Radiations et Radiations, Yves Lenoir (juillet 2013)

1. évaluation du nombre de leucémies infantiles de référence

Il n'est pas indiqué ni dans le papier de Kendall, ni dans celui de Pearce.

On le trouve à l'URL suivante des services statistiques britanniques (les meilleures du monde depuis des siècles) :

http://www.cancerresearchuk.org/cancer-info/cancerstats/types/leukaemia/incidence/#age

Voir pièce-jointe avec les courbes à part.

Il en ressort trois éléments significatifs :

a) en 2011, entre 0 et 14 ans l'incidence des leucémies de tout type est de 4,33/100 000

b) le taux de leucémies dans la population reste dans cet ordre de grandeur jusqu'à l'âge de 50 ans. Il croît ensuite sensiblement

c) entre 1980 et 2006, période couverte par l'étude de Pearce, le taux de leucémie corrigé de l'âge a cru notablement, passant de 7,2 à 9,2.

On conjecture que le phénomène est mondial dans les pays développés et que le taux moyen, 4, donné dans le livre japonais pour les années 45 à 75 a depuis sensiblement augmenté, sans doute aussi en grande partie du fait de l'augmentation de l'espérance de vie qui était d'une soixantaine d'années dans les années 40-55. Or l'incidence des leucémies croît sensiblement au delà de 50 ans comme rappelé ci-dessus.

On retient le chiffre de 4,33/100 000 comme incidence de référence, soit 43,3 / million et par an d'enfants entre 0 et 14 ans. On a donc 606,2 cas / million durant les 14 années d'enfance considérées.

2. Calcul de la dose moyenne par cas rajouté

Une dose rajoutée de 1 mGray à cette population de 1 million d'enfants va augmenter l'incidence des leucémies de 3,6%, soit de 21,8 cas pour une dose totale de 1000 Gray x personnes

la dose moyenne rajoutée /cas est donc de 45,8 Gy (1000 / 21,8)

3. Reprise du calcul des doses reçues à Hiroshima (prise en compte de l'efficacité des neutrons)

L'efficacité spécifique des neutrons n'est pas évoquée dans le chapitre des calculs de dose du livre japonais. On suppose donc qu'il n'est pas pris en compte et qu'il faut corriger la dose infligée par les neutrons du facteur CIPR. Cependant le spectre d'énergie des neutrons à Hiroshima est mal connu, sauf à l'hypocentre, à cause du ralentissement dû à la présence de vapeur d'eau dans l'air. Ainsi la proportion — ultra majoritaire de neutrons rapides émis par l'explosion va un peu diminuer avec la distance sans qu'une courbe soit fournie.

On néglige cette diminution (les neutrons thermiques sont bien plus dangereux que les neutrons rapides) et **on va appliquer le facteur d'efficacité CIPR de 5 pour cette catégorie** (Fig B4 p.323 de la version française de la CIPR 103 publiée par l'IRSN).

On reprend alors le tableur dans lequel on a effectué le calcul des doses où l'on tient compte de ce facteur 5 pour la part d'énergie déposée par les neutrons.

Le calcul (voir tableur joint-) donne une dose moyenne de 172,3 rem , soit **1,72 Sv** car il faut passer au Rem et au Sievert puisqu'on a tenu compte du facteur d'efficacité de 5 pour le rayonnement neutronique

4. Suite : reprise du passage correspondant du message préliminaire

Par souci d'exhaustivité et pour garder un caractère conservatif au calcul on va prendre en compte toutes les valeurs de la figure 9.12, de 1945 à 1975.
p 262 et suivante se trouvent les données sur les leucémies. Les données précoces (réparties entre leucémies aigües et chroniques) sont peu détaillées et ne concernent que les survivants à moins de 2000 m de l'hypocentre. J'ai supposé qu'en dessous de 1000 m il n'y avait pas de survivants, ce qui est pratiquement la réalité. La population concernée est donnée p. 399 : 24 253 personnes (sans informations sur la répartition entre adultes et enfants de moins de 14 ans)

Le nombre de leucémies/100 000 personnes et par an au Japon était à l'époque de 4, ce qui donne le risque pour 0 rad. (fig. 9.13 p 264)

