

Projected Cancer Risks From Computed Tomographic Scans Performed in the United States in 2007

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Background: The use of computed tomographic (CT) scans in the United States (US) has increased more than 3-fold since 1993 to approximately 70 million scans annually. Despite the great medical benefits, there is concern about the potential radiation-related cancer risk. We conducted detailed estimates of the future cancer risks from current CT scan use in the US according to age, sex, and scan type.

Methods: Risk models based on the National Research Council's "Biological Effects of Ionizing Radiation" report and organ-specific radiation doses derived from a national survey were used to estimate age-specific cancer risks for each scan type. These models were combined with age- and sex-specific scan frequencies for the US in 2007 obtained from survey and insurance claims data. We estimated the mean number of radiation-related incident cancers with 95% uncertainty limits (UL) using Monte Carlo simulations.

Results: Overall, we estimated that approximately 29 000

(95% UL, 15 000-45 000) future cancers could be related to CT scans performed in the US in 2007. The largest contributions were from scans of the abdomen and pelvis (n=14 000) (95% UL, 6900-25 000), chest (n=4100) (95% UL, 1900-8100), and head (n=4000) (95% UL, 1100-8700), as well as from chest CT angiography (n=2700) (95% UL, 1300-5000). One-third of the projected cancers were due to scans performed at the ages of 35 to 54 years compared with 15% due to scans performed at ages younger than 18 years, and 66% were in females.

Conclusions: These detailed estimates highlight several areas of CT scan use that make large contributions to the total cancer risk, including several scan types and age groups with a high frequency of use or scans involving relatively high doses, in which risk-reduction efforts may be warranted.

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THE USE OF COMPUTED TOMOGRAPHIC (CT) scans in the United States (US) has increased more than 3-fold since 1993 to approximately 70 million scans annually.¹ While CT scans can provide great medical benefits, there is concern about potential future cancer risks because they involve much higher

*See also pages 2049
and 2078*

radiation doses than conventional diagnostic x-rays.¹ The risks to individuals are likely to be small, but because of the large number of persons exposed annually, even small risks could translate into a considerable number of future cancers. To fully evaluate the long-term cancer risks from CT scans directly would require very large-scale studies with lifelong follow-up.² A more timely risk assessment can be obtained using risk projection models.³

In a previous study, we used risk projection models and detailed survey data on CT scan use in the United Kingdom (UK) in the early 1990s⁴ and estimated that approximately 0.2% of incident cancers in the UK could be attributable to CT scans.³ Based on our estimates, a recent review suggested that, because current use in the US is 10 times higher than it was in the UK in the early 1990s, this figure might now be as high as 1.5% to 2% in the US.⁵ While these crude estimates give an indication of the total public health impact, they do not provide any information on which types of CT scans or ages at exposure make the largest contributions to the risk, information that is needed for risk-reduction efforts.

Detailed estimates of the current frequency of CT scan use in the US by CT scan type are available in a new study.¹ We used information from that study combined with radiation risk models based on the National Research Council's "Biologi-

cal Effects of Ionizing Radiation” report⁶ to estimate the potential future cancer risks from CT scan use in the US in 2007. The aim of the study was to conduct a detailed evaluation of the overall potential public health impact of the current levels of use and to assess which age groups and scan types were associated with the highest risks.

METHODS

CT SCAN FREQUENCY

We estimated the frequency of different types of CT scans performed in the US in 2007 using a combination of data sources, primarily Medicare claims data and the IMV Medical Information Division survey of CT scan use in 2451 US facilities in 2007.^{1,7} Results were compared and cross-checked for consistency (eTable 1 [<http://www.archinternmed.com>]). Radiation-related cancer risks depend on sex and age at exposure. We estimated the age and sex distribution for each CT scan type using a large national commercial insurance database (NCID). These estimates were scaled to be applicable to the age-sex distribution of the US population and combined with the national frequency estimates.

