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Is there Unmeasured Indication Bias in Radiation-Related Cancer Risk Estimates from Studies of Computed Tomography?

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Abstract

Recently reported studies have associated radiation exposure from computed tomography (CT) scanning with small excess cancer risks. However, since existing medical records were used in these studies, they could not control for reasons for the CT scans and therefore, the results may have been confounded by indication. Here we conducted a study to estimate potential indication bias that could affect hazard ratios for colorectal, lung and female breast cancers by reasons for a CT scan. This involved a retrospective cohort study of electronic records from all patients aged 18–89 years without previous cancer diagnoses, who received at least one CT scan at Columbia University Medical Center in the period of 1994–2014. This investigation is not a study of CT-related cancer risks with adjustment for reasons, but an evaluation of the potential for confounding by indication in such studies. Among 75,968 patients, 212,487 CT scans were analyzed during a mean follow-up of 7.6 years. For colorectal and female breast cancers, no hazard ratio bias estimates for any of the CT reasons reached statistical significance. For lung cancer, significant biases occurred only in patients with unknown CT reasons and in patients with CTs for “abnormal findings” and in those with CTs for cancer- or nodule-related reasons. This retrospective cohort study among adults with ≥1 CT scan evaluates, for the first time, CT reason-specific indication biases of potential CT-related cancer risks. Overall, our data suggest that, in studies of adults who underwent CT scans, indication bias is likely to be of negligible importance for colorectal cancer and female breast cancer risk estimation; for lung cancer, indication bias is possible but would likely be associated with only a small modulation of the risk estimate.

INTRODUCTION

Computed tomography (CT) scans deliver higher radiation doses than most other diagnostic radiation procedures (1), and their use has increased dramatically in developed countries (2,

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3). Consequently, radiation-induced carcinogenesis due to CT scanning has become a public health concern. The annual number of CT scans in the U.S. in 2007 was 70-million, of which 20–30 million CT scans may have had limited clinical utility (4). Published retrospective cohort studies of CT-related radiation exposure among children have suggested increased risks for leukemia and brain tumors (5–8). These studies were criticized because the analyses failed to account for the reasons for the CT examinations, as they were not ascertained (9, 10). If the reasons were associated with a subsequent cancer diagnosis, confounding by indication could occur. However, other specially-designed studies have investigated cancer susceptibility syndromes, such as Down syndrome, as a potential source of indication bias and the potential was found to be negligible (11, 12).

While recently epidemiological studies have examined potential disease risks from pediatric CT scanning, studies of cancer risk from CT scans during adulthood are also relevant. Adults receive over 10 times more CT scans than children (13–15) and most radiation-induced cancers occur during middle or old age. While these CT risk studies are feasible in adults, large sample sizes are needed (16).

We conducted a retrospective cohort study to evaluate the association between the reasons for CT scans among adult patients of the Columbia University Medical Center (CUMC) and subsequent risk of lung, female breast or colorectal cancer. This investigation is not a study of CT-related cancer risks with adjustment for reasons, but rather serves as a basis to evaluate the potential for confounding by indication. The follow-up time is too short to assess radiation-related cancer risks.

METHODS

Study Population and Design

The study population included all patients who received a CT scan at CUMC in the period 1994–2014 at ages 18–89 years, and with at least one visit more than two years prior to their first post-1994 CT scan. Follow-up started one year after the first CT scan after 1994 for those who remained cancer-free for the one year. From electronic records, we abstracted data for each patient, including date of birth, sex, race, date of first visit at CUMC, cancer incidence and death. For all subjects, we determined the dates, reasons and body parts scanned for CT scans performed at CUMC until one year prior to cancer diagnosis or end of follow-up. We did not estimate quantitative radiation tissue dose. The requirement of one or more prior visits provided the basis for our assumption that those patients would likely also come to CUMC for a cancer diagnosis. We excluded patients who had missing information on the date of a CT scan. *Our a priori* selected outcomes were colorectal cancer, female breast cancer and lung cancer, the most common malignancies among adults. We ceased follow-up at the earliest date of diagnosis of any cancer, death or December 2014, whichever occurred earliest. Furthermore, patients with a benign first tumor were censored at the date of its diagnosis, since the incidence of a benign tumor might be a risk factor for one of the target cancers and thereby alter the referent hazard function. Cancer diagnoses were coded according to the WHO International Classification of Diseases (ICD-9). For a graphic illustration of the study population, see Fig. 1.