Voici le début du tableau déduit du graphique p 263 sur les leucémies précoces des survivants à moins de 2000 m de l'hypocentre (les témoignages montrent qu'elles frappent indistinctement adultes et enfants)

	aigüe	chronique	commentaire
1946	1		**le taux normal puisqu'on a environ 25 000 survivants**
1947	4	1	5 fois le taux normal
1948	12	5	17 fois le taux normal
1949	9	5	14 fois le taux normal
1950	15	8	23 fois le taux normal
1951	18	9	27 fois le taux normal
1952	12	6	
1953	16	8	
1954	10	5	
1955	9	6	
1956	5	3	
1957	9	2	
1958	10	5	
1959	11	2	
1960	7	2	
1961	7	2	
1962	7	4	

1963	8	3
1964	6	1
1965	1	0
1966	9	2
1967	3	2
1968	3	1
1969	0	0
1970	5	2
1971	2	0
1972	7	2
1973	2	1
1974	9	2
1975	4	1

total 220 89 TOTAL : 309
excédent : 279 pour une dose totale de 41 715 Sv x personnes

la dose par cas rajoutée est donc 149,5 Sv, soit 3,26 fois plus que pour les irradiations par scanner (45,8 Gy / cas).

5. Limite de la comparaison et conclusion.

On n'a pas pu trouver dans les données japonaises la distribution par âge des leucémies durant l'intégralité des trente années de l'étude résumée par la figure 9.12 dont les données sont présentées ci-dessus.

Cependant la figure 9.15 p 267 montre une forte disparité entre les cas de leucémies entre fin 1950 et fin 1971, par période de 5 ans, selon les tranches d'âge et trois intervalles d'irradiation. L'absence de données équivalentes pour la période 45-50 anéantit la possibilité d'estimer la dose par cas dans la tranche d'âge 0-14 ans.

En PJ :

- l'article de Kendall & al.
- l'article de Pearce & al.
- l'extrait des statistiques britanniques
- le tableur du calcul de la dose moyenne reçue par la cohorte des survivants à une distance comprise entre 1000 et 2000 m de l'hypocentre

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LEADING ARTICLE

A record-based case–control study of natural background radiation and the incidence of childhood leukaemia and other cancers in Great Britain during 1980–2006

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We conducted a large record-based case–control study testing associations between childhood cancer and natural background radiation. Cases (27 447) born and diagnosed in Great Britain during 1980–2006 and matched cancer-free controls (36 793) were from the National Registry of Childhood Tumours. Radiation exposures were estimated for mother's residence at the child's birth from national databases, using the County District mean for gamma rays, and a predictive map based on domestic measurements grouped by geological boundaries for radon. There was 12% excess relative risk (ERR) (95% CI 3, 22; two-sided $P = 0.01$) of childhood leukaemia per millisievert of cumulative red bone marrow dose from gamma radiation; the analogous association for radon was not significant, ERR 3% (95% CI -4, 11; $P = 0.35$). Associations for other childhood cancers were not significant for either exposure. Excess risk was insensitive to adjustment for measures of socio-economic status. The statistically significant leukaemia risk reported in this reasonably powered study (power $\sim$50%) is consistent with high-dose rate predictions. Substantial bias is unlikely, and we cannot identify mechanisms by which confounding might plausibly account for the association, which we regard as likely to be causal. The study supports the extrapolation of high-dose rate risk models to protracted exposures at natural background exposure levels.

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Keywords: cancer; childhood; radiation; radon; gamma rays

INTRODUCTION

There is abundant evidence that exposure to ionising radiation can cause cancer, particularly from data on the survivors of the Japanese atomic bombings and other groups receiving moderate or high doses at high-dose rates.[1] Ionising radiation is one of the few established exogenous risk factors for childhood leukaemia,[2] but again this evidence derives mainly from groups exposed to moderate or high doses and high-dose rates.[1]

A long-standing question is whether cancer risks detected in moderate/high dose and high-dose rate studies can be extrapolated to low doses or low-dose rates (which may be taken to be, respectively, <100 and <5 mGy/h of sparsely ionising radiation[3,4]). For example, some claim thresholds in the dose response for cancer, or even beneficial effects at low doses,[5] although the basis of this claim has been challenged.[6] Calculations, based on risk models derived from the atomic bomb survivors[7,8] suggest that about 15% of childhood leukaemia incidence in Great Britain is attributable to ubiquitous exposure to natural background radiation, although the uncertainties associated with this estimate are substantial. Many epidemiological studies have examined the putative association between childhood leukaemia and exposure to radiation from natural sources.[9–14] Although positive associations have been reported from some studies,[9–14] their interpretation has been problematical due to study deficiencies, for example participation bias, liability to 'ecological bias', or their being severely underpowered.[15]