A key assumption in the estimation of lifetime radiation-related cancer risk is the life expectancy of persons receiving CT scans.³ Typically, there is at least a 5-year lag period between radiation exposure and cancer diagnosis⁶; therefore, it is very unlikely that patients who do not survive that long would be diagnosed as having scan-related cancer. To address the problem of survival, we used the NCID data set to estimate the proportion of scans performed in patients who did not survive 6 months (2.8%), 1 year (4.3%), and 3 years (7.4%) (the maximum period available) after the scan, and we used linear extrapolation to estimate the proportion of scans performed in patients who did not survive 5 years (11%). We excluded these scans from the annual frequency estimates used in the risk calculations. We also used the NCID data set to estimate the age-specific proportion of scans that had an associated diagnosis code of cancer, with the age and sex distribution adjusted to correspond to the US population. We further excluded those scans under the assumption that they were also unlikely to be related to future cancers (9%) (eTable 2).

ORGAN-SPECIFIC DOSES

The CT dose index and other technical parameters (eg, peak kilovoltage and tube current-time product [milliamperes]) for each scan type were taken from the Food and Drug Administration’s National Evaluation of X-Ray Trends survey,⁸ a quality assurance survey that was conducted in 256 randomly selected US facilities. Several procedures were not included in that survey (coronary artery calcification, CT colonography, and CT angiography), and for those procedures we obtained parameters from recent protocols.⁹⁻¹¹ Parameters were entered into CT-expo to estimate organ-specific doses according to age and sex for each scan type.¹² Dose varies according to scanner model; therefore, we estimated mean doses across 6 models.⁸ Our effective dose estimates were very similar to those from a recent report, which included a literature review and direct phantom measurements (eTable 3).⁹

Pediatric CT scans can involve higher organ doses because of lower radiation attenuation in smaller patients.¹³ Recent surveys suggest that pediatric-specific settings are used increasingly in the US, which should lower doses.¹⁴ Therefore, we assumed that pediatric scans were performed using appropriate current-time product settings.¹⁵

RISK PROJECTION MODELS

The “Biological Effects of Ionizing Radiation” committee conducted a comprehensive review of the literature on health risks from low-level radiation exposure and developed cancer risk projection models for the US population. We used these risk models, with minor modifications, and developed additional models for sites that were not covered in their report (eTable 4).⁶ All models (except breast and thyroid) were developed using data from the latest follow-up of the Japanese atomic bomb survivors, as that study has the most detailed information available for most cancer sites.¹⁶ The models for breast and thyroid cancer were based on pooled analyses of the Japanese and other medically exposed cohorts.^{17,18} For solid cancers, we used a 5-year lag period and a linear dose-response model⁶ but assumed that the risk-per-unit dose was 1.5 times lower for doses equal to or less than 10 rad (to convert to grays, multiply by 0.01) than the risk at higher doses.⁶ This adjustment factor (known as a dose and dose rate reduction effectiveness factor) was allowed to vary in the uncertainty analysis (described below). For leukemia, we used a 2-year lag period, and the dose-response model was linear-quadratic.⁶

The risk calculations were performed with Analytica software¹⁹ using Monte Carlo simulation methods with Latin-hypercube sampling to estimate risks with uncertainty intervals, accounting for statistical uncertainties in the risk parameters and subjective uncertainties in the dose rate reduction effectiveness factor, as well as the transport of risks from the Japanese to the US population. We report the mean estimates from the simulations with 95% uncertainty limits (UL). We investigated the impact of additional uncertainties in the assumptions and data in a sensitivity analysis.

RESULTS

We estimated that, in total, approximately 72 million CT scans were performed in the US in 2007 (eTable 1). After we excluded scans obtained in the last 5 years of life and those with a related diagnosis code of cancer, the number of CT scans used for the calculation of future cancer risks was 57 million. The number of CT scans performed increased with age at exposure up to the age of 45 years, and nearly one-third of the scans (30%) were estimated to be performed in adults aged 35 to 54 years, 13% in those aged 18 to 34 years, and 7% in persons younger than 18 years (**Figure 1**). Approximately 60% of the scans were estimated to be performed in females. Age patterns were broadly similar across scan types (eTable 5).