For each outcome, we evaluated only scans to those body parts that would expose the target organ to a substantial dose, e.g., CT scans of the abdomen, pelvis and lower spine for colorectal cancer, and of the chest and upper spine for lung and breast cancer. A medical doctor (IS), who was blinded to outcome status, grouped reasons for scans into broad categories, e.g., pain, kidney issues, suspected cancer. Classification of reasons was challenging and involved some degree of judgment, particularly when records were cryptic or abbreviated. Therefore, categories were not defined *a priori*. Based on a keyword search, each CT scan was then classified to one or more categories (Supplementary Tables S1 and S2; <http://dx.doi.org/10.1667/RR14807.1.S1>). Note that each reason represents a clinician's judgment about the need for the CT scan and not a preliminary disease diagnosis.

Statistical Analysis

We followed an approach that is related to the Axelson and Steenland (17) formula to estimate the bias of radiation-related relative risks (RR) for colorectal, female breast and lung cancer due to indication for each specific reason. During a medical evaluation, a patient may receive a CT scan for a variety of reasons, some of which may be related ultimately to the specific outcome under epidemiological investigation. As shown in Table 1, the relevant data in a cohort study of the effects of CT scanning are the number of events, number of patients and disease rate for those who do not receive CT scans (d_0 , n_0 and I_0 , respectively), and those who receive a CT scan for outcome-related reasons (d_r , n_r and I_r) or other reasons that are not outcome-related (d_n , n_n and I_n .)

Since I_r may be related to prodromal symptoms associated with the outcome, in a study of the effects of CT scans on an outcome, most of the interest is typically in the estimation of $RR_n = I_n/I_0$, i.e., the relative risk of the outcome in those with a CT scan that was not related to the diagnosis under investigation relative to those without a CT scan. In the absence of knowledge of the reason for a CT scan, the observed estimate is $RR_{OBS} = \{I_r\pi + I_n(1 - \pi)\}/I_0$, where π is the probability of the outcome-related reason among patients with a CT scan. We rewrite this expression as:

$$\text{Bias} = RR_{OBS} / RR_n = \{\pi RR_r + (1 - \pi)\}, \quad (1)$$

where $RR_r = I_r/I_n$ represents the relative impact of the presumed outcome-related reason for the CT scan. Our study provides estimates of RR_r and μ and thus an estimate of a potential bias.

For each of the three outcomes, we fit the Cox proportional hazards regression model,

$$\log HR(r, z) = \sum_j \alpha_j z_j + \beta_0 d + d * \sum_i^k \beta_i r_i, \quad (2)$$

with age as the time scale and adjustment variables z_j (categorical year of birth, gender, race), a time-dependent CT exposure indicator d (no CT = 0, CT = 1) and the reasons r_i for the CT scan, where we extend Eq. (1) to allow for multiple categories. The $\exp(\beta_1), \dots$,

$\exp(\beta_{\text{pain}})$ are the reason-specific hazard ratios (HR) and estimate the various RR_r 's. For example, in analyses of colorectal cancer, the HR for pain as a reason, $\exp(\beta_{\text{pain}})$, compares patients who previously (lagged by 1 year) had an abdomen/pelvis/lower spine scan for “pain” with those who had a scan of the abdomen/pelvis/lower spine but for reasons “other than pain”. We approximated the variance of the bias using a Taylor series expansion for the product of two independent random variables (see Appendix for details). Confidence intervals for the bias were calculated assuming it is normally distributed. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

There were 212,487 CT scans among the 75,968 subjects (42.7% male). The average duration of follow-up was 7.6 years (median, 6.7 years; 75th percentile, 11.1 years; 90th percentile, 15.3 years; Tables 2 and 3). There were 98 diagnoses of colorectal cancer, 189 of lung cancer and 165 of female breast cancer.

Among 85,905 CT scans of the abdomen/pelvis/lower spine, among 33,734 patients, unique reasons were reported for 70,276 scans (81.8%). For 43,155 scans of the chest/upper spine, 19,375 scans (45.4%) had identifiable reasons. Those CT scans for which no reason was entered into the electronic records were assigned to category “unknown”. Multiple, very rare CT reasons were combined into the category of “others” (Tables 4–6 and Supplementary Table S1a–c; <http://dx.doi.org/10.1667/RR14807.1.S1>).

For colorectal cancer, none of the CT reason-specific hazard ratio bias estimates reached statistical significance (Table 4, Fig. 2). The individual HRs were significantly increased only for two CT reasons: “cancer” and “infection” (Table 4). These findings are consistent with expectations that colorectal cancer risk may be elevated in patients previously suspected to have malignant or premalignant conditions and/or certain infections. However, due to the low prevalence of these conditions, associated bias estimates were below 15% and were not statistically significant (Table 4).