A recent example of an investigation of the possible effects of natural background radiation upon the risk of childhood cancer is the UK Childhood Cancer Study (UKCCS), a large interview-based case–control study of childhood cancer throughout Great Britain during the early 1990s.[16] It was set up to examine five possible causitive factors, one of which was exposure to ionising radiation *in utero* or after birth, and the findings of analyses of exposure to gamma rays[13] and to radon[12] have been published. No association between gamma-ray exposure and the risk of any of the main types of childhood cancer was found, but as our calculations indicate[15] and as the UKCCS authors surmised, the gamma-ray branch of the study was underpowered. A negative association between the level of radon exposure and risk of childhood cancer (with similar patterns for each diagnostic grouping) was found, but our calculations indicate that the radon branch of the study had even less statistical power than the gamma-ray part. Moreover, the UKCCS suffered from incomplete and differential participation and the authors regarded this finding as artefactual, concluding that socio-economic differences between cases and controls, and between first choice controls and those actually interviewed, probably accounted for the observations.

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We report here a record-based case–control study investigating the effects of natural background radiation exposure on childhood leukaemia and other cancers, which is far larger than previous case–control studies. Our study design is similar to that of a record-based case–control study recently conducted in Denmark,[14] but it considers gamma rays as well as radon and is an order of magnitude larger, and therefore of much greater power.

MATERIALS AND METHODS

A fuller description of Materials and Methods is given in Supplementary Appendix 1.

The study population was children born and diagnosed with cancer or nonmalignant brain tumour in Great Britain between 1980 and 2006, recorded on the National Registry of Childhood Tumours,[17] an essentially complete population-based registry of cancers diagnosed in Great Britain before the fifteenth birthday. Birth registration details were available for almost all births in Britain. In all, 1 or 2 controls matched on sex and date of birth (to within 6 months) had already been selected from the same birth register as the case; 27 447 cases and 36 793 controls resulted.

Addresses of mothers at the time of birth of their child were assigned grid references using the ADDRESS-POINT system or, if this was not possible (about 4% of records), the less precise Code-Point.[18,19]

Ionising radiation exposure of cases and controls was estimated from the place of residence of the mother at the child's birth. Data on indoor absorbed dose rates from gamma rays with the directly ionising component of cosmic rays came from the National Survey of natural background radiation based on measurements made in 2283 houses in Great Britain;[20] for brevity we denote these as 'gamma-ray dose'. For this study we used mean gamma-ray dose rates in 459 English County Districts and comparable administrative areas in Wales and Scotland.[21]

Two sources of radon concentration estimates in the homes of study participants were used:

1. Mean exposures in County Districts, from the National Survey;[20] the radon analogues of the gamma-ray estimates.
2. A predictive radon map developed by the Health Protection Agency and British Geological Survey (HPA/BGS), which was based on the results of about 400 000 measurements of radon concentrations in homes grouped by grid squares and boundaries between different geological units.[22–24]

Our main analyses use gamma--ray-absorbed dose rate and radon concentration integrated from birth to diagnosis, approximating exposure from conception to 9 months before diagnosis. We also investigate other minimum latent periods of 0, 12 and 24 months, defined as the periods from birth to diagnosis: plus 9 months (approximating conception to diagnosis), minus 3 months (approximating conception to 12 months before diagnosis) and minus 15 months (approximating conception to 24 months before diagnosis).

The measured dosimetric quantities are proportional to tissue doses from the two components separately. To compare the risk estimates from this study with published estimates, it is necessary to calculate doses to the target tissue in question, and if the risks from gamma rays and radon are to be examined together doses from both sources must be calculated on the same basis. This could be done only for leukaemia, for which the relevant quantity is the red bone marrow (RBM) equivalent dose.

Socio-economic status (SES) is known to influence rates of childhood cancer, particularly leukaemia.[25] The principal measure of SES considered in the analysis was the Carstairs deprivation index, based upon the census ward in which the mother was living during the child's birth;[26] the main analysis included quintiles of the Carstairs index. Carstairs scores were available for all cases and controls in the study. An alternative measure of SES was the social class of the father, derived from his occupation as stated on the child's birth record. The occupational description was coded and social class category derived using classifications used by the Office of Population Censuses and Surveys, now the Office for National Statistics.[27,28] Paternal occupational social class derived in this way was available for about 90% of cases and controls and was based on self-reported data, which were sometimes ambiguous, although any inaccuracies should not be differential between cases and controls; analyses were restricted to the 85% of matched sets where both case and control(s) were assigned a value.

