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Evaluation of risks of cardiovascular disease from radiation exposure linked to computed tomography scans in the UK

Colin J Martin^{1,*} , Michael Barnard²  and Frank de Vocht^{3,4} ¹ Department of Clinical Physics and Bioengineering, University of Glasgow, Glasgow, United Kingdom² Department of Radiation Physics and Protection, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom³ Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, United Kingdom⁴ NIHR Applied Research Collaboration West (ARC West), Bristol, United Kingdom

* Author to whom any correspondence should be addressed.

E-mail: colinmartin1948@gmail.com**Keywords:** radiation effects, cardiovascular disease, cerebrovascular disease, radiation epidemiology, computed tomography doses

Abstract

Epidemiological studies of patient populations have shown that high doses of radiation increase risks of cardiovascular disease (CVD). Results from a recent meta-analysis of 93 epidemiological studies covering a wide range of doses provided evidence of a causal association between radiation exposure and CVD, and indicated excess relative risk per Gy for maximum dose below 500 mGy or delivered at low dose rates. These doses cover the range of organ doses expected from multiple diagnostic computed tomography (CT) scans. Dose-effect factors for the excess absolute risk of mortality from CVD following radiation exposure were derived from the meta-analysis. The present study uses these factors to estimate excess risks of mortality for various types of CVD, including cerebrovascular disease (CeVD), from CT scans of the body and head, assuming that the meta-analytic factors were accurate and represented a causal relationship. Estimates are based on cumulative doses to the heart and brain from CT scans performed on 105 574 patients on 12 CT scanners over a period of 5½ years. The results suggest that the excess number of deaths from CeVD could be 7 or 26 per 100 000 patients depending whether threshold brain doses of 200 mGy or 50 mGy, respectively are assumed. These results could have implications for head CT scans. However, the results rely on the validity of risk factors derived in the meta-analysis informing this assessment and which include significant uncertainties. Further incidence studies should provide better information on risk factors and dose thresholds, particularly for CeVD following head CT scans.

1. Introduction

Epidemiological studies of patient populations exposed to high doses of ionising radiations suggest a link between radiation dose and many types of cardiovascular disease (CVD) consequent on the receipt of high doses. These include ischaemic heart disease (IHD) [1–6] and cerebrovascular disease (CeVD) [7–14]. Higher incidences have been observed in patients treated with radiotherapy who receive doses of 5 Gy or more to the heart and brain, which will result in recognisable tissue damage [1]. Effects at higher doses show a dose-response association with for example patients having increased relative risks of mortality from cardiac disease of 1.25 following radiation therapy treatments of breast cancer with doses of 4–8 Gy to the heart [2–4] and relative risks of coronary heart disease of 2–3 have been observed in patients receiving doses of 20–30 Gy to the heart from radiation treatment for Hodgkins lymphoma [1]. Studies of patients treated with radiotherapy for head and neck cancer show increases in the incidence of CeVD [7–13]. Patients may receive doses to the brain from 0.1 Gy up to >50 Gy, with those towards the upper end of the range having a substantially higher risk of mortality from CeVD. Patients receiving doses over about 10 Gy may have a ten-fold increase in incidence of stroke [9]. A long term study with 55 y follow-up of over 15 000 individuals

Table 1. Meta-analysis of higher quality ERRs for CVD mortality for various disease endpoints per Gy for studies with low dose (<500 mGy) and/or low dose rate (<5 mGy h⁻¹) with 95% confidence intervals (CIs) [26].

Disease endpoint	No. of studies	Meta analysis ERR for all data per Gy
IHD	15	0.397 (0.047–0.747)
Other heart disease	9	0.474 (0.057–0.891)
Other CVD	8	0.595 (0.175–1.015)
CeVD	14	0.539 (0.157–0.921)

treated for tinea capitis who received a mean dose of 1.5 Gy to the brain reported a 20% increase in the incidence of stroke per Gy [14].