The projected number of incident cancers per 10 000 scans generally decreased with increasing age at exposure (**Table 1**). The risk per 10 000 scans varied according to scan type, with consistently high risks for chest or abdomen CT angiography and whole-body CT. The projected risks were generally higher in females than in males for scans that exposed the chest because of the additional risk of breast cancer and the higher lung cancer risk coefficients (eTable 4).

When we combined the age- and sex-specific annual frequencies with the estimated risk per 10 000 scans, it was estimated that, overall, approximately 29 000 (95% UL, 15 000-45 000) future cancers could be related to the number of CT scans performed in the US in 2007 (**Table 2**). The largest contributions were from the scan

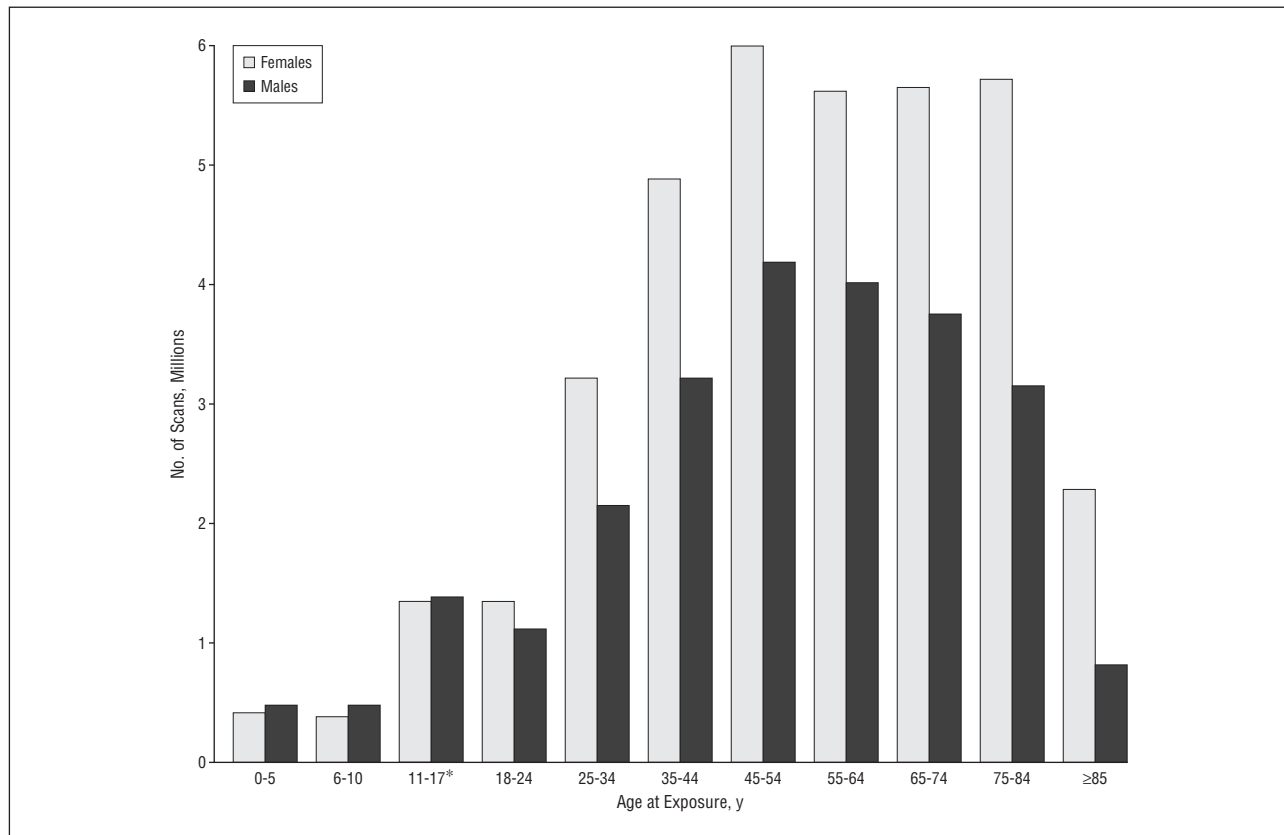


Figure 1. Estimated number of computed tomographic (CT) scans performed in the United States in 2007 (after exclusions), according to sex and age at exposure. The number of CT scans were estimated using the survey data for total number of scans of each type. *The age distribution of CT scans comes from the national commercial insurance database, excluding CT scans that had a diagnosis code of cancer or that were performed in the last 5 years of life.

Table 1. Mean Lifetime Cancer Risk per 10 000 CT Scans,^a According to CT Scan Type and Age at Exposure

Age at Exposure, y	Type of CT Scan												
	Head		Spine			Abdomen and Pelvis	CTA				Whole Body	CTC	CAC