The analysis used conditional logistic regression (within matched case-control sets)[29] implemented in STATA.[30] In the main analysis a log-linear logistic model was fitted via maximum likelihood,[29] in which $RR_i = \exp[\alpha_1 D_i + \alpha_2 S_i]$ (D_i = cumulative lagged dose, S_i = Carstairs score). Confidence intervals (CI) were Wald-based, calculated using the Fisher information.[31] The *P*-values presented were calculated from likelihood ratio tests, and were two-sided.

RESULTS

Table 1 gives a breakdown of the number of cases and controls by age at diagnosis. Tables S1 and S2 give the breakdown of cases and controls by, respectively, calendar year of birth and diagnosis, and age at diagnosis. When comparisons are made between cases and their matched controls the mean absolute difference (that is, regardless of whether positive or negative) between the dates of birth is 13.5 days, with 95% being within 5 weeks. However, controls were born both before and after their matching case and the mean difference is less than 1 day.

Further details, including information on migration of cases (that is, from the birth address by the time of diagnosis) are presented in Tables S3–S5; equivalent migration information for controls is not available. For all childhood cancers combined, address at diagnosis was the same as address at birth for about 50% of cases and a further 20% had moved <2 km. Of those diagnosed in the first years of life, 96% still resided in the County District (CD) in which they were born, whereas for those diagnosed at age 14 years this figure dropped to 75%; over the age range 0–14 years, 83% had not moved CD before diagnosis. Clearly, the proportion of cases that had moved by the time of diagnosis increases with age at diagnosis, and thus varies somewhat with cancer type (Tables S3, S4) being rather higher for lymphomas (mean age at diagnosis 8.9 years). The mean separation between maternal residence at birth of cases and matched controls is about 11 km.

Table S6 gives a breakdown of the study population by Carstairs quintile and by father's social class as deduced from his occupation as given on the birth certificate. The proportion of cases and that of controls in the various categories were similar.

Estimates of indoor gamma-ray dose rate and radon concentration are available for all cases and controls. The approximate matching of cases and controls on place of birth results in a proportion of case–control sets having the same estimated radiation exposure. This arises more frequently for the gamma-ray dose rate, which is determined by the CD of maternal residence at the child's birth. The number of cases with a gamma-ray dose rate different from their control(s) was 14 308 (52% of all cases), whereas over 95% of cases and controls were assigned different radon concentrations. If gamma-ray dose rates or radon concentrations are the same for cases and controls then cumulative doses will differ only because of differences in the at-risk periods, although typically this results in smaller differences in cumulative doses than from different dose rates or concentrations.

Gamma-ray dose rates were distributed approximately normally with a mean for controls of 94.7 (SD 15.6; range 38.1–159.7) nGy/h, whereas radon concentrations were approximately log-normally distributed with a geometric mean of 16.4 and a geometric SD of 2.0 (arithmetic mean 21.3 and SD 22.6; range 1.2–692) Bq/m^3 for controls. The observation of log-normal distributions of radon concentrations is a common one.[32,33] However, the dose accumulated between birth and diagnosis is of greater aetiological relevance than dose rates or activity concentrations, and this depends on the age at diagnosis for the disease in question. Distributions of gamma-ray doses by attained age for cases and controls are given in Table S7 for the disease groupings

Table 1. Distribution of numbers of cases and controls by grouped age at diagnosis and diagnostic grouping