Increased risks of both IHD and CeVD have also been observed in the Life Span Study cohort of the Japanese atomic bomb survivors receiving a range of doses, from low to high, the latter producing tissue damage (1950–2003) [15–17]. Approximately 60% of radiation-related excess non-cancer deaths in this group have been attributed to circulatory disease [18]. Evidence that increased risks from CVD incidence and mortality may extend down to radiation dose levels below 100 mSv has been provided by epidemiological studies of exposed workers. The INWORKS project includes pooled cohorts of over 300 000 workers from France, the UK and USA employed in nuclear industries who had dosimetry records for external radiation exposure [19, 20]. These studies show a linear dose-response relationship for IHD mortality with an average ERR of 0.17 per Sv [90% CI 0.002, 0.36] and CeVD mortality (ERR 0.49 [90% CI, 0.11, 0.92]). There have been a variety of other studies suggesting higher incidences of IHD and CeVD from radiation exposures, examples being in workers at the Mayak nuclear plant in the USSR, but in this group there is little evidence of excess mortality [21–23] and among liquidators involved in the clean-up after the Chernobyl nuclear reactor accident [24, 25].

Recently Little *et al* [26] carried out a systematic review and meta-analysis of 93 epidemiological studies with limited overlap and derived meta-analytic excess relative risks (ERRs) for incidence and mortality from the four sub-categories of CVD. They comment that the results suggest that risks are statistically significantly higher ($P = 0.002$) for mortality endpoints compared with those for incidence for IHD, CeVD and all CV, and the ERRs per Gy for incidence and mortality were significantly elevated for low dose (<500 mGy) and/or low dose rate (<5 mGy h⁻¹) data. ERRs for mortality from low dose and low dose rate studies that the authors classified as higher quality; i.e. lower risk of bias (based on the ROBINS-I framework) are given in table 1 [27]. Other studies included in the analysis show significant heterogeneity that may be due to residual confounding factors, different baseline population disease rates, different disease endpoints, and measurement or other errors in exposure assessment. However, the heterogeneity is markedly reduced among the group of higher quality studies with a maximum dose of less than 500 mGy or low dose rate.

Increased risks at lower doses, if shown to be causal, could have implications for diagnostic medical and occupational radiation exposures. Medical diagnosis and treatment represent the largest source of exposure of the population from artificial sources and computed tomography (CT) scans make up the largest part of the diagnostic component [28, 29]. It is important to understand the potential implications of any adverse effects for patients from these exposures; particularly if the dose-response associations do indeed extend down to low doses. At the time of the initial study no estimates of risks of CVD from epidemiological studies of exposed populations had been published [30].

In the present study we conduct a further evaluation of doses to a group of over one hundred thousand patients having CT scans at three UK hospitals over a period of five and a half years [30]. Doses to the heart and brain were analysed, although it is acknowledged that there may be other target tissues, such as the carotid arteries for CeVD. The aim is to use the dose-effect factors for radiation associated mortality from CVD that are now available to estimate mortality rates that could result from medical imaging exposures if the dose-effect associations are causal across the complete dose range.

2. Methods

2.1. Dose data collection

The Radimetrics™ dose management software (version 3.0A; Bayer AG Berlin, GDR) is installed on a virtual machine hosted at the Oxford University Hospitals NHS Foundation Trust (OUH). Image data including dose sheets from 12 CT scanners at three hospital sites, which are forwarded to the Radimetrics platform from the picture archiving and communication system (PACS) for processing. Dose data in the form of the dose length product and the volume averaged CT dose index (CTDI_{vol}), and scan parameters for each examination were extracted from the digital imaging communications in medicine (DICOM) fields of the

Table 2. Summary estimates of excess absolute risk (EAR) of radiation induced mortality (% per Gy) over the remainder of the subject's lifetime and 95% confidence intervals (CIs) from meta-analysis of mortality data for various types of CVD [26]. Results are based on data from all studies analysed and derived using population data on deaths from CVD for England and Wales from 2003 and 2021.

Cardiovascular disease	EAR CIs using 2003 data (% per Gy)	EAR and CIs using 2021 data (% per Gy)
IHD	1.30 (0.84–01.75)	0.64 (0.41–0.87)
Other heart disease	0.18 (0.11–0.25)	0.21 (0.12–0.29)
Other CVD	0.61 (–0.10–1.31)	0.41 (–0.07–0.88)
CeVD	2.04 (1.01–3.07)	0.94 (0.46–1.41)
All CVD	3.94 (2.85–5.03)	2.33 (1.69–2.98)

images. The CT scanners and the methods used to extract the data are described in Martin and Barnard [30]. The Radimetrics platform uses a Monte Carlo simulator to model the x-ray interactions with stylised patient phantoms to assess organ and tissue doses [31, 32]. A phantom is selected for each patient based on age, sex and mid-scan diameter. Simulations are run for different scan protocols to evaluate the energy deposited in every organ, data are stored in a look-up table, and organ doses for individual scans are scaled based on values of CTDI_{vol}. The displayed CTDI_{vol} values were calibrated on a 16 cm CT phantom for head scans and a 32 cm phantom for body scans.