For lung cancer, biases significantly >1 occurred only in patients with unknown CT reasons, in those with CT scans for cancer-related reasons (e.g., lung nodule, density) and in those with CT scans for “abnormal findings” (Table 5, Fig. 2). The first two of these CT reasons, as well as two others (“inflammation” and “lung issues”) produced significantly elevated HRs (Table 5). The results for “inflammation”, “lung issues” and “cancer, nodule, density” categories are intuitively explainable because patients with such CT reasons may have been predisposed to cancer, for example, because they could have been tobacco smokers. The results for “unknown” CT reasons are less clear.

The patterns for female breast cancer were similar to those for colorectal cancer: none of the reason-specific biases reached statistical significance, and cancer HRs were significantly elevated only for the “screening” CT category (Table 6, Fig. 2). Therefore, patients who underwent screening CT procedures were expectedly more likely to be later diagnosed with breast cancer, but the low prevalence of such procedures resulted in negligible bias.

Using a two-sided sign test, CT reason-specific HRs were below or above 1 for each of the three cancer outcomes with frequencies consistent with random variation ($P=0.58$ for colorectal cancer, $P=0.09$ for lung cancer and $P=0.99$ for female breast cancer). Of the bias estimates for 57 reasons, 40 (70%) are between -2% and 2% , and 46 (81%) are between -5% and 5% . Three of the 57 bias estimates (5.3%, i.e., what would be expected by chance) differed significantly from 1.0.

Hazard ratios, $\exp(\beta_0)$ in Eq. (2), were 0.53 [95% confidence interval (CI): 0.26–1.09, $P=0.09$] for colorectal cancer and CT scans of the abdomen/pelvis/lower spine, and 1.02 (95% CI: 0.58–1.80, $P=0.94$) and 1.38 (95% CI: 0.62–3.08, $P=0.43$) for lung and female breast cancer, respectively, and chest/upper spine CT scans, compared to patients who had CT scans to distal unrelated body parts. The main results were very similar when we started follow-up six months (instead of 12 months) after the first CT scan and when we reduced the lag period from 12 to 6 months.

DISCUSSION

This is the first quantitative study of the potential confounding of CT-related radiation cancer risk due to reasons for CT scans. Hazard ratios for specific reasons, although varying widely, were symmetrically distributed around unity and significance P values were consistent with random variation, indicating that most reasons were probably unrelated to cancer risk. When combined with the relatively low prevalence of CT scans for specific reasons, the estimated biases of radiation-related RRs were negligible for the majority of reasons.

Previous work has demonstrated that studies of cancer risk due to radiation exposure from CT scans among adults are feasible, although sample sizes in the order of 0.4–1.3 million exposed adults are needed (16). Our results are reassuring for such a study. During a relatively short follow-up (median: 6.7 years, 75th percentile: 11.1 years), which makes the observation of cancers due to CT-related radiation unlikely, most reasons were not associated with substantially increased or decreased hazard ratios. Our data do not allow conclusions about indication bias in studies of pediatric CT exposure and risk of leukemia and brain tumors since the indications for relevant CT scans likely differ substantially by age.

CT scans associated with the largest potential bias were those performed for unknown reasons (89% bias for colorectal cancer, 131% for lung cancer and 51% for female breast cancer). It is unclear why a substantial fraction of CT scans had no associated reason in the electronic system, since this response occurred when the treating clinicians did not record the reasons for these CT scans. It may be that the category includes the rare and less clear indications, or indicates the less comprehensive recording of indication information by hospital personnel, or that patients with unknown CT reasons more often had malignant/premalignant conditions. If true, it would be difficult in an epidemiological study to identify these patients by information about the reason for their scans unless investigators directly interviewed patients.

Our study has several strengths. It involves a large cohort of patients from a major hospital in New York City and uses patient-specific information on reasons for CT scans and cancer diagnosis. A careful classification of reasons for CT scans resulted in broad groups of indications. The HRs for reasons of CT scans appear plausible, which suggests that the methodology can detect an association. For example, the significantly elevated hazard ratio for breast cancer due to “screening” might be due to the fact that patients who visit the hospital for a screening CT scan probably have a higher risk of breast cancer than other patients, although this is a rare occurrence.

Nevertheless, our study also has several weaknesses. Ascertainment of CT scans and cancer incidence is likely incomplete since we only include information from CUMC files. By limiting our cohort to patients with at least one visit to CUMC two or more years prior to their first CT scan, we attempt to exclude patients who may have visited other hospitals for major health problems. In addition, despite our large cohort size, the numbers of cases for the different cancers are relatively few. As a consequence, many reason-specific RRs are based on few exposed cases, which leads to wide confidence intervals. Furthermore, with regard to the reasons for CT scans, we had to rely on the level of detail recorded in the electronic system and an expert-opinion classification of this information into broad categories. Misclassification likely occurred and would generally attenuate RRs, i.e., bias could be slightly underestimated. Finally, as with most studies of CT-related radiation exposure and cancer risk, we did not have data available on other risk factors for the outcomes of interest. It is conceivable that the reason for a CT scan might be correlated with a risk factor and with the outcome, e.g., cough among smokers. However, this correlation is not unexpected and contributes to making the reason for a CT scan a potential confounder.