Disease grouping	*ICCC3 codes*	*Age group (years)*					*Mean age (years)*
		<1	*1–4*	*5–9*	*10–14*	*0–14*	
Cases							
Lymphoid leukaemia	11	337	4182	1904	844	7267	5.1
Acute myeloid leukaemia	12	237	521	288	270	1316	5.2
Other leukaemias	13–15	115	190	91	79	475	4.7
Total leukaemia	11–15	689	4893	2283	1193	9058	5.1
Hodgkin lymphoma	21	0	82	275	582	939	10.6
Non-Hodgkin lymphoma except Burkitt lymphoma	22	14	273	371	325	983	7.8
All lymphomas	21–25	23	468	803	1025	2319	8.9
Brain and CNS tumours	31–36	584	2351	2231	1419	6585	6.3
Other malignant tumours	41–122	2015	4101	1638	1731	9485	4.8
All cancer except leukaemia	21–122	2622	6920	4672	4175	18 389	5.8
Total childhood cancer	11–122	3311	11 813	6955	5368	27 447	5.6
Males: total childhood cancer	11–122	1760	6447	3953	2945	15 105	5.6
Females: total childhood cancer	11–122	1551	5366	3002	2423	12 342	5.5
Controls							
Lymphoid leukaemia	11	428	5339	2561	1243	9571	5.2
Acute myeloid leukaemia	12	306	649	393	389	1737	5.5
Other leukaemias	13–15	148	226	117	113	604	4.9
Total leukaemia	11–15	882	6214	3071	1745	11 912	5.3
Hodgkin lymphoma	21	0	113	385	890	1388	10.7
Non-Hodgkin lymphoma except Burkitt lymphoma	22	18	333	476	475	1302	8.1
All lymphomas	21–25	29	603	1096	1546	3274	9.2
Brain and CNS tumours	31–36	743	3097	3033	2124	8997	6.5
Other malignant tumours	41–122	2602	5186	2210	2612	12 610	5.1
All cancer except leukaemia	21–122	3374	8886	6339	6282	24 881	6.1
Total childhood cancer	11–122	4256	15 100	9410	8027	36 793	5.8

Abbreviation: CNS, central nervous system.

all leukaemias and in Table S8 for all other cancers. As expected, there is a strong tendency for higher doses to have been accrued by those diagnosed at older ages. Differences between case and control distributions are not obvious by inspection of these data and a comparative analysis as described in Supplementary Appendix 1 is required; the resulting variation in relative risk (RR) with cumulative dose is presented below.

Table S9 and S10 give the variation with Carstairs quintile of the cumulative gamma-ray dose and radon exposure for cases and controls; for radon there is a clear tendency for more affluent groups to have higher exposures whereas no such trend is seen for gamma rays.

The correlation between radon concentration and gamma-ray dose rate is 0.09 ($P<0.001$); this is highly statistically significant because of the large numbers involved, but the correlation is not strong.

As shown in Table S11 the mean cumulative RBM equivalent dose from gamma rays and radon combined over the period from birth to diagnosis for the first controls is 4.0 mSv with a range from 0 (for those diagnosed at birth) up to about 31 mSv. On average, radon contributed about 10% of the RBM equivalent dose, although contributions were very variable with a range 1–80%.

Table 2 gives results for the main trend analysis using gamma-ray and radon exposures integrated from birth to diagnosis, with Carstairs quintiles included in the model. Significantly elevated excess relative risks (ERRs) were found for cumulative gamma-ray doses for total leukaemias (ICCC3 codes 11–15) (9% ERR per mGy; 95% CI 2, 17; $P=0.01$), lymphoid leukaemia (10% ERR per mGy; 95% CI 2, 19; $P=0.01$), and all cancers (3% ERR per mGy; 95% CI 0, 7; $P=0.04$). Lymphoid leukaemia is the largest component of the all leukaemias group (7267/9058 cases) and leukaemia makes up about one-third of all childhood cancers (9058/27 447 cases), and so these findings are not independent. There were no significantly raised risks of other types of childhood cancer. For the grouping of all childhood cancers excluding leukaemia the RR was raised (1.02), but the difference from 1.0 was far from being statistically significant. The radon RRs were elevated for several disease groupings, but none was close to statistical significance. Table 2 includes disease groupings of interest to the UK Committee On Medical Aspects of Radiation in the Environment.[34,35] The RRs per Carstairs quintile show the expected higher incidence of leukaemia in more affluent groups.[36]

The Figure 1 shows smoothed RR by cumulative gamma-ray dose group with fitted trend lines for all leukaemias combined and for all other cancers. There was a progressive increase in leukaemia ERR with dose: the excess was always positive, and statistically significant for doses >4.1 mGy. Although there were substantial uncertainties, the pattern for other cancers was somewhat different, with the ERR slightly and nonsignificantly negative up to about 12 mGy, above which there was a progressive non-significant increase in risk; because of the much greater leverage of the high-dose points this upturn at comparatively high dose resulted in an overall (nonsignificant) positive trend.