Only those fields relevant for the study were exported from the records for the analysis. This included protocol name, date performed, device, patient medical record number (MRN), gender, age at exam, organ doses and effective dose. Data on patient organ doses were accumulated over a period of 5½ years from CT scans performed between 26 October 2015 and 6 May 2021. Cumulative data were downloaded into an Excel™ (Microsoft Corp, Redmond, WA, USA) spreadsheet for 215 194 CT examinations performed on 105 757 patients receiving scans over the period, 65 394 of whom had body scans and 58 430 head scans. If a patient had received both head and body examinations during the analysis period, these were listed as 'head/body' and included the number of each examination type. MRNs were removed and each replaced with a unique nonidentifiable key, using a lookup table to link the key to each MRN. Once checked and the accuracy of the assigning of keys was confirmed, all patient MRN data were removed. The cumulative doses for the heart and brain from all the scans performed were evaluated, together with the effective doses from weighted sums of doses to individual organs. The doses from Radimetrics software are recorded in mSv, but it is more appropriate for doses to organs and tissues to be given as mean absorbed doses in mGy [33]. Therefore, since all exposures are from x-rays and the two quantities are identical, doses are expressed in mGy. The methods are described in more detail in Martin and Barnard [30].

2.2. Risk data

The meta-analysis by Little *et al* [26] provided an estimate of the aggregate estimate of ERR of mortality and incidence per Gy over the remainder of the subject's lifetime across subsets of the studies using standard statistical methods. Risk of bias was systematically assessed for each study using the ROBINS-I framework [27]. Values of ERR derived for types of CVD for the higher quality studies with lowest risk of bias, low dose and low dose rate studies that are relevant to the present analysis are shown in table 1. The pooled values of ERRs for CVD mortality from the meta-analysis of all the studies were used to derive population-based estimates of excess absolute risks of mortality per Gy averaged over populations for France, Germany, USA, Canada, and Japan, as well as values for England and Wales based on data from 2003 and 2021 (table 2). The risk value for the England and Wales 2003 group was the highest at 3.94% per Gy for all CVDs and that for the 2021 group the lowest at 2.33% per Gy among all the risk data.

2.3. Processing of CT scan dose data

The dose data were analysed using an Excel spreadsheet. During the 5½ year period of the study 5.14% of the 105 757 patients had five or more CT scans and 0.66% more than ten scans, and 0.68% received effective doses over 100 mSv. The dose data set was analysed separately for heart dose and brain dose. The patients were predominantly in the age range 40 y to 90 y [30], but while the study by Little *et al* [26] suggested some increase in the ERRs of CVD incidence with age at exposure, there were no data on changes in mortality presented, and we therefore used age-independent values of ERRs. For context it should be noted that ERRs in the Life Span Study were higher for the youngest age group for CeVD [15, 34], but not for heart disease [15, 35]. Patients in the present study were simply grouped by organ dose and the dose ranges for the two organs were chosen to give sufficient patient numbers for analysis and to allow the influence of any threshold dose for demonstration of the effects to be investigated for the whole group (table 3). However, the predicted

Table 3. Numbers within the cohort of 105 757 scanned patients receiving doses to the heart or brain within different dose ranges. Those above 20 mGy were used for the analyses.

Heart dose	No. of patients (<i>N</i>)	Brain dose	No. of patients (<i>N</i>)
<20 mGy	78 247	<20 mGy	50 247
20–50 mGy	20 466	20–50 mGy	29 745
50–100 mGy	5499	50–100 mGy	15 619
100–200 mGy	1358	100–200 mGy	7621
200–300 mGy	149	200–500 mGy	2294
>300 mGy	38	0.5–1 Gy	215
		>1 Gy	16

mortalities among the proportion of patients within the study population under 60 y of age following either head or body CT scans were estimated to give an indication of the effect of patient age distribution.