In conclusion, our data suggest that, in studies of adults who underwent CT scans, indication bias is likely to be of negligible importance for colorectal cancer and female breast cancer risk estimation; for lung cancer, indication bias is possible but would likely be associated with only a small modulation of the risk estimate.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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APPENDIX

Calculation of Variance of Bias

The variance of the bias is approximated by a Taylor series for the product of two independent random variables (18).

$$\text{Var}(\text{Bias}) = \text{Var}[(RR_r - 1) * \pi] = \text{Var}(RR_r) * \text{Var}(\pi) + [E(RR_r - 1)]^2 * \text{Var}(\pi) + [E(\pi)]^2 * \text{Var}(RR_r).$$

(A1)

We assume that π and RR_r are independent and that RR_r is lognormally distributed. Since π is estimated from a large number, N , of patients with a CT scan to the relevant region ($N = 33,734$ for abdomen/pelvis/lower spine; $N = 19,308$ for chest/upper spine; $N = 10,482$ for chest/upper spine for females), $\text{Var}(\pi) = \pi * (1 - \pi)/N$ is very small (<0.00001). That is, the variance of the bias is approximated by:

$$\text{Var}(\text{Bias}) = [E(\pi)]^2 * \text{Var}(RR_r), \quad (\text{A2})$$

where $E(\pi) = \pi$ and $\text{Var}(RR_r) = RR_r^2 * [\exp(\sigma^2) - 1]$ with σ^2 the variance of the corresponding regression coefficient, $\log(RR_r)$, in the Cox regression. This means that confidence intervals of the bias will be wide if a reason is common and/or associated with a large HR. Received: April 20, 2017; accepted: October 11, 2017; published online: December 5, 2017