Table 3 gives results for leukaemia in terms of RR per mSv cumulative RBM equivalent dose. There was a 12% ERR (95% CI 3, 22; $P=0.01$) of total childhood leukaemia per mSv RBM dose from natural gamma radiation. Analyses were also carried out using estimates of combined (radon plus gamma ray) equivalent dose to the RBM. The results of this analysis were generally similar to the gamma ray results: for example, for all leukaemias 7% ERR per mSv (95% CI 1, 13; $P=0.02$).

Very similar results to the main analysis were obtained if alternative measures of SES rather than Carstairs quintile were used (Tables S12, S13), or if there was no modification by any measure of SES (Table S14); adjustment for SES appears to make little difference to the magnitude of the risk or its degree of statistical significance. For the analysis using social class based on (self-reported) father's occupation, the *P*-values were somewhat larger; this analysis included only 85% of the total

Table 2. Trend analysis by childhood cancer diagnostic grouping

ICCC3 codes	*Diagnostic grouping*	*Number of cases*	*Number of controls*	*Relative risk*											
				Radon				*Gamma*				*Quintiles of carstairs index*			
				RR[a]	*95% CI*		P	*RR*[b]	*95% CI*		P	*RR*[c]	*95% CI*		P
11	Lymphoid leukaemia	7267	9571	1.24	0.94	1.64	0.13	**1.10**	1.02	1.19	0.01	**0.96**	0.93	0.98	0.001
12	Acute myeloid leukaemia	1316	1737	0.72	0.37	1.40	0.34	1.04	0.89	1.21	0.60	0.96	0.90	1.02	0.22
13–15	Other leukaemias	475	604	1.04	0.41	2.61	0.94	1.19	0.90	1.57	0.23	1.10	0.99	1.22	0.07
11–15	Total leukaemia	9058	11 912	1.12	0.88	1.43	0.35	**1.09**	1.02	1.17	0.01	**0.96**	0.94	0.99	0.002
21	Hodgkin lymphoma	939	1388	1.07	0.67	1.70	0.79	1.04	0.93	1.16	0.53	1.03	0.95	1.11	0.47
22	NHL	983	1302	1.29	0.69	2.39	0.43	1.04	0.89	1.21	0.61	1.07	1.00	1.16	0.06
21–25	Total lymphoma	2319	3274	1.14	0.80	1.62	0.47	1.01	0.93	1.09	0.86	1.04	1.00	1.09	0.08
11, 22	Lymphoid leukaemia + NHL	8250	10 873	1.24	0.96	1.60	0.10	**1.09**	1.02	1.16	0.02	**0.97**	0.95	0.99	0.01
11–15, 22	Total leukaemia + NHL	10 041	13 214	1.14	0.91	1.43	0.27	**1.08**	1.02	1.15	0.01	**0.97**	0.95	1.00	0.02
31–36	Brain and CNS tumours	6585	8997	1.15	0.88	1.50	0.32	1.02	0.96	1.09	0.49	0.98	0.95	1.01	0.14
41–122	Other malignant tumours	9485	12 610	0.99	0.80	1.23	0.95	1.02	0.96	1.08	0.57	0.98	0.96	1.01	0.19
21–122	All cancers except leukaemia	18 389	24 881	1.06	0.91	1.24	0.43	1.02	0.98	1.06	0.38	0.99	0.97	1.01	0.21
11–122	Total childhood cancer	27 447	36 793	1.08	0.95	1.23	0.25	**1.03**	1.00	1.07	0.04	**0.98**	0.97	0.99	0.01

Abbreviations: CI, confidence interval; CNS, central nervous system; NHL, non-Hodgkin lymphoma; RR, relative risk. Model includes cumulative radon exposure, cumulative gamma-ray exposure and quintiles of Carstairs index of deprivation. Exposure period taken as birth to diagnosis. RRs in bold are significantly different from 1.00 ($P<0.05$), RRs in bold and underlined are significantly different from 1 ($P<0.01$). [a]RR for each 10^3 Bq/m^{3}years increase in cumulative radon exposure. [b]RR for each mGy increase in cumulative gamma-ray exposure. [c]RR for each quintile increase on the Carstairs index of deprivation.

number of cases. Little difference resulted from analyses in which radon was excluded from the model (Table S15), or if attention was restricted to those case–control sets that had the most precise GridSquare/AP radon estimates (Table S16; this analysis included about 83% of the total number of cases and controls), or in which County District averages were used in place of HPA/BGS estimates for radon concentrations (Table S17).