	Head	Chest	Cervical	Lumbar	Thoracic		Chest	Head	Abdomen	Pelvis			
Females													
3	8	40	70	20	70	20	NA	NA	NA	NA	60	NA	NA
15	4	30	50	10	40	20	60	30	20	20	40	10	10
30	2	10	5	7	10	10	20	4	10	10	20	6	5
50	1	7	2	6	9	8	10	2	9	8	10	5	3
70	1	3	1	2	3	3	5	1	4	3	5	3	1
Males													
3	9	10	10	20	20	20	NA	NA	NA	NA	30	NA	NA
15	5	9	10	10	8	20	20	10	20	10	20	10	2
30	3	5	3	7	5	10	8	5	10	5	10	6	1
50	2	4	2	6	4	9	8	3	10	3	10	5	1
70	1	3	1	4	3	5	5	2	6	2	3	3	1

Abbreviations: CAC, coronary artery calcification; CT, computed tomographic; CTA, CT angiography; CTC, CT colonography; NA, pediatric protocols not available.

^aEstimated for a single-phase scan and presented to 1 significant figure.

types performed most frequently: abdomen and pelvis (n=14 000) (95% UL, 6900-25 000), chest (n=4100) (95% UL, 1900-8100), and head (n=4000) (95% UL, 1100-8700), as well as from the highest-dose scans (chest CT angiography) (n=2700) (95% UL, 1300-5000). Two-thirds of the projected cancers were estimated to occur in women primarily because of higher frequency of use

(60% of scans) and because of the higher breast and lung cancer risks from scans that expose the chest (described above).

Approximately one-third of the projected cancers (35%) were from scans performed between the ages of 35 and 54 years, whereas 15% were from scans performed before the age of 18 years (**Figure 2**). The break-

Table 2. Projected Number of Future Cancers That Could Be Related to CT Scans Performed in the United States in 2007, According to CT Scan Type^a