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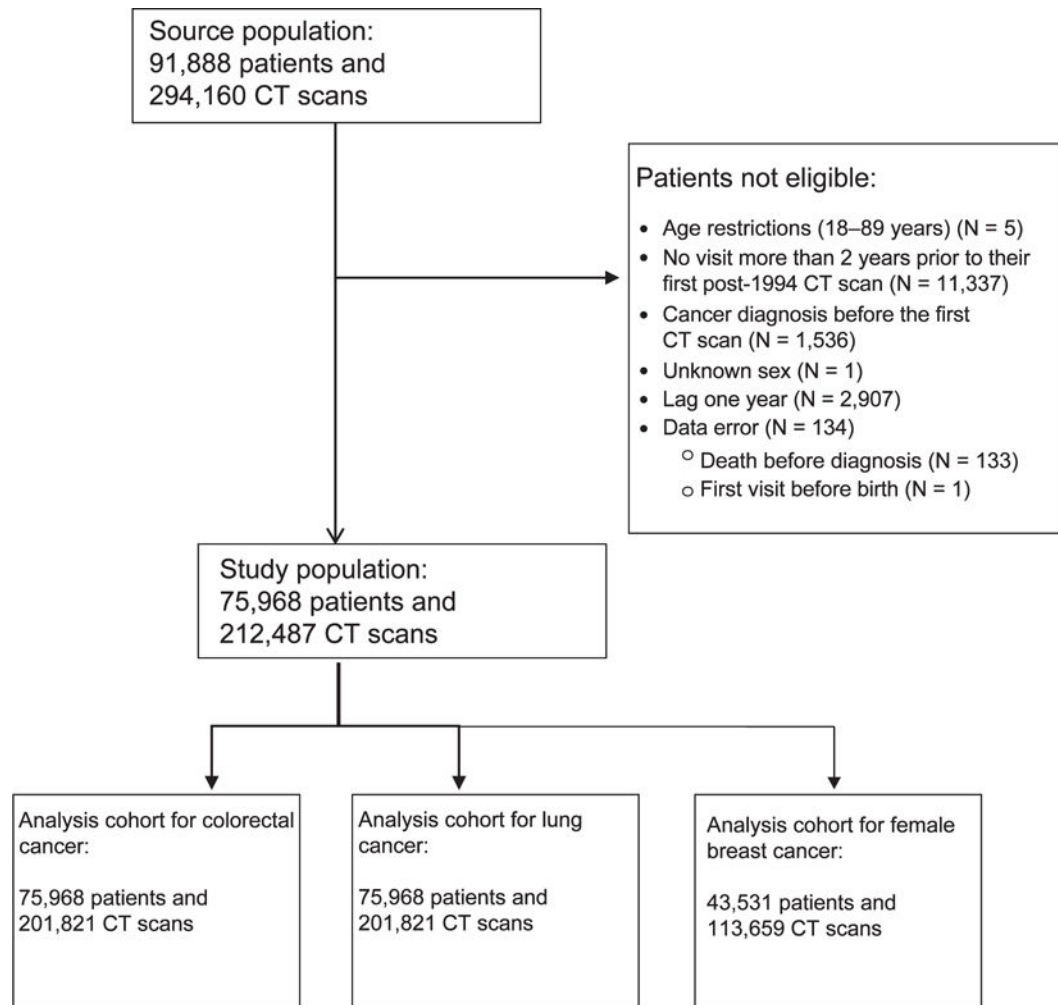
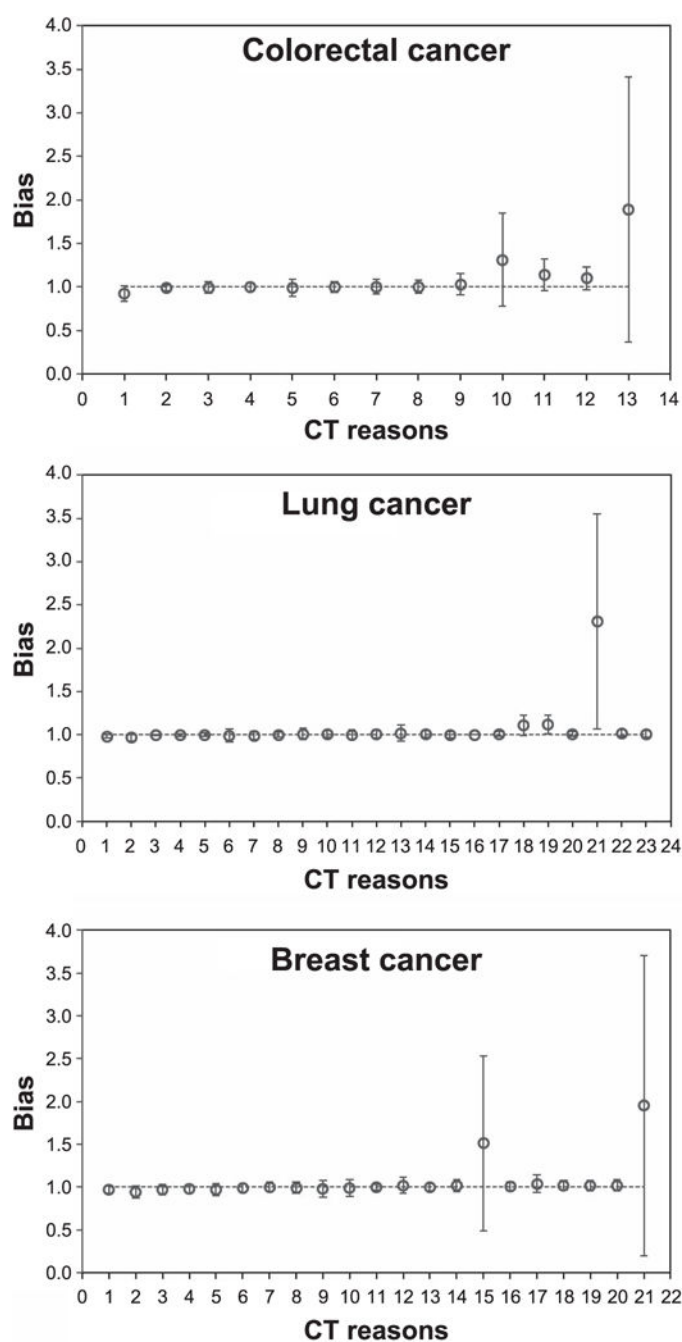


FIG. 1.
Flow chart of the study population.

**FIG. 2.**

Computed tomography (CT) reason-specific hazard ratio bias estimates (symbols) and their 95% confidence intervals (error bars) for colorectal, lung and breast cancer. The different reasons for the CT scans are listed sequentially on the x-axis in the same order as in Tables 4–6 for colorectal cancer, lung cancer and breast cancer, respectively.

TABLE 1

Relevant Data for CT Scan Cohort Study

	CT scan = no	CT scan = yes	
		Outcome-related reason	Not outcome-related reason
No. of events	d_0	d_r	d_n
No. of patients	n_0	n_r	n_n
Disease rate	I_0	I_r	I_n

Notes. Relevant data are shown in terms of the number of events, number of patients and disease rate for those who did not receive CT scans (d_0 , n_0 and I_0 , respectively), and those who received a CT scan for outcome-related reasons (d_r , n_r and I_r) or other reasons that are not outcome-related (d_n , n_n and I_n).

