.62	1.2	0.87	0.59	1.3
382 Suppurative and unspecified otitis media	50	56	0.94	0.64	1.4	0.95	0.61	1.5
383 Mastoiditis and related conditions	3	5	0.63	0.15	2.6	0.84	0.3	2.3
384 Other disorders of tympanic membrane	9	9	1.1	0.42	2.7	1.1	0.48	2.4
385 Other disorders of middle ear and mastoid	10	5	2.1	0.72	6.2	1.7	0.69	4.0
386 Vertiginous syndromes and other disorders of vestibular system	96	98	1.0	0.77	1.4	1.0	0.72	1.5
388 Other disorders of ear	119	105	1.2	0.92	1.5	1.2	0.84	1.7
389 Hearing loss	339	345	1.0	0.89	1.2	1.0	0.78	1.4
392 Rheumatic chorea	3	2	1.6	0.26	9.4	1.3	0.41	3.8
394 Diseases of mitral valve	22	20	1.1	0.63	2.1	1.1	0.63	2.1
395 Diseases of aortic valve	9	8	1.2	0.45	3.0	1.1	0.5	2.6
396 Diseases of mitral and aortic valves	52	65	0.84	0.58	1.2	0.85	0.56	1.3
397 Diseases of other endocardial structures	39	40	1.0	0.66	1.6	1.0	0.64	1.7
398 Other rheumatic heart disease	14	16	0.92	0.45	1.9	0.95	0.48	1.9
401 Essential hypertension	1028	1053	1.0	0.93	1.1	1.0	0.79	1.3
402 Hypertensive heart disease	109	96	1.2	0.92	1.6	1.2	0.85	1.7
403 Hypertensive chronic kidney disease	107	98	1.2	0.88	1.5	1.2	0.81	1.6
404 Hypertensive heart and chronic kidney disease	16	27	0.63	0.34	1.2	0.69	0.37	1.3
405 Secondary hypertension	11	12	0.95	0.42	2.2	0.98	0.47	2.1
410 Acute myocardial infarction	155	180	0.9	0.73	1.1	0.91	0.66	1.2
411 Other acute and subacute forms of ischemic heart disease	127	133	1.0	0.78	1.3	1.0	0.72	1.4
412 Old myocardial infarction	131	157	0.86	0.69	1.1	0.87	0.63	1.2
413 Angina pectoris	181	214	0.87	0.71	1.1	0.87	0.65	1.2
414 Other forms of chronic ischemic heart disease	384	408	0.97	0.84	1.1	0.97	0.74	1.3

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
415 Acute pulmonary heart disease	43	43	1.1	0.69	1.6	1.1	0.66	1.7
416 Chronic pulmonary heart disease	65	80	0.85	0.62	1.2	0.86	0.58	1.3
420 Acute pericarditis	8	8	1.0	0.39	2.8	1.1	0.46	2.4
421 Acute and subacute endocarditis	6	7	0.91	0.3	2.7	0.97	0.4	2.4
423 Other diseases of pericardium	22	24	0.96	0.54	1.7	0.98	0.55	1.8
424 Other diseases of endocardium	247	278	0.92	0.78	1.1	0.92	0.69	1.2
425 Cardiomyopathy	90	89	1.1	0.79	1.4	1.1	0.74	1.5
426 Conduction disorders	157	140	1.2	0.95	1.5	1.2	0.86	1.6
427 Cardiac dysrhythmias	585	573	1.1	0.98	1.2	1.1	0.85	1.4
428 Heart failure	432	443	1.0	0.89	1.2	1.0	0.78	1.3
429 Ill-defined descriptions and complications of heart disease	239	268	0.94	0.79	1.1	0.94	0.71	1.3
430 Subarachnoid hemorrhage	5	11	0.48	0.17	1.4	0.65	0.27	1.6
431 Intracerebral hemorrhage	41	57	0.76	0.51	1.1	0.78	0.5	1.2
432 Other and unspecified intracranial hemorrhage	15	25	0.63	0.33	1.2	0.69	0.37	1.3
433 Occlusion and stenosis of precerebral arteries	93	115	0.83	0.63	1.1	0.84	0.59	1.2
434 Occlusion of cerebral arteries	116	150	0.81	0.63	1.0	0.81	0.58	1.1
435 Transient cerebral ischemia	158	167	0.99	0.8	1.2	0.99	0.72	1.4
436 Acute, but ill-defined, cerebrovascular disease	207	241	0.9	0.74	1.1	0.9	0.67	1.2
437 Other and ill-defined cerebrovascular disease	116	121	1.0	0.79	1.3	1.0	0.73	1.4
438 Late effects of cerebrovascular disease	145	148	1.0	0.83	1.3	1.0	0.76	1.4
440 Atherosclerosis	127	155	0.85	0.68	1.1	0.86	0.62	1.2
441 Aortic aneurysm and dissection	32	63	0.53	0.34	0.81	0.56	0.35	0.89
442 Other aneurysm	10	11	0.95	0.4	2.2	0.98	0.46	2.1
443 Other peripheral vascular disease	173	180	1.0	0.81	1.2	1.0	0.73	1.4
444 Arterial embolism and thrombosis	20	27	0.78	0.44	1.4	0.82	0.46	1.5
446 Polyarteritis nodosa and allied conditions	25	24	1.1	0.63	1.9	1.1	0.62	1.9
447 Other disorders of arteries and arterioles	35	32	1.1	0.71	1.9	1.1	0.69	1.9
448 Disease of capillaries	11	9	1.3	0.54	3.1	1.2	0.57	2.7