Type of CT Scan	No. of Scans, ^b Millions (%)	No. of Cancers					
		Females		Males		Total	
		Mean (95% UL)	%	Mean (95% UL)	%	Mean (95% UL)	%
Head	18.7 (33)	1900 (500-4400)	11	2100 (600-4300)	19	4000 (1100-8700)	14
Chest	7.1 (12)	3100 (1400-6100)	17	1000 (500-2000)	9	4100 (1900-8100)	14
Cervical spine	1.8 (3)	700 (200-1700)	4	300 (100-600)	3	1000 (300-2300)	3
Thoracic spine	0.3 (<1)	200 (80-300)	1	50 (20-100)	<1	250 (10-400)	1
Lumbar spine	2.2 (4)	700 (300-1600)	4	500 (200-1100)	5	1200 (400-2700)	4
Abdomen/pelvis	18.3 (32)	8500 (4200-15 000)	47	5500 (2600-9600)	50	14 000 (6900-25 000)	48
CTA chest	2.3 (4)	2200 (1100-4200)	12	500 (200-900)	5	2700 (1300-5000)	9
CTA other ^c	1.6 (3)	400 (200-900)	2	500 (200-1100)	5	900 (300-1900)	3
Whole body	0.3 (<1)	300 (100-500)	2	100 (50-200)	1	400 (200-600)	1
Colonography	0.2 (<1)	70 (30-120)	<1	50 (20-100)	<1	120 (60-200)	<1
Calcium scoring	0.6 (1)	150 (70-300)	1	30 (10-60)	<1	180 (80-400)	<1
Other ^d	3.5 (6)	10 (3-20)	<1	20 (1-80)	<1	30 (4-100)	<1
Total ^e	56.9 (100)	18 000 (9000-28 000)	100	11 000 (6000-16 000)	100	29 000 (15 000-45 000)	100

Abbreviations: CT, computed tomographic; CTA, CT angiography; UL, uncertainty limits.

^aThe numbers are presented to a maximum of 2 significant figures.

^bExcluding CT scans with a diagnosis code of cancer or that were performed in the last 5 years of life.

^cAbdomen, pelvis, and head.

^dPrimarily extremity CT scans and bone mineral density.

^eTotals are not equal to the sum for males and females because of rounding.

down by cancer site showed that lung cancer was the most common projected radiation-related cancer (n=6200) (95% UL, 2300-13 000) followed by colon cancer (n=3500) (95% UL, 1000-6800) and leukemia (n=2800) (95% UL, 800-4800) (eFigure). The cancer sites with the highest risks were common cancers with a high frequency of exposure to that organ (eg, colon from CT of the abdomen and pelvis and lung from CT of the chest) or higher radiosensitivity (eg, red bone marrow and leukemia).

COMMENT

The rapid increase in CT scan use in the US has raised concerns about potential cancer risks, because when a large number of people are exposed, even small risks could translate into a large number of future cancers in the population. Our estimates suggest that approximately 29 000 (95% UL, 15 000-45 000) future cancers could be related to CT scan use in the US in 2007. The detailed estimates highlight a number of areas that could be associated with particularly high risks, including several scan types that either are very common (CT of the abdomen and pelvis, chest, and head) or involve relatively high doses (CT angiography of the chest). To date, attention has focused on risks from pediatric CT scans. However, our estimates suggest that in terms of absolute numbers the potential public health impact of current use patterns is highest for adults aged 35 to 54 years, particularly women, because of the high frequency of use.

To our knowledge, these are the only detailed estimates of the potential future cancer risks based on current US age- and sex-specific CT scan patterns. Our previous risk projections were based on UK data from the

1990s, when CT scan use was much less common, and no equivalent information was available for the US at that time.³ A number of other studies have used risk-projection methods to estimate risks for specific scan types (eg, chest CT or CT angiography), but those did not take into account the frequency of use in the US.²⁰⁻²² Several recent studies have also estimated risks to individuals from specific patterns of use with hospital records data.^{23,24} These studies highlight the potential risks to some individuals who receive multiple CT scans, but they cannot be used to estimate the total risk at the population level, which requires national survey data.

A commonly quoted estimate for excess cancer mortality from radiation exposure is 1 death per 2000 scans (assuming an effective dose of 10 mSv per scan and a risk of 5% per sievert).²⁵ Based on this crude approach, 57 million scans would result in about 29 000 future cancer deaths. Our detailed calculations suggested that these scans would result in about 29 000 incident cancers and, assuming approximately 50% mortality, these incident cancer cases would translate into about 14 500 cancer deaths. The main reason that the crude estimate is much higher is that it assumes that the age-distribution of patients undergoing CT scans is the same as that of the general population, whereas it is much older on average.¹