An analysis was also undertaken considering radon concentration or gamma-ray dose rate as a measure of radiation exposure rather than cumulative exposure (Table S18). Most of the RRs were above unity, but none reached statistical significance under a two-sided test.

RRs for males were generally similar to those for females (for example, for total leukaemia 1.10 and 1.08 per mGy increase in cumulative gamma-ray exposure, respectively) (Table S19). For gamma rays, tests for heterogeneity between the sexes were not significant for any disease grouping listed.

Table S20 shows RR for leukaemia and for lymphoid leukaemia by single year of age at diagnosis. There is little pattern for radon exposure. The gamma-ray results show some pattern with attained age, but this should not be overinterpreted and formal tests for heterogeneity are not significant ($P>0.2$).

The main analysis uses exposure integrated from the date of birth to the date of diagnosis, roughly equivalent to the period from conception to diagnosis minus a latent period of 9 months. Other minimum latent periods (0, 12 and 24 months) were investigated, but no substantial changes were seen in RR, or in levels of statistical significance (Table S21; for latent periods of 12 and 24 months the analyses include about 96 and 85% of the total number of records, respectively).

Table S22 shows the results of an analysis analogous to the main analysis, but excluding second controls. This included 27 377 cases and the same number of controls, that is almost all the cases, but only about 74% of the total number of controls. The number of cases is lower than that in the main analysis because a few were matched to a second control only.

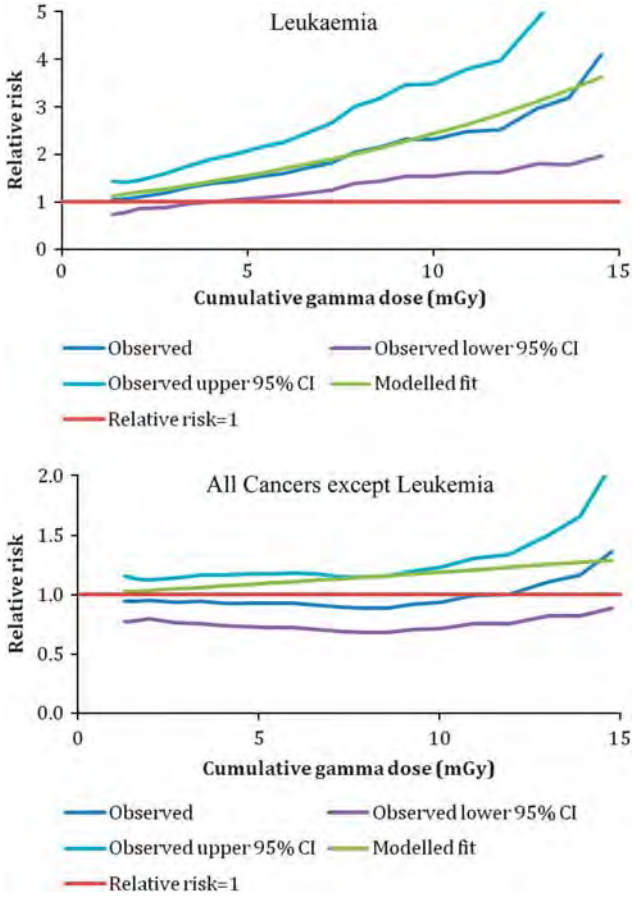

Figure 1. Observed (and 95% CI) and fitted relative risk for leukaemia (panel 1) and for all other cancers (panel 2) by cumulative gamma ray dose.

DISCUSSION

Our most striking finding was the statistically significant positive trend in the risk of childhood leukaemia with increasing dose of naturally occurring gamma radiation, of a magnitude comparable to that predicted by previous calculations based on standard risk and dose models. Excess risks were largely

Table 3. Trend analysis for leukaemia and cumulative RBM equivalent doses from radon and gamma rays, separately and combined

	Relative risk per mSv for model containing gamma ray and radon RBM doses separately								*Relative risk per mSv for model including combined RBM doses from gamma rays and radon*			
	Radon				*Gamma*				*Gamma and radon*			
	RR[a]	*95% CI*		P	*RR*[b]	*95% CI*		P	*RR*[c]	*95% CI*		P
Lymphoid leukaemia	1.07	0.98	1.16	0.13	**1.13**	1.02	1.24	0.01	**1.09**	1.03	1.16	0.01
Acute myeloid leukaemia	0.91	0.75	1.10	0.34	1.05	0.87	1.28	0.60	0.98	0.86	1.11	0.74
Other leukaemias	1.01	0.77	1.33	0.94	1.25	0.87	1.78	0.23	1.09	0.89	1.34	0.40
Total leukaemia	1.03	0.96	1.11	0.35	**1.12**	1.03	1.22	0.01	**1.07**	1.01	1.13	0.02