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
451 Phlebitis and thrombophlebitis	71	63	1.2	0.85	1.7	1.2	0.79	1.8
453 Other venous embolism and thrombosis	86	92	0.98	0.73	1.3	0.99	0.68	1.4
454 Varicose veins of lower extremities	92	106	0.91	0.69	1.2	0.92	0.64	1.3
455 Hemorrhoids	169	152	1.2	0.95	1.5	1.2	0.86	1.6
456 Varicose veins of other sites	3	8	0.39	0.1	1.5	0.64	0.24	1.7
457 Noninfectious disorders of lymphatic channels	66	19	3.7	2.2	6.2	3.2	1.9	5.5
458 Hypotension	167	190	0.93	0.75	1.1	0.93	0.68	1.3
459 Other disorders of circulatory system	198	186	1.1	0.94	1.4	1.1	0.85	1.5
460 Acute nasopharyngitis [common cold]	61	45	1.4	0.98	2.1	1.4	0.92	2.2
461 Acute sinusitis	126	134	0.99	0.77	1.3	0.99	0.71	1.4
462 Acute pharyngitis	111	116	1.0	0.78	1.3	1.0	0.72	1.4
463 Acute tonsillitis	4	3	1.4	0.32	6.4	1.2	0.44	3.5
464 Acute laryngitis and tracheitis	26	18	1.5	0.84	2.8	1.5	0.8	2.6
465 Acute upper respiratory infections of multiple or unspecified sites	313	316	1.0	0.9	1.2	1.0	0.8	1.4
466 Acute bronchitis and bronchiolitis	264	316	0.86	0.73	1.0	0.86	0.65	1.1
470 Deviated nasal septum	9	4	2.4	0.74	7.7	1.7	0.68	4.3
472 Chronic pharyngitis and nasopharyngitis	73	76	1.0	0.73	1.4	1.0	0.69	1.5
473 Chronic sinusitis	98	111	0.93	0.71	1.2	0.93	0.66	1.3
476 Chronic laryngitis and laryngotracheitis	7	5	1.5	0.46	4.6	1.3	0.52	3.2
477 Allergic rhinitis	142	170	0.87	0.7	1.1	0.88	0.64	1.2
478 Other diseases of upper respiratory tract	58	71	0.85	0.6	1.2	0.87	0.58	1.3
480 Viral pneumonia	8	8	1.0	0.39	2.8	1.1	0.46	2.4
481 Pneumococcal pneumonia [Streptococcus pneumoniae pneumonia]	15	19	0.84	0.43	1.6	0.88	0.46	1.7
482 Other bacterial pneumonia	48	52	0.97	0.66	1.4	0.98	0.63	1.5
485 Bronchopneumonia, organism unspecified	5	8	0.66	0.21	2.0	0.8	0.33	2
486 Pneumonia, organism unspecified	401	435	0.96	0.84	1.1	0.96	0.73	1.2
487 Influenza	39	37	1.1	0.7	1.7	1.1	0.67	1.8
490 Bronchitis, not specified as acute or chronic	136	156	0.91	0.72	1.1	0.91	0.66	1.3

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
491 Chronic bronchitis	110	124	0.93	0.72	1.2	0.93	0.66	1.3
492 Emphysema	55	50	1.2	0.79	1.7	1.1	0.74	1.8
493 Asthma	163	170	1.0	0.81	1.3	1.0	0.74	1.4
494 Bronchiectasis	15	13	1.2	0.58	2.6	1.2	0.6	2.4
496 Chronic airway obstruction, not elsewhere classified	272	303	0.93	0.79	1.1	0.93	0.71	1.2
507 Pneumonitis due to solids and liquids	56	67	0.88	0.62	1.3	0.9	0.59	1.4
510 Empyema	5	4	1.3	0.35	4.8	1.2	0.45	3.2
511 Pleurisy	209	157	1.4	1.2	1.8	1.4	1.0	1.9
512 Pneumothorax and air leak	38	22	1.8	1.1	3.1	1.7	1.0	2.9
514 Pulmonary congestion and hypostasis	91	97	0.99	0.74	1.3	0.99	0.69	1.4
515 Postinflammatory pulmonary fibrosis	42	34	1.3	0.83	2.1	1.3	0.79	2.1
516 Other alveolar and parietoalveolar pneumonopathy	7	5	1.5	0.47	4.7	1.3	0.53	3.3
517 Lung involvement in conditions classified elsewhere	7	8	0.92	0.33	2.5	0.98	0.42	2.3
518 Other diseases of lung	319	347	0.98	0.84	1.1	0.98	0.74	1.3
519 Other diseases of respiratory system	47	38	1.3	0.86	2	1.3	0.81	2.1
521 Diseases of hard tissues of teeth	6	4	1.6	0.45	5.6	1.3	0.51	3.5
522 Diseases of pulp and periapical tissues	5	10	0.53	0.18	1.5	0.69	0.29	1.7
523 Gingival and periodontal diseases	7	6	1.2	0.41	3.6	1.2	0.48	2.8
524 Dentofacial anomalies, including malocclusion	41	38	1.1	0.73	1.8	1.1	0.7	1.8
525 Other diseases and conditions of the teeth and supporting structures	7	6	1.2	0.41	3.7	1.2	0.48	2.9
526 Diseases of the jaws	10	8	1.3	0.52	3.3	1.2	0.56	2.8
527 Diseases of the salivary glands	34	35	1.0	0.64	1.6	1.0	0.62	1.7
528 Diseases of the oral soft tissues excluding lesions specific for gingiva and tongue	66	54	1.3	0.91	1.9	1.3	0.85	1.9
529 Diseases and other conditions of the tongue	14	12	1.2	0.57	2.6	1.2	0.58	2.4
530 Diseases of esophagus	376	390	1.0	0.88	1.2	1.0	0.77	1.3
531 Gastric ulcer	47	47	1.1	0.71	1.6	1.1	0.68	1.7
532 Duodenal ulcer	19	18	1.1	0.59	2.1	1.1	0.59	2.1

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
533 Peptic ulcer site unspecified	45	54	0.87	0.59	1.3	0.89	0.57	1.4
535 Gastritis and duodenitis	128	145	0.93	0.74	1.2	0.94	0.68	1.3
536 Disorders of function of stomach	107	131	0.85	0.66	1.1	0.86	0.61	1.2
537 Other disorders of stomach and duodenum	14	17	0.86	0.42	1.7	0.9	0.46	1.8
540 Acute appendicitis	4	9	0.47	0.14	1.5	0.67	0.26	1.7
550 Inguinal hernia	18	22	0.85	0.46	1.6	0.89	0.48	1.6
552 Other hernia of abdominal cavity with obstruction but without mention of gangrene	12	8	1.6	0.65	3.9	1.4	0.65	3.1
553 Other hernia of abdominal cavity without mention of obstruction or gangrene	140	142	1.1	0.83	1.3	1.1	0.76	1.5
555 Regional enteritis	6	8	0.79	0.28	2.3	0.89	0.37	2.1
556 Ulcerative enterocolitis	10	18	0.58	0.27	1.3	0.67	0.33	1.4
557 Vascular insufficiency of intestine	22	23	1.0	0.57	1.8	1.0	0.57	1.8
558 Other and unspecified noninfectious gastroenteritis and colitis	131	161	0.85	0.68	1.1	0.86	0.62	1.2
560 Intestinal obstruction without mention of hernia	83	106	0.81	0.61	1.1	0.82	0.57	1.2
562 Diverticula of intestine	260	249	1.1	0.95	1.3	1.1	0.84	1.5
564 Functional digestive disorders not elsewhere classified	372	362	1.1	0.93	1.2	1.1	0.82	1.4
565 Anal fissure and fistula	11	7	1.7	0.64	4.3	1.5	0.64	3.3
566 Abscess of anal and rectal regions	5	8	0.66	0.22	2.0	0.81	0.33	2.0
567 Peritonitis and retroperitoneal infections	10	13	0.81	0.36	1.9	0.88	0.42	1.8
568 Other disorders of peritoneum	18	15	1.3	0.64	2.5	1.2	0.64	2.4
569 Other disorders of intestine	165	162	1.1	0.87	1.3	1.1	0.79	1.5
570 Acute and subacute necrosis of liver	3	4	0.78	0.18	3.5	0.94	0.33	2.7
571 Chronic liver disease and cirrhosis	21	22	0.99	0.55	1.8	1.0	0.56	1.8
572 Liver abscess and sequelae of chronic liver disease	11	12	0.96	0.42	2.2	0.99	0.47	2.1
573 Other disorders of liver	46	44	1.1	0.73	1.7	1.1	0.7	1.7
574 Cholelithiasis	101	93	1.1	0.86	1.5	1.1	0.79	1.6
575 Other disorders of gallbladder	41	46	0.94	0.62	1.4	0.95	0.6	1.5