Although cancer risks from CT scans have not been demonstrated directly, radiation is one of the most extensively studied carcinogens, and there is direct evidence from studies of the Japanese atomic bomb survivors, nuclear workers, and patients receiving multiple diagnostic x-rays that radiation doses of the magnitude delivered by several scans (5-10 rad) can cause cancer and that the magnitude of the risk at these doses is largely consistent with the risks at higher doses.²⁶ To accu-

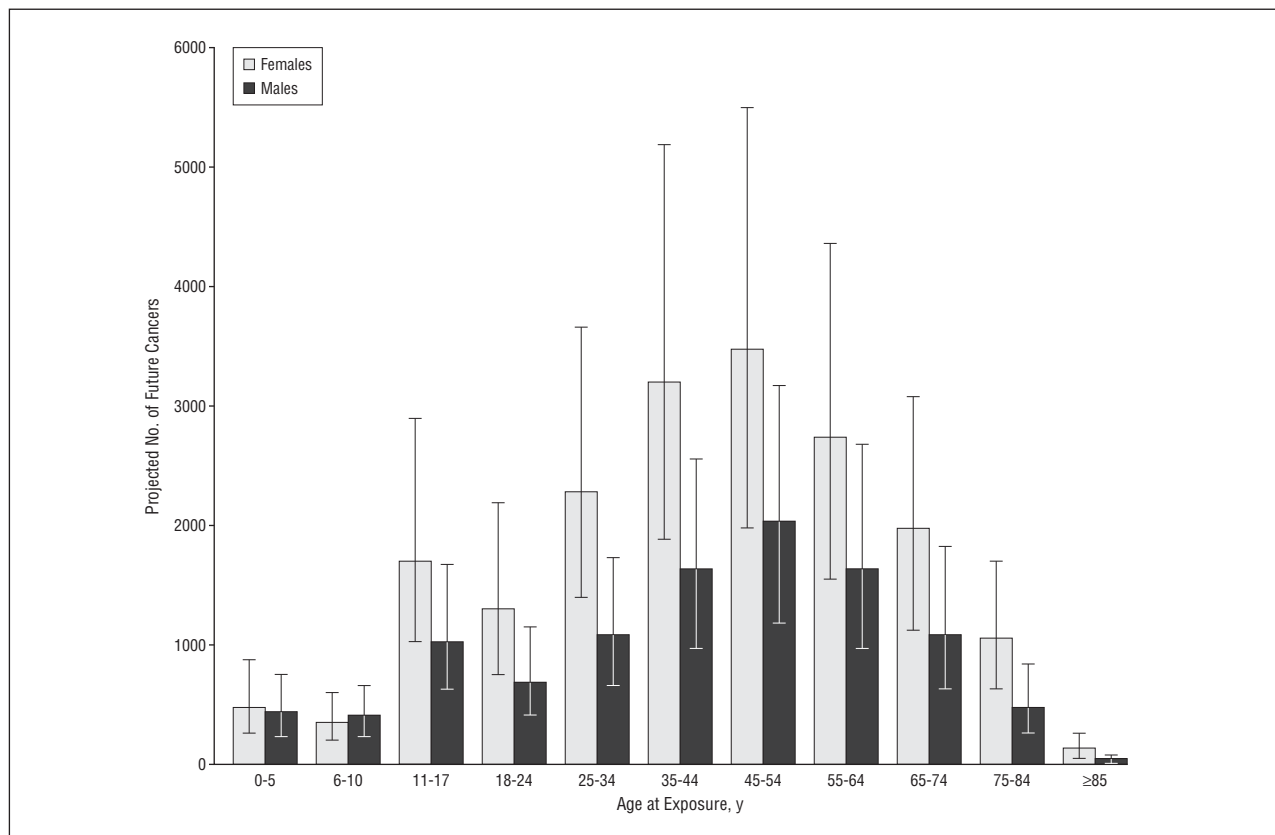


Figure 2. Projected number of future cancers (mean and 95% uncertainty limits) that could be related to computed tomographic scan use in the United States in 2007, according to age at exposure.