TABLE 2

Characteristics of Patients from CUMC who Received at Least One CT Scan Aged 18–89 Years in the Period 1994–2014

	Subjects	
	N	%
Sex		
Male	32,437	42.7
Female	43,531	57.3
Race		
White	35,201	46.3
Black	11,751	15.5
Other	29,016	38.2
Age at CT scan		
18–29	14,416	19.0
30–39	12,390	16.3
40–49	13,377	17.6
50–59	12,261	16.1
60–69	10,293	13.6
70–79	8,634	11.4
80	4,598	6.1
Year of first examination		
1994–1999	12,826	16.9
2000–2004	18,640	24.5
2005–2009	23,167	30.5
2010	21,335	28.1
Birth year		
1929	8,477	11.2
1930–1939	8,395	11.1
1940–1949	10,574	13.9
1950–1959	13,218	17.4
1960–1969	13,065	17.2
1970–1979	11,224	14.8
1980	11,015	14.5
Number of CT scans		
1	31,524	41.5
2	20,939	27.6
3–10	21,144	27.8
11–20	1,926	2.5
21	435	0.6
First cancer diagnosis during follow-up		
None	71,363	93.9
Colorectal cancer	98	0.3

	Subjects	
	N	%
Female breast cancer	165	0.1
Lung cancer	189	0.2
Other malignant cancers	1,278	1.7
Benign tumors	2,874	3.8

TABLE 3

Number of CT Scans by Sex and Body Part among Patients from CUMC Who Received at Least One CT Scan Aged 18–89 Years in the Period 1994–2014

Body part	Male		Female		All	
	N	Percentage	N	Percentage	N	Percentage
Head and neck	34,948	37.9	43,733	36.5	78,681	37.0
Chest ^a	17,342	18.7	21,233	17.7	38,575	18.2
Abdomen and pelvis ^b	34,774	37.5	48,837	40.8	83,611	39.4
Upper spine ^a	2,754	3.0	2,289	1.9	5,043	2.4
Lower spine ^b	917	1.0	1,438	1.2	2,355	1.1
Extremities	1,549	1.7	1,600	1.3	3,149	1.5
Miscellaneous/unknown	436	0.5	637	0.5	1,073	0.5

^a Only these CT scans are used for lung and female breast cancer analyses.

^b Only these CT scans are used for colorectal cancer analyses.

Estimated Hazard Ratios and Biases for Colorectal Cancer by Reason for CT Scan of the Abdomen/Pelvis/Lower Spine among Patients from CUMC who Received at Least One CT Scan Aged 18–89 Years in the Period 1994–2014

TABLE 4

CT scan reasons		N (%) ^a	Cases	HR ^b	95% CI	P value	Prevalence (%) ^c	Bias	95% CI
Ever (vs. never) abdomen/pelvis/lower spine CT scan for reason									
1	Kidney	11,269 (13.1)	2	0.39	0.09–1.68	0.21	13.19	0.92	0.83–1.01
2	Lesions	1,857 (2.2)	1	0.53	0.07–4.25	0.55	2.43	0.99	0.95–1.02
3	Trauma	2,112 (2.5)	1	0.78	0.10–6.11	0.78	3.02	0.99	0.93–1.06
4	Heart/lung	2,707 (3.2)	2	0.89	0.21–3.76	0.89	3.42	1.00	0.95–1.05
5	Bleeding	4,744 (5.5)	2	0.90	0.20–4.05	0.89	6.19	0.99	0.90–1.09
6	Status	2,418 (2.8)	2	1.02	0.23–4.50	0.98	3.34	1.00	0.94–1.06
7	Other	4,516 (5.3)	4	1.04	0.36–3.02	0.94	7.13	1.00	0.92–1.09
8	Liver/pancreas	5,063 (5.9)	4	1.08	0.35–3.27	0.90	5.43	1.00	0.93–1.08
9	Intestinal/gastric	8,777 (10.2)	7	1.28	0.55–3.00	0.57	11.03	1.03	0.91–1.16
10	Pain	37,540 (43.7)	18	1.69	0.85–3.38	0.14	44.57	1.31	0.77–1.84
11	Infection	7,468 (8.7)	8	2.64	1.17–6.00	0.02	8.25	1.14	0.95–1.32
12	Cancer	4,035 (4.7)	9	2.83	1.28–6.27	0.01	5.41	1.10	0.97–1.23
13	Unknown	15,629 (18.2)	4	3.53	1.14–10.95	0.03	34.99	1.89	0.36–3.41

Notes. HR = hazard ratio; CI = confidence.

^aPercentage relative to 85,905 abdomen/pelvis/lower spine CT scans. Some scans have multiple reasons.