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
576 Other disorders of biliary tract	24	20	1.3	0.71	2.3	1.2	0.69	2.3
577 Diseases of pancreas	35	49	0.75	0.49	1.2	0.78	0.48	1.2
578 Gastrointestinal hemorrhage	195	227	0.91	0.75	1.1	0.91	0.68	1.2
579 Intestinal malabsorption	9	13	0.73	0.31	1.7	0.82	0.38	1.7
580 Acute glomerulonephritis	3	5	0.63	0.15	2.6	0.83	0.3	2.3
581 Nephrotic syndrome	6	10	0.63	0.23	1.7	0.76	0.33	1.8
582 Chronic glomerulonephritis	22	22	1.1	0.59	1.9	1.1	0.59	1.9
583 Nephritis and nephropathy not specified as acute or chronic	41	39	1.1	0.72	1.7	1.1	0.69	1.8
584 Acute kidney failure	119	132	0.96	0.75	1.2	0.96	0.69	1.3
585 Chronic kidney disease (ckd)	152	159	1.0	0.81	1.3	1	0.74	1.4
586 Renal failure, unspecified	68	67	1.1	0.77	1.5	1.1	0.72	1.6
588 Disorders resulting from impaired renal function	21	18	1.2	0.66	2.3	1.2	0.65	2.2
590 Infections of kidney	47	42	1.2	0.78	1.8	1.2	0.74	1.8
591 Hydronephrosis	32	36	0.93	0.58	1.5	0.95	0.57	1.6
592 Calculus of kidney and ureter	37	26	1.5	0.91	2.5	1.4	0.85	2.4
593 Other disorders of kidney and ureter	225	219	1.1	0.9	1.3	1.1	0.81	1.5
594 Calculus of lower urinary tract	3	4	0.78	0.18	3.5	0.94	0.33	2.7
595 Cystitis	89	64	1.5	1.1	2.0	1.5	0.99	2.1
596 Other disorders of bladder	36	41	0.92	0.59	1.4	0.94	0.58	1.5
597 Urethritis not sexually transmitted and urethral syndrome	17	12	1.5	0.71	3.1	1.4	0.7	2.8
599 Other disorders of urethra and urinary tract	676	706	1.0	0.91	1.1	1.0	0.79	1.3
600 Hyperplasia of prostate	3	5	0.62	0.15	2.6	0.83	0.3	2.3
610 Benign mammary dysplasias	85	79	1.1	0.82	1.5	1.1	0.76	1.6
614 Inflammatory disease of ovary fallopian tube pelvic cellular tissue and peritoneum	8	8	1.1	0.4	2.8	1.1	0.46	2.4
616 Inflammatory disease of cervix vagina and vulva	110	103	1.1	0.86	1.5	1.1	0.79	1.6
617 Endometriosis	9	8	1.2	0.45	3.1	1.1	0.51	2.6
618 Genital prolapse	78	99	0.82	0.61	1.1	0.83	0.57	1.2
619 Fistula involving female genital tract	2	2	1.0	0.15	7.4	1.1	0.34	3.4
620 Noninflammatory disorders of ovary fallopian tube and broad ligament	15	19	0.82	0.42	1.6	0.87	0.45	1.7

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
621 Disorders of uterus not elsewhere classified	43	38	1.2	0.76	1.8	1.2	0.72	1.9
622 Noninflammatory disorders of cervix	21	20	1.1	0.62	2.1	1.1	0.62	2.1
623 Noninflammatory disorders of vagina	36	50	0.76	0.49	1.2	0.78	0.49	1.2
624 Noninflammatory disorders of vulva and perineum	17	15	1.2	0.6	2.4	1.2	0.61	2.3
625 Pain and other symptoms associated with female genital organs	130	131	1.0	0.82	1.3	1.0	0.75	1.5
626 Disorders of menstruation and other abnormal bleeding from female genital tract	19	25	0.79	0.44	1.4	0.83	0.46	1.5
627 Menopausal and postmenopausal disorders	159	200	0.81	0.66	1.0	0.82	0.6	1.1
629 Other disorders of female genital organs	2	3	0.7	0.12	4.2	0.93	0.3	2.8
680 Carbuncle and furuncle	7	8	0.92	0.33	2.5	0.98	0.42	2.3
681 Cellulitis and abscess of finger and toe	77	87	0.94	0.69	1.3	0.94	0.65	1.4
682 Other cellulitis and abscess	293	281	1.1	0.95	1.3	1.1	0.84	1.5
684 Impetigo	17	15	1.2	0.6	2.4	1.2	0.61	2.3
685 Pilonidal cyst	2	2	1.1	0.15	7.6	1.1	0.34	3.4
686 Other local infections of skin and subcutaneous tissue	62	66	0.98	0.69	1.4	0.99	0.66	1.5
690 Erythematous dermatosis	56	49	1.2	0.82	1.8	1.2	0.78	1.9
691 Atopic dermatitis and related conditions	43	40	1.1	0.74	1.7	1.1	0.71	1.8
692 Contact dermatitis and other eczema	305	345	0.91	0.78	1.1	0.91	0.69	1.2
693 Dermatitis due to substances taken internally	15	18	0.88	0.44	1.7	0.92	0.48	1.8
695 Erythematous conditions	72	74	1.0	0.74	1.4	1.0	0.7	1.5
696 Psoriasis and similar disorders	34	21	1.7	0.99	2.9	1.6	0.92	2.8
697 Lichen	8	10	0.83	0.33	2.1	0.9	0.4	2
698 Pruritus and related conditions	64	70	0.97	0.69	1.4	0.97	0.65	1.5
700 Corns and callosities	154	149	1.1	0.87	1.4	1.1	0.79	1.5
701 Other hypertrophic and atrophic conditions of skin	177	137	1.4	1.1	1.7	1.4	1.0	1.9
702 Other dermatoses	353	377	0.99	0.85	1.1	0.99	0.75	1.3
703 Diseases of nail	249	244	1.1	0.9	1.3	1.1	0.81	1.4
704 Diseases of hair and hair follicles	44	33	1.4	0.9	2.2	1.4	0.85	2.2