rately quantify risks from CT scans directly would require long-term follow-up of very large populations,² which is why we used an indirect modeling approach to provide more timely risk projections. The models are based on the so-called linear, no-threshold theory, which holds that, at low radiation doses, excess cancer risks associated with radiation exposure are directly proportional to dose. This theory has long been the basis for radiation protection recommendations by international and national expert committees concerned with radiation protection,^{6,27,28} although not without challenge from believers in a low-dose threshold dose below which there is no radiation-related cancer risk.²⁹ The evidence in support of a threshold is relatively weak because at very low doses statistical power is lacking to detect variations on low-dose linearity, such as an assumed threshold at 0.5 rad.²⁸ Biological evidence also does not generally support the likelihood of a threshold as even the most efficient DNA repair processes are imperfect.²⁶ Therefore, the linear no-threshold approach is a reasonable method based on biological and epidemiological evidence for estimating cancer risks from low-doses of radiation exposure.

Nevertheless, there are a number of uncertainties and assumptions involved in these risk projections. A particular strength of this study is that we developed methods to quantify the uncertainties in the risk models, including statistical uncertainties in the risk parameters and subjective uncertainties in the magnitude of the risk at low doses, as well as the transport of risks from the Japa-

nese to the US population. We further summarized the impact of alternative assumptions and additional uncertainties, which are described below and summarized in **Table 3**. Formal inclusion of these additional uncertainties would have increased the width of the uncertainty intervals.

There is clear experimental evidence that exposure to low-energy x-rays results in more chromosome aberrations and cell transformations per unit dose than gamma rays (the primary source of exposure from the atomic bombs).³⁰ It is less clear whether this also applies to cancer risks in humans, because there are no epidemiological studies with directly comparable populations that have been exposed to different types of radiation.³⁰ If the experimental findings are applicable, then the risk models from the Japanese atomic bomb survivors may underestimate risk for low-energy x-rays, possibly by a factor of 2.0 (Table 3).⁶ Another possible source of underestimation is that risk models were not available for some cancer sites because the number of cases in the Japanese atomic bomb survivors study was too small ($n < 100$) for reliable estimation.¹⁶ The sites that we included account for approximately 80% of annual cancers in the US,³¹ suggesting that we could have underestimated risk by up to 20%, assuming similar levels of radiosensitivity for the included and excluded cancer sites. Conversely, several included sites have not been clearly established as being radiation inducible (eg, prostate cancer).⁶ The risk coefficients were low for these sites and had a lower bound of 0 (eTable 4). If these sites had been excluded,

Table 3. Sensitivity Analysis of the Impact of Varying the Assumptions and Parameters Expressed as Maximum Percentage of Change in the Mean Projected Number of Cancers

Alternative Parameter or Assumption	Maximum Change, %
Relative biological effectiveness of x-rays, 2.0	+100
Inclusion of cancer sites without detailed risk models	+20
Exclusion of cancer sites that are not confirmed radiation inducible	-17
Radiation-related solid cancer latency, 10 y	-4
Uncertainty in organ dose estimates	±15
Pediatric scans obtained with adult settings ^a	+5
Uncertainty in CT scan frequency	±30
All-cause mortality rates 10% higher than general population	-5
All-cause mortality rates 50% higher than general population	-20
Inclusion of CT scans with a diagnosis code of cancer	+13

^aA detailed description of these alternative assumptions is provided in the "Methods" and "Comment" sections. CT indicates computed tomographic.

the total cancer risk would have been reduced by 17% (Table 3).