The numbers of deaths from CVD resulting from the CT scan exposures predicted by the excess mortality values for the different disease types were derived by multiplying the cumulative organ dose (in Gy) for each individual patient by the excess absolute risk (*EAR*) from the UK mortality risk data (table 2, column 3) for each disease expressed as a fraction, and summing the results for the *N* patients within each defined dose range (table 3) using equation (1) (where *i* is the *i*th patient, *N* is the number in the group, *EAR* is the excess absolute risk per Gy expressed as a fraction, organ dose (heart or brain) is the value for the *i*th patient in Gy)

$$\text{Predicted number of deaths in dose range} = \sum_{i=1}^{i=N} \text{EAR} \times \text{Organ dose}_i. \quad (1)$$

The predicted numbers of deaths over the remaining lifetimes of the patients were normalised to apply to 100 000 patients having CT scans for easier interpretation, by multiplying by 100 000/105 757. A similar approach was used to determine the predicted excess numbers of deaths from heart and circulatory diseases linked just to body CT scans and from CeVDs linked just to head CT scans. The *EAR* of radiation induced mortality values (table 2) were also used to calculate excess mortality from ten body or head CT scans from typical doses in UK hospitals to give an indication of the risk linked to the type of examination. For this, values for the National Diagnostic Reference Levels (DRLs) in terms of the volume averaged CT dose index (CTDI_{vol}) for CT scans of the chest and head have been used to represent doses to the heart and brain respectively [36]. The CTDI_{vol} values are measurements derived to give approximate measures of doses to tissues within the scanned regions for standard phantoms representing the body and head. The DRL values are the 3rd quartile of the distribution of median doses for UK hospitals included in the survey.

Since doses from diagnostic medical exposures are generally low, the values of threshold doses for any effect of radiation on CVD will have a significant influence on the potential mortalities. Shimizu *et al* [15] state that based on the Life Span Study of the Japanese atomic bomb survivors, the best estimate of a threshold dose for CeVD is 500 mGy, but that this is highly uncertain and might be between 0 Gy and 2 Gy, while their best estimate for a threshold dose for heart disease is 0 Gy. The possibility of no threshold dose below which radiation induced CVD effects can occur based on the Life Span Study is supported by some [37] and disputed by others [38]. The International Commission on Radiological Protection, classified CVD as a tissue reaction and derived a nominal threshold dose of 500 mGy equating to a 1% lifetime risk, but this is a proposed value to facilitate practical decision making, rather than a true dose threshold linked to the effect. Since there is no definitive dose that can be used as a threshold dose, calculations have been made using a selection of possible threshold doses from 50 mGy upwards to assess the significance of any threshold value chosen.

In order to evaluate how the excess mortalities from CVD compare with those from the induction of cancer—as a well-recognised risk—for patients receiving effective doses over 100 mSv, a comparison is made with cancer mortality data. Although there have been several studies of the occurrence of brain tumours and leukaemia in populations of young persons given CT scans that have derived values of ERR for incidence of haematological malignancies, the ages are different from those in the present study and are difficult to compare directly [39, 40]. It should be noted that findings of studies of this type could be subject to reverse causation, whereby the indication for the original scan could bias the results [41]. ICRP Publication 147 [33] uses available cancer incidence data taking account of variations with age and sex to derive lifetime risks of cancer incidences per unit effective dose (Sv) from distributions of dose resulting from CT scans of different parts of the body [42]. The cancer incidence factors for head scans and chest abdomen pelvis scans, as representative of body scans, for a Euro-American population, were used to calculate excess lifetime risks of

cancer incidence for each patient having a CT scan from the effective doses. A summed cancer incidence was then calculated for patients receiving effective doses within selected ranges using the equation:

$$\text{Cancer incidence sum} = \sum_{i=1}^{i=N} \text{sex} = \text{F, M} \quad \text{LRCI}_{\text{sex,CT,age}} \times \text{Effective dose}_{\text{CT},i} \quad (2)$$