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
705 Disorders of sweat glands	8	8	1.1	0.4	2.8	1.1	0.46	2.4
706 Diseases of sebaceous glands	189	159	1.3	1.0	1.6	1.3	0.94	1.7
707 Chronic ulcer of skin	202	223	0.96	0.8	1.2	0.96	0.72	1.3
708 Urticaria	37	40	0.98	0.62	1.5	0.99	0.61	1.6
709 Other disorders of skin and subcutaneous tissue	220	184	1.3	1.1	1.6	1.3	0.97	1.8
710 Diffuse diseases of connective tissue	24	22	1.1	0.64	2.0	1.1	0.64	2.0
711 Arthropathy associated with infections	11	7	1.6	0.63	4.2	1.4	0.64	3.2
712 Crystal arthropathies	17	11	1.6	0.76	3.5	1.5	0.73	3.0
713 Arthropathy associated with other disorders classified elsewhere	2	5	0.42	0.08	2.2	0.74	0.25	2.2
714 Rheumatoid arthritis and other inflammatory polyarthropathies	77	75	1.1	0.77	1.5	1.1	0.72	1.6
715 Osteoarthritis and allied disorders	699	714	1.0	0.94	1.2	1.0	0.81	1.3
716 Other and unspecified arthropathies	249	257	1.0	0.85	1.2	1.0	0.76	1.3
717 Internal derangement of knee	48	36	1.4	0.92	2.2	1.4	0.86	2.2
718 Other derangement of joint	67	54	1.3	0.91	1.9	1.3	0.85	1.9
719 Other and unspecified disorders of joint	690	710	1.1	0.96	1.2	1.1	0.83	1.4
720 Ankylosing spondylitis and other inflammatory spondylopathies	7	14	0.53	0.21	1.3	0.66	0.3	1.5
721 Spondylosis and allied disorders	180	171	1.1	0.92	1.4	1.1	0.83	1.5
722 Intervertebral disc disorders	219	207	1.1	0.93	1.4	1.1	0.83	1.5
723 Other disorders of cervical region	227	216	1.1	0.93	1.4	1.1	0.84	1.5
724 Other and unspecified disorders of back	591	622	0.98	0.87	1.1	0.98	0.76	1.3
725 Polymyalgia rheumatica	33	42	0.81	0.52	1.3	0.84	0.51	1.4
726 Peripheral enthesopathies and allied syndromes	317	313	1.1	0.92	1.3	1.1	0.82	1.4
727 Other disorders of synovium tendon and bursa	230	224	1.1	0.9	1.3	1.1	0.81	1.5
728 Disorders of muscle ligament and fascia	233	246	1.0	0.84	1.2	1.0	0.76	1.3
729 Other disorders of soft tissues	638	615	1.1	1.0	1.3	1.1	0.88	1.5

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
730 Osteomyelitis periostitis and other infections involving bone	20	20	1.1	0.57	2	1.1	0.58	2.0
731 Osteitis deformans and osteopathies associated with other disorders classified elsewhere	11	9	1.3	0.53	3.1	1.2	0.56	2.7
732 Osteochondropathies	3	6	0.52	0.13	2.1	0.75	0.28	2.1
733 Other disorders of bone and cartilage	537	537	1.1	0.97	1.2	1.1	0.85	1.4
734 Flat foot	13	15	0.92	0.44	1.9	0.95	0.48	1.9
735 Acquired deformities of toe	109	105	1.1	0.84	1.4	1.1	0.77	1.5
736 Other acquired deformities of limbs	51	42	1.3	0.85	1.9	1.3	0.8	2
737 Curvature of spine	57	52	1.2	0.79	1.7	1.1	0.75	1.8
738 Other acquired musculoskeletal deformity	30	32	0.98	0.6	1.6	1.0	0.59	1.7
739 Nonallopathic lesions not elsewhere classified	33	36	0.96	0.6	1.5	0.97	0.59	1.6
742 Other congenital anomalies of nervous system	3	7	0.45	0.12	1.7	0.69	0.26	1.9
743 Congenital anomalies of eye	21	21	1.1	0.57	1.9	1.1	0.58	1.9
745 Bulbus cordis anomalies and anomalies of cardiac septal closure	5	3	1.7	0.41	7.3	1.4	0.49	3.8
746 Other congenital anomalies of heart	23	21	1.1	0.64	2.1	1.1	0.63	2.1
747 Other congenital anomalies of circulatory system	15	18	0.88	0.44	1.7	0.92	0.48	1.8
750 Other congenital anomalies of upper alimentary tract	13	11	1.3	0.56	2.8	1.2	0.58	2.5
751 Other congenital anomalies of digestive system	2	10	0.21	0.05	0.96	0.52	0.18	1.5
752 Congenital anomalies of genital organs	2	4	0.51	0.09	2.8	0.81	0.27	2.4
753 Congenital anomalies of urinary system	20	13	1.6	0.81	3.3	1.5	0.77	2.9
754 Certain congenital musculoskeletal deformities	14	10	1.5	0.66	3.3	1.4	0.66	2.9
755 Other congenital anomalies of limbs	14	12	1.2	0.57	2.7	1.2	0.59	2.4
756 Other congenital musculoskeletal anomalies	22	25	0.97	0.54	1.7	0.98	0.55	1.8
757 Congenital anomalies of the integument	23	8	3.1	1.4	6.9	2.4	1.1	4.9
759 Other and unspecified congenital anomalies	13	7	1.9	0.78	4.9	1.6	0.73	3.6

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
769 Respiratory distress syndrome in newborn	2	3	0.69	0.12	4.1	0.92	0.3	2.8
779 Other and ill-defined conditions originating in the perinatal period	3	2	1.6	0.26	9.4	1.3	0.41	3.8
780 General symptoms	930	930	1.1	0.98	1.2	1.1	0.84	1.4
781 Symptoms involving nervous and musculoskeletal systems	302	304	1.1	0.9	1.2	1.1	0.8	1.4
782 Symptoms involving skin and other integumentary tissue	531	567	0.98	0.87	1.1	0.98	0.76	1.3
783 Symptoms concerning nutrition metabolism and development	273	263	1.1	0.93	1.3	1.1	0.83	1.5
784 Symptoms involving head and neck	405	414	1.0	0.91	1.2	1.0	0.8	1.4
785 Symptoms involving cardiovascular system	395	354	1.2	1.1	1.4	1.2	0.94	1.6
786 Symptoms involving respiratory system and other chest symptoms	934	931	1.1	0.99	1.2	1.1	0.85	1.4
787 Symptoms involving digestive system	558	573	1.1	0.94	1.2	1.1	0.82	1.4
788 Symptoms involving urinary system	394	434	0.94	0.82	1.1	0.94	0.72	1.2
789 Other symptoms involving abdomen and pelvis	565	552	1.1	0.95	1.2	1.1	0.83	1.4
790 Nonspecific findings on examination of blood	261	273	1.0	0.87	1.2	1.0	0.77	1.4
791 Nonspecific findings on examination of urine	72	56	1.4	0.98	2.0	1.4	0.91	2.1
792 Nonspecific abnormal findings in other body substances	52	54	1.0	0.69	1.5	1.0	0.66	1.6
793 Nonspecific (abnormal) findings on radiological and other examination of body structure	369	317	1.3	1.1	1.5	1.3	0.98	1.7
794 Nonspecific abnormal results of function studies	232	264	0.92	0.77	1.1	0.92	0.69	1.2
795 Other and nonspecific abnormal cytological, histological, immunological, and dna test findings	50	44	1.2	0.8	1.8	1.2	0.76	1.9
796 Other nonspecific abnormal findings	265	308	0.9	0.76	1.1	0.9	0.68	1.2
797 Senility without mention of psychosis	8	6	1.4	0.49	4.1	1.3	0.54	3.1
798 Sudden death cause unknown	2	2	1.0	0.15	7.4	1.1	0.34	3.4