^bOne regression was performed with adjustment for categorical year of birth, gender and race (white, black, other) and including a time-dependent binary variable ever versus never had a CT scan of the abdomen/pelvis/lower spine and a time-dependent binary variable for each reason with categories: ever had an abdomen/pelvis/lower spine scan for that reason, never had an abdomen/pelvis/lower spine scan for that reason (i.e., had such a scan for another reason) (reference).

^cPrevalence of subjects who ever had an abdomen/pelvis/lower spine CT scan for each particular reason during follow-up. For example, the RR is 2.64 for ever having had a CT scan to the abdomen/pelvis/lower spine for the reason “infection” compared to not having had such a scan for this particular reason. Since 8.25% of all subjects with a scan to the abdomen/pelvis/lower spine ever had at least one such scan for “infection” as a reason, $\pi_1 = 0.0825$. Relative bias is therefore $2.64 * 0.0825 + (1 - 0.0825) = 1.14$ or 14%.

Estimated Hazard Ratios and Biases for Lung Cancer by Reason for CT Scan of the Chest/Upper Spine among Patients from CUMC who Received at Least One CT Scan Aged 18–89 Years in the Period 1994–2014

TABLE 5

CT scan reasons ^d		N (%) ^a	Cases	HR ^b	95% CI	P value	Prevalence (%) ^c	Bias	95% CI
1	Abnormal findings	817 (1.9)	3	0.44	0.14–1.40	0.16	3.78	0.98	0.96–1.00
2	Shortness of breath	1,518 (3.5)	3	0.50	0.16–1.58	0.24	6.61	0.97	0.93–1.01
3	Esophagus Abdominal organs	435 (1.0)	2	0.65	0.15–2.75	0.56	0.44	1.00	0.99–1.00
4	Sarcoid Lupus Autoimmune	249 (0.6)	1	0.67	0.09–4.92	0.69	0.94	1.00	0.98–1.01
5	Immune suppression HIV	258 (0.6)	1	0.80	0.11–6.02	0.82	1.02	1.00	0.98–1.02
6	Fall Trauma Injury	2,059 (4.7)	5	0.86	0.34–2.20	0.76	9.12	0.99	0.91–1.06
7	Infection	1,929 (4.4)	10	0.93	0.47–1.83	0.83	7.28	0.99	0.95–1.04
8	Dissection Aneurysm	803 (1.8)	5	1.07	0.43–2.69	0.89	3.05	1.00	0.97–1.03
9	Others	2,172 (5.0)	12	1.09	0.59–2.01	0.79	9.31	1.01	0.94–1.07
10	COPD Emphysema Bronchitis	1,468 (3.4)	14	1.11	0.59–2.09	0.74	5.54	1.01	0.97–1.05
11	Spinal and bone problems	789 (1.8)	3	1.12	0.34–3.70	0.85	3.55	1.00	0.95–1.06
12	Cardiac	1,542 (3.5)	10	1.13	0.58–2.21	0.71	6.55	1.01	0.96–1.06
13	Pain	2,333 (5.4)	8	1.16	0.55–2.45	0.70	10.57	1.02	0.92–1.11
14	Cough	766 (1.8)	6	1.25	0.54–2.90	0.61	3.49	1.01	0.97–1.05
15	Dyspnea	221 (0.5)	1	1.36	0.19–9.88	0.76	1.03	1.00	0.97–1.04
16	Bleeding	297 (0.7)	3	1.44	0.43–4.87	0.56	0.13	1.00	1.00–1.00
17	Syndrome Disease	364 (0.8)	5	1.75	0.69–4.41	0.24	1.59	1.01	0.98–1.04
18	Lung issues	4,354 (10.)	37	1.75	1.12–2.74	0.01	14.94	1.11	0.99–1.23
19	Cancer Nodule Density	3,255 (7.5)	43	1.92	1.24–2.96	<0.01	12.58	1.12	1.01–1.22

CT scan reasons ^d	N (%) ^a	Cases	HR ^b	95% CI	P value	Prevalence (%) ^c	Bias	95% CI
20 Screening	509 (1.2)	5	2.06	0.79–5.40	0.14	1.27	1.01	0.99–1.04
21 Unknown	23,780 (54.6)	89	2.75	1.53–4.95	<0.01	75.14	2.31	1.07–3.56
22 Inflammation	296 (0.7)	5	2.85	1.10–7.37	0.03	1.28	1.02	0.99–1.06
23 Alcohol/drugs	38 (0.1)	1	7.47	0.98–57.11	0.05	0.18	1.01	0.98–1.05

Notes. HR = Hazard ratio; CI = Confidence interval; COPD=Chronic obstructive pulmonary disease; HIV=Human immunodeficiency virus.

^aPercentage relative to 43,155 chest/upper spine CT scans. Some scans have multiple reasons.