CT = head, body
age = 0 – 10, 90 – 99

where $\text{LRCI}_{\text{sex,CT,age}}$ = Total lifetime risk of cancer incidence risk coefficient from ICRP Publication 147, relating to the sex, age at exposure and type of CT scan for each patient [33] and i represents the i th patient of N within the selected dose range. An adjustment factor equal to the ratios of the number of deaths from cancer over the incidence rate was applied to the results to derive a value for cancer mortality for comparison with results for CVD mortality. Two approaches were used to derive the adjustment factor. UK data for cancer incidence and mortality were taken from the Institute for Health Metrics and Evaluation (IHME) database on the Global Health Burden of Disease [43] and the total number of deaths for all named types of cancer in the UK over a 10 year period (2010–2019) was divided by the total cancer incidence, which gave an adjustment factor of 0.42. The second method derived the proportions of cancers of each type from the IHME database within the UK over the same period, multiplied these by values for lethality taken from ICRP Publication 103 (table A.4.5) [44], and summed the data over all cancer types. The ICRP Publication includes values for the main radiation related types of cancer and gives a value of 0.49 for application to other cancers. However, the table does not include a specific factor for the prostate, that makes up 13% of the UK cancer incidence and has a relatively low mortality. Therefore, a specific lethality factor of 0.24 based on available data from the UK was used for prostate cancer. The overall mortality adjustment factor derived using this method was 0.49 and this was applied to predict the number of deaths from cancer in the study group.

3. Results

Predicted numbers of excess deaths for the various types of CVD among the patients in the study are plotted in the form of bar charts in figure 1. The values were calculated by applying equation (1) to all patients with a dose to the heart or the brain for CeVD, within the selected dose ranges for each group. The exposure of the brain in the patient population is greater, because the frequency of repeat scans of the head for individual patients was greater (table 3), and the predicted number of deaths from CeVD among all the patients scanned was substantially higher than for other types of CVD. The data suggest that there could be up to 30 excess deaths from all types of CVD per 100 000 patients scanned in the 5½ year period resulting from the exposures, but this is critically dependant on the threshold dose used for the estimation. If the threshold dose to the brain was as low as 50 mGy, then the predicted number of excess deaths from CeVD per 100 000 patients would be 26, whereas if the threshold was 200 mGy, then the prediction would be seven extra deaths. In the same way, if the threshold dose to the heart was 50 mGy, then the number of excess deaths from IHD, other heart disease and other CVD per 100 000 patients could be seven, whereas, if it was 200 mGy, only 0.6 additional death is predicted.

Since potential risks of CeVD from exposure of the brain in head CT scans could be substantially higher than those for other types of CVD from exposure of the heart in body CT scans, patient dose data for head and body CT scans have been analysed separately. The risk data from Little *et al* [26] has been applied to derive predicted numbers of excess deaths for head or body CT scans separately. For these calculations a threshold of 100 mGy to the heart or brain was chosen. Risks were calculated for the patients among the group of 65 394 given body scans who received over 100 mGy to the heart, and results were normalised to provide the number of deaths from different categories of heart disease per 100 000 patients having body scans. In a similar manner, risks were calculated for patients among the group of 58 430 having head scans who received over 100 mGy to the brain. Results for both groups are given in table 4. Proportions of patients under 60 y were separated out and the number of expected deaths evaluated to give an indication of numbers in the younger age group, although the results from the meta-analysis suggest that risks are similar [26]. The results again indicate that, if the risk factors are correct, then CeVD from head scans could be the more significant risk from medical exposures (given the threshold dose were as low as 100 mGy).

In order to provide a comparison between potential excess mortality from CVD and that from cancer, factors on the total lifetime risk of cancer incidence per Sv effective dose by age at exposure and sex in ICRP Publication 147 were applied using equation (2) [33]. The results were then multiplied by a ratio of cancer mortality to incidence for the UK population. The excess mortality rates for cancer relating to effective doses