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
799 Other ill-defined and unknown causes of morbidity and mortality	364	356	1.1	0.93	1.2	1.1	0.82	1.4
801 Fracture of base of skull	4	3	1.4	0.32	6.3	1.2	0.43	3.5
802 Fracture of face bones	23	19	1.3	0.7	2.4	1.3	0.69	2.3
805 Fracture of vertebral column without mention of spinal cord injury	83	79	1.1	0.82	1.5	1.1	0.76	1.6
806 Fracture of vertebral column with spinal cord injury	10	8	1.3	0.53	3.4	1.3	0.56	2.8
807 Fracture of rib(s) sternum larynx and trachea	59	44	1.4	0.97	2.1	1.4	0.9	2.2
808 Fracture of pelvis	45	40	1.2	0.78	1.8	1.2	0.74	1.9
810 Fracture of clavicle	8	9	0.93	0.36	2.4	0.98	0.43	2.2
811 Fracture of scapula	5	5	1.0	0.3	3.6	1.1	0.41	2.8
812 Fracture of humerus	71	57	1.3	0.93	1.8	1.3	0.86	1.9
813 Fracture of radius and ulna	77	77	1.1	0.77	1.4	1.1	0.72	1.5
814 Fracture of carpal bone(s)	40	44	1.0	0.66	1.5	1.0	0.64	1.6
815 Fracture of metacarpal bone(s)	23	24	1.0	0.57	1.8	1.0	0.57	1.8
816 Fracture of one or more phalanges of hand	27	24	1.3	0.75	2.2	1.3	0.73	2.2
818 Illdefined fractures upper limb	9	13	0.67	0.29	1.6	0.77	0.36	1.6
820 Fracture of neck of femur	137	152	0.94	0.74	1.2	0.94	0.68	1.3
821 Fracture of other and unspecified parts of femur	49	44	1.2	0.78	1.8	1.2	0.74	1.8
822 Fracture of patella	13	13	1.1	0.49	2.3	1.1	0.52	2.2
823 Fracture of tibia and fibula	37	29	1.3	0.8	2.1	1.3	0.76	2.1
824 Fracture of ankle	48	30	1.7	1.1	2.7	1.6	0.99	2.6
825 Fracture of one or more tarsal and metatarsal bones	32	30	1.1	0.68	1.8	1.1	0.66	1.9
826 Fracture of one or more phalanges of foot	24	19	1.3	0.73	2.4	1.3	0.71	2.3
829 Fracture of unspecified bones	35	46	0.82	0.53	1.3	0.84	0.52	1.4
831 Dislocation of shoulder	15	18	0.88	0.44	1.7	0.92	0.48	1.8
835 Dislocation of hip	7	4	1.8	0.53	6.2	1.5	0.56	3.7
836 Dislocation of knee	20	19	1.1	0.59	2.1	1.1	0.59	2
838 Dislocation of foot	4	2	2.0	0.37	11	1.4	0.47	4.2
839 Other multiple and ill-defined dislocations	30	36	0.86	0.53	1.4	0.88	0.53	1.5
840 Sprains and strains of shoulder and upper arm	108	83	1.4	1.0	1.8	1.4	0.96	2.0

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
841 Sprains and strains of elbow and forearm	5	5	1.1	0.31	3.7	1.1	0.42	2.8
842 Sprains and strains of wrist and hand	39	52	0.79	0.52	1.2	0.81	0.51	1.3
843 Sprains and strains of hip and thigh	47	41	1.2	0.8	1.9	1.2	0.76	1.9
844 Sprains and strains of knee and leg	79	86	0.98	0.72	1.3	0.98	0.68	1.4
845 Sprains and strains of ankle and foot	81	89	0.96	0.71	1.3	0.96	0.66	1.4
846 Sprains and strains of sacroiliac region	39	43	0.94	0.61	1.4	0.95	0.59	1.5
847 Sprains and strains of other and unspecified parts of back	177	176	1.1	0.86	1.3	1.1	0.78	1.4
848 Other and ill-defined sprains and strains	80	64	1.3	0.96	1.8	1.3	0.89	1.9
850 Concussion	14	11	1.5	0.72	3.3	1.4	0.7	2.9
851 Cerebral laceration and contusion	5	8	0.66	0.21	2	0.8	0.33	2.0
852 Subarachnoid subdural and extradural hemorrhage following injury	13	21	0.65	0.33	1.3	0.72	0.37	1.4
853 Other and unspecified intracranial hemorrhage following injury	8	10	0.77	0.31	1.9	0.86	0.39	1.9
854 Intracranial injury of other and unspecified nature	50	36	1.5	0.95	2.2	1.4	0.89	2.3
860 Traumatic pneumothorax and hemothorax	9	4	2.4	0.73	7.7	1.7	0.68	4.3
861 Injury to heart and lung	2	2	1.1	0.15	7.5	1.1	0.34	3.4
864 Injury to liver	2	2	1.0	0.15	7.4	1.1	0.34	3.4
867 Injury to pelvic organs	2	3	0.7	0.12	4.2	0.93	0.3	2.8
870 Open wound of ocular adnexa	6	3	1.8	0.54	6.3	1.5	0.57	3.8
871 Open wound of eyeball	8	3	2.8	0.74	10.6	1.8	0.67	4.8
872 Open wound of ear	4	5	0.84	0.23	3.1	0.95	0.36	2.5
873 Other open wound of head	126	103	1.3	1.0	1.7	1.3	0.92	1.8
877 Open wound of buttock	2	4	0.53	0.1	2.9	0.82	0.27	2.5
879 Open wound of other and unspecified sites except limbs	66	69	1.0	0.76	1.4	1.0	0.71	1.5
880 Open wound of shoulder and upper arm	3	4	1.6	0.88	3.0	1.5	0.83	2.8
881 Open wound of elbow forearm and wrist	23	26	1.0	0.59	1.7	1.0	0.59	1.8
882 Open wound of hand except finger(s) alone	19	27	0.74	0.41	1.3	0.78	0.44	1.4
883 Open wound of finger(s)	34	27	1.3	0.8	2.2	1.3	0.77	2.2