^bOne regression was performed with adjustment for categorical year of birth, gender and race (white, black, other) and including a time-dependent binary variable: ever versus never had a CT scan of the chest/upper spine scan, and a time-dependent binary variable for each reason with categories: ever had a chest/upper spine scan and for that reason versus never had a chest/upper spine scan for that reason (reference).

^cPrevalence of subjects who ever had a chest/upper spine CT scan for each particular reason during follow-up.

^dFor multiple sclerosis, effusion, asthma, congestive heart failure, embolism, neurologic, kidney, perforation and others, there were no cases, and so they are not included in this table.

TABLE 6

Estimated Hazard Ratios and Biases for Female Breast Cancer by Reason for CT Scan of the Chest/Upper Spine among Patients from CUMC who Received at least one CT Scan Aged 18–89 Years in the Period 1994–2014

CT scan reasons ^d	N (%) ^a	Cases	HR ^b	95% CI	P value	Prevalence (%) ^c	Bias	95% CI
1 COPD Emphysema Bronchitis	1,468 (3.4)	3	0.50	0.14–1.77	0.28	5.53	0.97	0.93–1.01
2 Pain	2,333 (5.4)	4	0.51	0.18–1.48	0.21	11.88	0.94	0.87–1.01
3 Others	2,172 (5.0)	5	0.69	0.27–1.75	0.43	8.93	0.97	0.91–1.03
4 Infection	1,929 (4.4)	4	0.71	0.25–2.01	0.52	6.38	0.98	0.93–1.03
5 Cancer Nodule Density	3,255 (7.5)	11	0.75	0.37–1.52	0.43	13.10	0.97	0.90–1.04
6 Cough	766 (1.8)	2	0.76	0.18–3.19	0.71	3.81	0.99	0.94–1.04
7 Neurologic	499 (1.2)	1	0.80	0.11–5.97	0.83	2.42	1.00	0.94–1.05
8 Cardiac	1,542 (3.5)	4	0.87	0.31–2.45	0.80	6.68	0.99	0.93–1.06
9 Lung issues	4,354 (10.0)	11	0.88	0.41–1.88	0.73	14.58	0.98	0.88–1.08
10 Shortness of breath	1,518 (3.5)	3	0.91	0.28–2.97	0.87	7.84	0.99	0.90–1.09
11 Syndrome Disease	364 (0.8)	2	1.19	0.27–5.22	0.82	1.76	1.00	0.97–1.04
12 Fall Trauma Injury	2,059 (4.7)	5	1.25	0.46–3.41	0.66	7.20	1.02	0.92–1.11
13 CHF	338 (0.8)	1	1.33	0.18–10.07	0.78	1.17	1.00	0.96–1.05
14 Abnormal findings	817 (1.9)	4	1.61	0.57–4.59	0.37	3.79	1.02	0.95–1.09
15 Unknown	23,780 (54.6)	42	1.69	0.77–3.68	0.19	74.38	1.51	0.49–2.54
16 Bleeding	297 (0.7)	1	1.69	0.20–14.25	0.63	0.97	1.01	0.96–1.06
17 Spinal and bone problems	789 (1.8)	4	2.09	0.68–6.41	0.20	3.89	1.04	0.94–1.14
18 Esophagus Abdominal organs	435 (1.0)	3	2.31	0.67–7.94	0.43	1.87	1.02	0.97–1.08
19 Effusion	519 (1.2)	2	2.32	0.52–10.44	0.27	1.48	1.02	0.96–1.08
20 Kidney	164 (0.4)	1	4.27	0.57–32.06	0.16	0.55	1.02	0.95–1.08
21 Screening	509 (1.2)	3	4.93	1.32–18.39	0.02	24.08	1.95	0.19–3.70

Notes. HR = hazard ratio; CI = confidence interval; COPD = chronic obstructive pulmonary disease; CHF = congestive heart failure.

^aPercentage relative to 43,155 chest/upper spine CT scans. Some scans have multiple reasons.

^bOne regression was performed with adjustment for categorical year of birth and race (white, black, other) and, including a time-dependent binary variable ever versus never, had a CT scan of the chest/upper spine scan and a time-dependent binary variable for each reason, with categories: ever had a chest/upper spine scan and for that reason; never had a chest/upper spine scan for that reason (reference).

^cPrevalence of subjects who ever had a chest/upper spine CT scan for each particular reason during follow-up.

^dFor multiple sclerosis, dyspnea, alcohol/drugs, asthma, sarcoid, embolism, dissection, perforation, inflammation and immunosuppression/human immunodeficiency virus, there were no cases, and so they are not included in this table.

HR = hazard ratio; CI = confidence interval; COPD = chronic obstructive pulmonary disease; CHF = congestive heart failure.