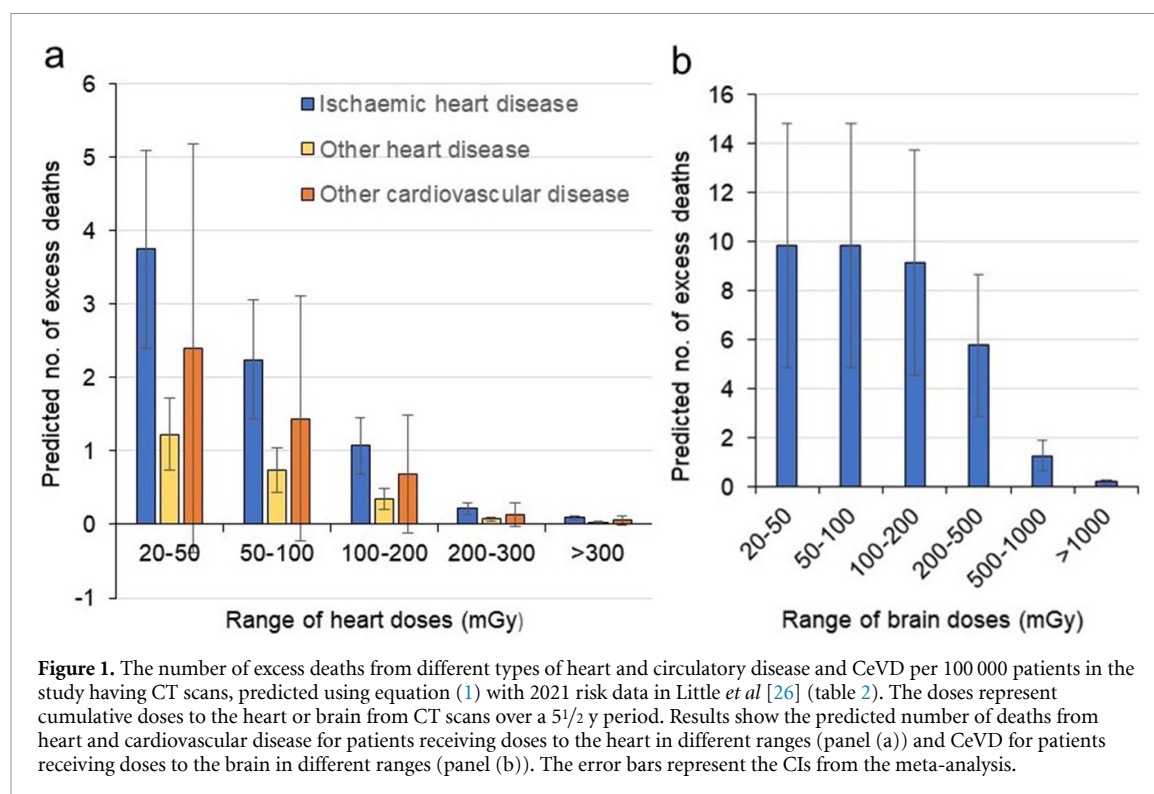


Table 4. Predicted excess mortality per 100 000 patients from different types of CVD among patients receiving CT scans of the body or scans of the head, over a 5½ year period from the survey data assuming a 100 mGy dose threshold for the effect [26, 30]. The errors represent 95% confidence intervals on the risk data. Results are compared with data on cancer mortality calculated using ICRP cancer incidence factors [33] taking account of differences in age and sex with different dose thresholds with an adjustment factor applied to derive mortality.

Disease type (CT scan)	Organ/Tissue exposed	Deaths among all patients receiving >100 mGy	Deaths among patients under 60 y receiving >100 mGy
Ischaemic heart disease (Body CT)	Heart	2.2 ± 0.8	0.5 ± 0.2
Other heart disease (Body CT)	Heart	0.7 ± 0.4	0.2 ± 0.05
Other cardiovascular disease (Body CT)	Heart	1.4 ± 1.6	0.3 ± 0.4
Cerebrovascular disease (Head CT)	Brain	29.5 ± 15	10.5 ± 5.2
Cancer (Effective dose with age related risk factors ICRP 147) [33]	Dose quantity and threshold	Cancer mortality among all patients	Cancer mortality among patients under 60 y
Cancer (body and/or head CT)	Effective dose >100 mSv	1.2(2.5) ^a	0.6(1.2) ^a
Cancer (body and/or head CT)	Effective dose >20 mSv	7.4(15) ^a	3.9(8) ^a

^a Values for cancer incidence, from which mortalities were derived, are given in brackets.

over 100 mSv were lower than the excess mortalities predicted for CVD. However, for lower thresholds of effective dose of, for example, 20 mSv, or if the linear no threshold model were applied, the numbers would increase substantially due to the large number of patients receiving smaller numbers of scans with lower cumulative doses (table 4).

The 2021 UK risk data (table 2) have been used to evaluate the risks for patients undergoing ten CT scans (table 5) using doses based on the UK national DRLs for chest and head CT scans. These results suggest that the excess risk of mortality from CeVD may be an order of magnitude higher than for CVD involving exposure of the heart if indeed the EAR factors accurately reflect a causal link between radiation exposure and CeVD, because of the higher doses to the brain from head CT scans than those to the heart from body CT scans.

Table 5. Excess absolute risks of death from types of CVD from ten CT scans over a patient's lifetime calculated using risk data from Little *et al* [26].