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
884 Multiple and unspecified open wound of upper limb	7	8	1.3	0.81	1.9	1.2	0.77	2.0
890 Open wound of hip and thigh	11	4	2.9	0.93	9.1	2.0	0.79	4.9
891 Open wound of knee leg (except thigh) and ankle	35	46	0.8	0.52	1.2	0.82	0.51	1.3
892 Open wound of foot except toe(s) alone	11	12	0.97	0.43	2.2	1.0	0.48	2.1
893 Open wound of toe(s)	11	10	1.2	0.5	2.8	1.2	0.54	2.5
894 Multiple and unspecified open wound of lower limb	12	11	1.1	0.5	2.6	1.1	0.54	2.4
895 Traumatic amputation of toe(s) (complete) (partial)	8	4	2.1	0.63	6.9	1.6	0.62	4.0
897 Traumatic amputation of leg(s) (complete) (partial)	2	4	0.51	0.09	2.8	0.81	0.27	2.4
905 Late effects of musculoskeletal and connective tissue injuries	23	23	1.1	0.61	1.8	1.1	0.6	1.9
906 Late effects of injuries to skin and subcutaneous tissues	5	3	1.2	0.57	2.7	1.2	0.59	2.4
909 Late effects of other and unspecified external causes	2	2	1.1	0.15	7.6	1.1	0.34	3.4
910 Superficial injury of face neck and scalp except eye	24	30	0.84	0.49	1.4	0.87	0.5	1.5
911 Superficial injury of trunk	10	8	1.1	0.48	2.4	1.1	0.51	2.2
913 Superficial injury of elbow forearm and wrist	29	29	1.1	0.63	1.8	1.1	0.62	1.8
914 Superficial injury of hand(s) except finger(s) alone	11	11	1.1	0.52	2.5	1.1	0.55	2.3
915 Superficial injury of finger(s)	3	6	1.1	0.39	2.8	1.1	0.46	2.4
916 Superficial injury of hip thigh leg and ankle	27	26	1.1	0.67	1.9	1.1	0.66	2
917 Superficial injury of foot and toe(s)	12	15	0.67	0.38	1.2	0.72	0.4	1.3
918 Superficial injury of eye and adnexa	28	24	1.3	0.74	2.2	1.2	0.72	2.2
919 Superficial injury of other multiple and unspecified sites	69	62	1.2	0.85	1.7	1.2	0.79	1.8
920 Contusion of face, scalp, and neck except eye(s)	108	108	1.1	0.82	1.4	1.1	0.76	1.5
921 Contusion of eye and adnexa	15	18	0.88	0.45	1.8	0.92	0.48	1.8
922 Contusion of trunk	113	129	0.92	0.72	1.2	0.93	0.66	1.3
923 Contusion of upper limb	103	103	1.1	0.81	1.4	1.1	0.75	1.5
924 Contusion of lower limb and of other and unspecified sites	213	232	0.99	0.82	1.2	0.99	0.74	1.3

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
930 Foreign body on external eye	13	12	0.94	0.54	1.6	0.96	0.55	1.7
931 Foreign body in ear	6	2	1.9	0.72	5.2	1.6	0.69	3.7
933 Foreign body in pharynx and larynx	8	17	1.2	0.66	2.2	1.2	0.65	2.2
934 Foreign body in trachea bronchus and lung	7	5	1.7	0.92	3.2	1.6	0.87	2.9
935 Foreign body in mouth esophagus and stomach	8	6	0.97	0.6	1.6	0.98	0.59	1.6
938 Foreign body in digestive system, unspecified	2	2	0.52	0.1	2.9	0.81	0.27	2.4
942 Burn of trunk	3	9	0.62	0.4	0.97	0.66	0.41	1.1
943 Burn of upper limb except wrist and hand	3	4	1.4	0.49	4.1	1.3	0.54	3.1
944 Burn of wrist(s) and hand(s)	6	7	0.85	0.52	1.4	0.87	0.52	1.5
945 Burn of lower limb(s)	6	9	0.77	0.31	1.9	0.85	0.39	1.9
948 Burns classified according to extent of body surface involved	4	5	0.84	0.23	3.1	0.95	0.36	2.5
949 Burn unspecified site	9	10	0.95	0.39	2.3	0.99	0.45	2.2
952 Spinal cord injury without evidence of spinal bone injury	2	3	0.69	0.12	4.1	0.92	0.3	2.8
955 Injury to peripheral nerve(s) of shoulder girdle and upper limb	4	2	2.1	0.39	11.6	1.4	0.48	4.3
958 Certain early complications of trauma	15	15	0.99	0.49	2.0	1.0	0.52	2.0
959 Injury other and unspecified	371	355	1.1	0.96	1.3	1.1	0.85	1.5
964 Poisoning by agents primarily affecting blood constituents	5	2	2.7	0.51	13.7	1.6	0.54	4.7
965 Poisoning by analgesics antipyretics and antirheumatics	4	3	1.4	0.32	6.3	1.2	0.43	3.5
972 Poisoning by agents primarily affecting the cardiovascular system	4	12	0.35	0.11	1.1	0.55	0.22	1.4
977 Poisoning by other and unspecified drugs and medicinal substances	11	9	1.3	0.53	3.1	1.2	0.56	2.7
989 Toxic effect of other substances chiefly nonmedicinal as to source	11	10	1.1	0.49	2.7	1.1	0.53	2.4
991 Effects of reduced temperature	4	2	2.1	0.39	11.6	1.4	0.48	4.3
992 Effects of heat and light	3	4	0.78	0.17	3.5	0.93	0.33	2.6
994 Effects of other external causes	3	2	1.6	0.27	9.5	1.3	0.41	3.9

ICD9 Category	Breast cancer cohort frequency	Comparison cohort frequency	Conventional hazard ratio and 95% CI			Semi-Bayes hazard ratio and 95% CI		
			HR	LCL	UCL	HR	LCL	UCL
995 Certain adverse effects not elsewhere classified	192	198	1.0	0.84	1.3	1.0	0.76	1.4
996 Complications peculiar to certain specified procedures	126	98	1.4	1.1	1.8	1.4	0.96	1.9
997 Complications affecting specified body system not elsewhere classified	69	82	0.88	0.64	1.2	0.89	0.61	1.3
998 Other complications of procedures not elsewhere classified	120	99	1.3	0.99	1.7	1.3	0.91	1.8
999 Complications of medical care not elsewhere classified	21	10	2.2	1.0	4.7	1.9	0.93	3.8