We estimated doses using scanner types and settings from a population-based national survey.⁸ The proportion of multislice scanners currently in use in the US has increased since this survey was conducted, and doses from multislice scanners could be higher or lower than those from single-slice scanners, depending on the parameter settings that are used.^{32,33} However, our effective dose estimates based on the National Evaluation of X-Ray Trends survey⁸ were very similar to estimated current mean doses in a recent report that included a literature review as well as recent direct measurements.⁹ Variation in the mean organ dose estimates can be approximately 15% or more,³⁴ which has a similar impact on the risk estimates (since risk is proportional to dose). Although there is evidence that pediatric-specific settings are used increasingly, the total risk estimate would have been increased by 5% if all pediatric scans had been performed with adult settings (Table 3). In practice, there is wide variation in CT doses, depending on the purpose of the scan, number of phases, scanner type, settings, and patient size. Results from a recent dose survey for CT coronary angiography illustrate the potential variability.³⁵

A key strength of our study was the use of detailed information on current patterns of CT scan use according to age, sex, and scan type. Although there was no single data source that included all this information, cross-checking of the data sources showed consistency. For example, based on the NCID database, there were an estimated 19 million scans performed on adults older than 65 years compared with 20 million in Medicare. Both sources also agreed on the estimated proportion of scans obtained in women (60%). The uncertainties in the frequency data include the extrapolation from the NCID to the general population and the assumption that the Medicare claims database is representative of all patients older than 65 years. The potential magnitude of uncertainty is difficult to quantify but is not thought to be more than

30%.¹ The combination of site-specific surveys and insurance claim databases should have reduced the possibility of systematic biases because CT scans not currently covered by insurance plans would have been collected in the IMV survey.⁷

Although we excluded CT scans that were performed in the last 5 years of life, it is likely that many patients who survive longer than this still have a shorter life expectancy than the general population (assumed in the calculations). In our previous study, we estimated that a 10% to 50% increase in all-cause mortality rates would result in 5% to 20% lower cancer risk projections (Table 3).³ We also excluded CT scans with an associated diagnosis code of cancer. A number of the excluded scans probably did not result in a cancer diagnosis, and it is also possible that patients could develop a new cancer as a result of follow-up scans. If we had included these scans, the risk estimates would have been increased by 13% (Table 3).

Brenner and Hall⁷ used a crude approach based on our previous calculations and suggested that 1.5% to 2% of cancers in the US might now be attributable to CT scans. Our current estimates are for CT scans obtained in 2007, and because cancer risks remain elevated for many decades after radiation exposure, these projected radiation-related cancers would be spread out over many decades. However, if CT scan use remains at the current level or increases further, then our results suggest that eventually 29 000 (95% UL, 15 000-45 000) cancers every year could be related to past CT scan use, which is equivalent to approximately 2% (1%-3%) of the 1.4 million cancers that are diagnosed annually in the US.³¹ Therefore, in several decades, the attributable risk may reach the level suggested by Brenner and Halls' crude calculation, but at present it is likely to be lower, as current cancers would be related to CT scan use in the 1980s and 1990s, when levels of use were lower.¹

Reduction in risk could be achieved in a number of ways, including decreasing the number of unnecessary procedures as well as the dose per procedure. The American College of Radiology appropriateness criteria³⁶ are an important tool for helping physicians to make the most appropriate imaging decisions for specific conditions, and widespread use of these criteria should reduce unnecessary CT scans. Mechanisms to evaluate appropriate dose levels, as well as guidance for reducing dosages, including reference levels for radiation dose,³⁷ are available, and participation in radiation dose registries, such as the recently initiated American College of Radiology registry, can provide institutions with feedback on their radiation exposure levels in comparison with other institutions.³⁸

Changes made to practice now could help to avoid the possibility of reaching the level of attributable risk suggested above (2%). Our detailed estimates highlight several areas of use in which the public health impact may be largest, specifically abdomen and pelvis and chest CT scans in adults aged 35 to 54 years. To date, the emphasis on cancer risks has been on pediatric CT scans. There is evidence that doses have begun to be successfully reduced as a result of campaigns such as Image Gently.³⁹ Further work is needed to investigate the balance of the

risks and benefits from CT scan use and to assess the potential for dose or exposure reduction.

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