CT scan	Organ irradiated	UK DRL ^a CTDI _{vol} (mGy)	Organ dose from 10 CT scans (mGy)	Disease	Excess risk of mortality
Chest	Heart	8.5 mGy	85 mGy	IHD	1 in 1800
Chest	Heart	8.5 mGy	85 mGy	Other heart disease	1 in 6000
Chest	Heart	8.5 mGy	85 mGy	Other CVD	1 in 3000
Head	Brain	47 mGy	470 mGy	CeVD	1 in 230

^a UKHSA 2023 www.gov.uk/government/publications/diagnostic-radiology-national-diagnostic-reference-levels-ndrls/ndrl.

4. Discussion

Factors for estimating the excess mortality from IHD, other types of heart disease and CVD, and CeVD following radiation exposure derived from a systematic review and meta-analysis of epidemiological data [26] have been used to predict potential numbers of deaths that might result from medical CT scan exposures. The study used dose data for 105 757 patients given CT scans in three hospitals over a period of 5½ years. Results suggest that if the risk factors reported in Little *et al* [26] represent a true causal relationship between CVD mortality and radiation exposure, and any dose threshold was 100–200 mGy or less, then the excess mortality from IHD as a result of radiation exposure could be similar to the excess numbers developing cancer, while the numbers of excess CeVD mortality could be substantially larger.

However, the estimates of mortality risk incorporate considerable uncertainty due to the heterogeneity of many of the studies, residual confounding factors, and interpretational factors [45]. Few of the studies included the influence of possible modifying factors of lifestyle, medical, or environmental variables, particularly the risk factors relating to CVD such as smoking, obesity, diabetes, hypertension and hypercholesterolaemia, although Little *et al* state that the available evidence does not suggest that lifestyle, environmental, or medical risk factors appreciably modify the ERR related to radiation [26] and data from the UK and the Mayak cohort particularly do not indicate these factors significantly bias associations [46]. The risks were averaged over the population, although the data on differences in CVD incidence with age at exposure show that the risks may be lower in younger adults [26] while no substantial differences were reported with sex. This contrasts with studies of the Japanese atomic bomb survivors that suggest risks may decline with age at exposure [15] and the INWORKS study of radiation workers that indicates women have a higher associated ERR than men [20]. Even for the conservative 95% CI lower limit of the estimates presented in tables 1 and 3, estimates for excess mortality remain significant, although this does not take account of any biases that might have influenced derivation of the risk factors. Overall, the risk of CeVD from head CT scans based on these factors is an order of magnitude higher than that for other CVD from body CT scans (tables 4 and 5), as a result of the higher dose to the brain than to the heart (table 3). If the values did represent a true reflection of the excess mortality, then this would have implications for head CT scans.

There are several important considerations in relation to these estimates. In particular, the numbers are critically dependent on any dose threshold that is assigned between 50 mGy and 200 mGy. If a threshold does exist the predicted number of excess deaths could be far lower and dependent on the dose value selected. If the threshold dose to the brain for induction of CeVD was 50 mGy, then the number of excess deaths from the group of patients studied could be about 26, whereas if it was 200 mGy it would be seven and if it was 500 mGy the prediction would be one excess death. Similarly, if the threshold dose to the heart for induction of IHD, other heart disease, and other CVD was 50 mGy, then the number of excess deaths from the group of patients studied could be about seven, if it was 200 mGy it would only be less than one.

Another consideration is that head CT scans give high doses to the brain, but tissues in the neck would receive much lower doses and these may be involved in the effects reported. The carotid arteries may receive significant doses in many of the radiotherapy studies and have been identified as a potential site at particular risk for induction of CeVD at higher doses [12]. The Radimetrics dose system does not give doses to the carotid arteries, but the thyroid lies in a similar region of the neck and this was used as a surrogate. In this study, whereas 9.6% of patients having head CT scans received cumulative doses to the brain over 100 mSv, only 1.3% of patients had thyroid/carotid artery doses over 100 mSv.

It should be noted that this study is based on a review of patient CT scan data over a period of 5½ years and in practice patients are likely to have other investigations as well as more CT scans in the years ahead, so the total doses received over periods of 10, 20 or even 50 years will be much greater, as would be the dose-dependent risk assuming the effect of such doses is cumulative. Studies of the incidence of CeVD among those having head CT scans could shed light on whether the estimated numbers of excess deaths used

in this study are realistic and, perhaps more importantly, whether threshold dose levels for any effects do exist and what these might be [39, 40].