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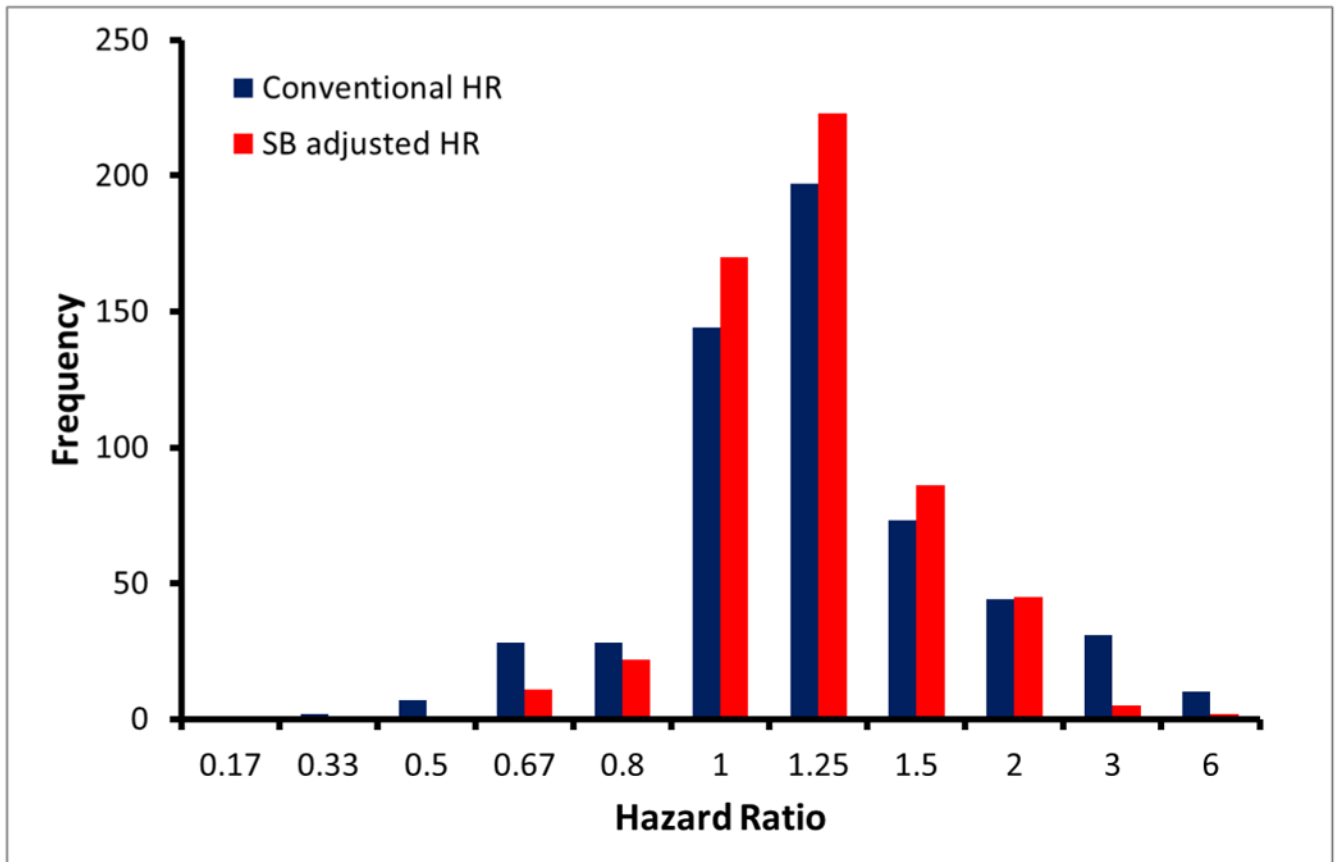


Fig. 1. Histogram distribution of 564 conventional and semi-Bayes (EB) adjusted hazard ratios comparing occurrence of ICD9 codes among breast cancer survivors with a matched comparison cohort

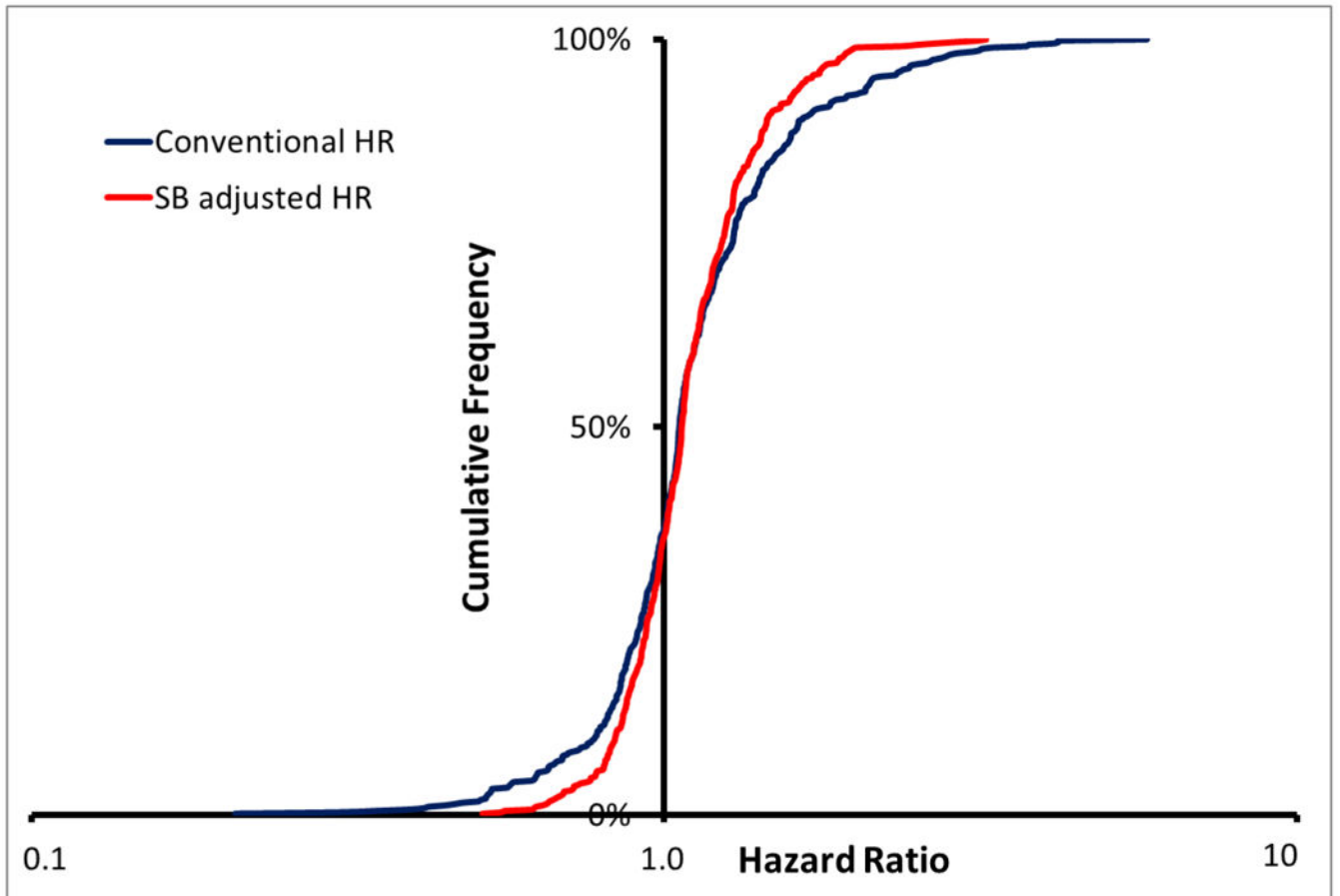


Fig 2. Cumulative distribution of 564 conventional and semi-Bayes (EB) adjusted hazard ratios comparing occurrence of ICD9 codes among breast cancer survivors with a matched comparison cohort