5. Limitations of the study

An important limitation of these estimations of excess CVD mortality is that they are entirely reliant on the validity of the dose-response associations derived from one meta-analysis of epidemiological studies and the studies selected for inclusion in the analysis [26]. The paper by Little *et al* is a comprehensive study and represents the first attempt to estimate radiation dose-effect factors for CVD, based on a systematic review of 93 studies carried out by a large group of experienced epidemiologists. However, it is difficult to assess the whole process used in derivation of risk factors as there are considerable differences in disease endpoints, with both incidence and mortality being used, and a variety of cardiac conditions; IHD, hypertension, heart failure, valve disease and others being used in different studies. Heart disease is more difficult to categorise than cancer and there may also be possible misclassifications of causes of death for example in studies of the Japanese atomic bomb survivors [47, 48]. Moreover, the observational epidemiology studies contributing to the meta-analysis will have been subject to issues of residual confounding factors and interpretational factors which may have impacted on the summary estimates. Although the significant heterogeneity observed between the different studies in the meta-analysis may represent statistical variation, it is worth pointing out some of the anomalies that might be of particular relevance. The INWORKS study of workers exposed at occupational dose levels shows higher risks for cohorts from British Nuclear Fuels and the UK Atomic Weapons Establishment by which the positive association is heavily influenced [20]. Comparison of data for workers at the Mayak plant with workers at Sellafield, UK, showed that whereas the excess risk of mortality from IHD per unit dose reported among Sellafield workers was eight times higher than that for the Mayak workers, the estimated doses in the latter were eight times higher, and such variations between incidence and mortality rates in different studies highlight the current uncertainty in this area [49]. It has also been observed that some markedly high risks among the Chernobyl liquidators are for those working for the shortest periods of time [24, 25]. As stated earlier in this paper Little *et al* [26] reported that risks were higher among lower dose, lower dose rate and fractionated studies than in others involving higher doses. This raises further questions about the shape of the exposure-response association, but of relevance to the current study is that the data from the meta-analysis uses summary estimates based on the higher quality studies only, which covered the dose ranges that can occur from multiple CT scans.

A second limitation of this study relates to the methods used. Doses to organs at risk of for CeVD (brain) and other CVD (heart) were taken from a Radimetrics dose management system, which calculated the doses based on standard phantoms. There will, however, have been differences from the actual organ doses for some patients [50]. Calculations of risk for cancer incidence from effective dose also use age and sex factors based on chest abdomen pelvis CT scans as an approximation for all body scans. The calculations of the risk of mortality from ten body or ten head CT scans use values for the corresponding DRL in terms of CTDI_{vol} as a surrogate for the dose to the heart or brain, respectively. These represent average values for the dose in the region scanned within a standard phantom and although derived from national surveys only approximate to the dose to the respective organ. Finally, the calculations do not take account of the health conditions of individual patients which may shorten their lives, resulting in an overestimation of true risk.

6. Conclusions

This study has shown that if risk factors based on the systematic review and meta-analysis by Little *et al* [26] are both accurate and causal, then the excess number of deaths from CVD and in particular CeVD resulting from radiation exposure due to medical imaging could be similar to, or even much greater than, those from excess cancers. Although the benefits of imaging to patient management should outweigh these relatively small additional risks, they reinforce the need to ensure that all exposures are justified and the radiological protection optimised. This could have particular implications for induction of CeVD as doses to the brain from head CT scans are larger than corresponding doses to the heart from body scans. The predicted mortality risk for CeVD from a head CT scan is an order of magnitude higher than that for CVD from a body CT scan. However, the results are critically dependent on the level set for any threshold dose. Studies of the incidence of CeVD following head CT scans should have the potential to provide information on the risk factors and the level of any dose threshold.

Data availability statement

The data cannot be made publicly available upon publication because they are not available in a format that is sufficiently accessible or reusable by other researchers. The data that support the findings of this study are available upon reasonable request from the authors.

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Conflict of interest

The authors declare that they have no conflict of interests.

Ethical statement

All procedures performed in studies involving human data were in accordance with the ethical standards of the institutional research committee. All data patient medical record numbers were removed from the data files prior to analysis.

ORCID iDs

Colin J Martin  <https://orcid.org/0000-0002-0784-9002>

Michael Barnard  <https://orcid.org/0000-0003-3323-1158>

Frank de Vocht  <https://orcid.org/0000-0003-3631-627X>

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