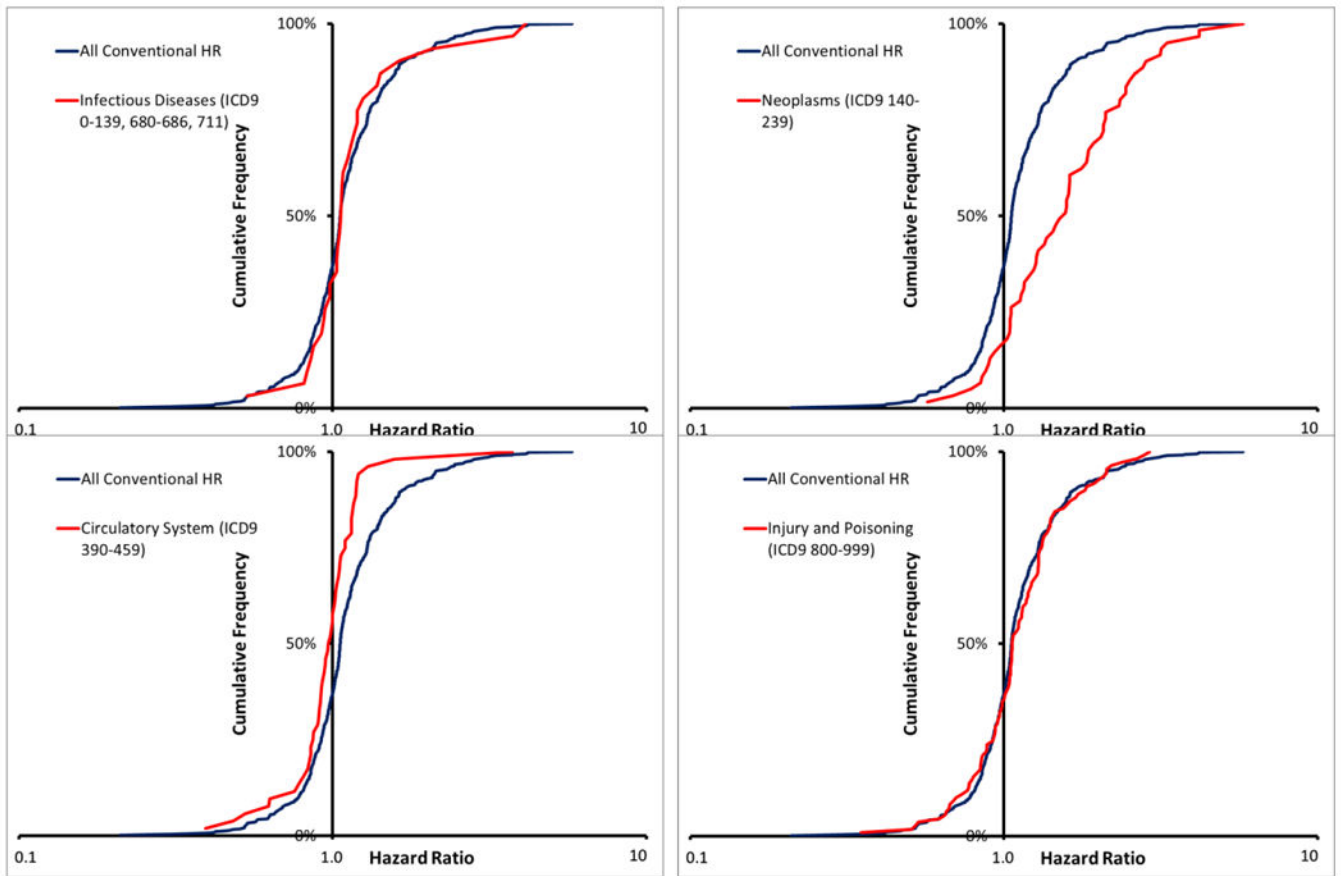


Fig 3. Cumulative distribution of conventional hazard ratios comparing occurrence of ICD9 codes among breast cancer survivors with a matched comparison cohort, overall and within disease categories

Table 1
Characteristics of Older Five-Year Survivors of Early Breast Cancer and Matched Comparison Cohort

	Breast Cancer Survivor Cohort* (n = 1,361)		Comparison Cohort† (n = 1,361)		
	No.	%	No.	%	
Sociodemographic					
Age Category at Beginning of Follow-up (years)					
70-74	502	37	502	37	
75-79	417	31	417	31	
80+	442	32	442	32	
Race/ethnicity					
Caucasian, Non-Hispanic	1115	82	1147	84	
African-American, Non-Hispanic	137	10	125	9.2	
Hispanic	72	5.3	62	4.6	
Asian/Pacific Islander	37	2.7	27	2.0	
Native American	0	0	0	0	
Comorbidity Burden at Five Years after Index Date					
Prevalent Comorbidities included in mCCI ‡ (index weight)					
Myocardial infarction	(1)	80	5.9	80	5.9
Congestive heart failure	(1)	140	10	117	8.6
Peripheral vascular disease	(1)	60	4.4	67	4.9
Cerebrovascular disease	(1)	96	7.1	98	7.2
Dementia	(1)	64	4.7	76	5.6
Chronic pulmonary disease	(1)	172	13	184	14
Connective tissue disease	(1)	36	2.6	62	4.6
Ulcer disease	(1)	75	5.5	73	5.4
Diabetes	(1)	202	15	169	12
Mild liver disease	(1)	7	0.51	6	0.44
Hemiplegia	(2)	24	1.8	25	1.8
Moderate or severe renal disease	(2)	17	1.2	15	1.1
Diabetes with end organ damage	(2)	31	2.3	31	2.3

	Breast Cancer Survivor Cohort* (n = 1,361)		Comparison Cohort† (n = 1,361)	
	No.	%	No.	%
Leukemia, lymphoma or tumor ^d	112	8.2	75	5.5
Moderate or severe liver disease ⁽³⁾	14	1.0	2	0.15
AIDS ⁽⁶⁾	0	0.00	0	0.00
Metastatic solid tumor ⁽⁶⁾	6	0.44	4	0.29
Modified Charlson Comorbidity Index ^{§,¶}				
mCCI 0	741	54	755	55
mCCI 1-2	502	37	487	36
mCCI 3+	118	8.7	119	8.7

* Older five-year breast cancer survivors diagnosed 1990–1994 with early stage I and II breast cancer at age 65 or older followed for 10 years beginning on the first day of the sixth year after index date (date of breast cancer diagnosis).

† Comparison cohort matched for health system and age, who were free of breast cancer at matched enrollment date and followed for 10 years beginning on the first day of the sixth year after index date (date of matched breast cancer patient's diagnosis).

‡ Participants may be counted in multiple comorbidities.

§ Prevalent breast cancer at enrollment date excluded.

¶ Prevalent breast cancer at enrollment date excluded from modified Charlson Comorbidity Index (mCCI), which is calculated from the sum of comorbidity weights listed in the table (Charlson et al 1987).