Abbreviations: CI, confidence interval; RBM, red bone marrow; RR, relative risk. Model includes cumulative RBM equivalent dose (mSv) and quintiles of Carstairs index of deprivation. Exposure period taken as from birth to diagnosis. RRs in bold are significantly different from 1.00 ($P<0.05$). RRs in bold and underlined are significantly different from 1.00 ($P<0.01$). [a]RR for each mSv increase in RBM equivalent dose from radon. [b]RR for each mSv increase in RBM equivalent dose from gamma rays. [c]RR for each mSv increase in RBM equivalent dose from gamma rays and radon combined.

insensitive to adjustment for different measures of SES, to different estimates of radon exposure or to different assumed minimum latent periods.

The 95% CI on our leukaemia risk estimate is wide, but it is, nonetheless, instructive to compare the leukaemia risk that we observed with estimates derived from the Japanese atomic bomb survivors, who were exposed to higher acutely delivered doses. Table S23 shows that the cumulative leukaemia incidence risk at age 15 years predicted by the relative risk model derived here (and assuming 1 mSv per year to the RBM) is somewhat higher, at about 0.019%, than that predicted by the UNSCEAR 2006 models,[1] 0.010%, and by the BEIR VII models,[37] 0.007%. At attained ages greater than 4 years derived risks were higher than those predicted by both the UNSCEAR[1] and BEIR VII models[37]; at younger ages our derived risks were below those of UNSCEAR but higher than those of BEIR VII. However, given the substantial uncertainties in all estimates there is reasonable agreement between the risk predictions. These risks should be compared with the cumulative background risk of leukaemia incidence to age 15 years, which is around 0.06%.[17]

The results of the analysis using radon exposure rate or gamma-ray dose rate (Table S18) throw light on effects of exposures *in utero*, as the dose received during any antenatal period will be proportional to the radon concentration or gamma-ray dose rate. The dose received *in utero* will generally be smaller than the dose accumulated to diagnosis because the latter is usually incurred over a longer period. The results suggest that for leukaemia cumulative exposure (including the postnatal period) is the more important measure of exposure. The risk we derive in terms of cumulative RBM dose, 12% ERR per mSv (95% CI 3, 22), is similar to that obtained from the largest obstetric X-ray exposure study, 5.1% ERR per mGy (95% CI 2.8, 7.6).[38]

For types of childhood cancer other than leukaemia, no gamma-ray risk was elevated to an extent that approaches statistical significance (Table 2). We conclude that such risks, if they exist, are less than those of leukaemia. This is consistent with what is known about radiation-related risks for the typical cancers of childhood other than leukaemia: although the risks from antenatal exposure are similar to that for leukaemia, the risks from postnatal exposure are likely to be materially lower.[1,38] The power of our study to estimate the predicted risk of these other cancers was therefore markedly lower than that for estimating leukaemia risk.

A weaker (and statistically non-significant) association between childhood leukaemia and radon exposure was found in our study. This was what might be expected given the much lower assessed RBM doses from this source.[15] Our results were compatible with an association between childhood leukaemia and radon exposure of about the size that would be suggested by standard risk and dose calculations, and also with the results of studies reporting a positive association, in particular those of a recent case–control study of leukaemia and other childhood cancers in relation to radon exposure in Denmark.[39] However, the CIs on our RRs were wide enough for the results also to be consistent with no effect. For childhood cancers other than leukaemia, no significant associations with radon exposure were found.

A number of other case–control studies have investigated associations between natural background radiation and childhood cancer.[3,39,40] No consistent association has been found. However, power calculations[15] suggest that all previous case–control studies were underpowered (as were, to a lesser extent, geographical correlation studies). A power calculation using the methods of Little *et al*.[15] indicates that, after making allowance for cases and controls being assigned the same gamma-ray exposure rate, this study still has a power of about 50% to detect the predicted association between gamma-ray exposure and childhood leukaemia.

The study reported here considers only the gamma-ray and radon components of dose from natural background radiation; it does not assess the impact of the dose received from the ingestion of naturally occurring radionuclides in food and drink. Other sources of radiation exposure, in particular exposures incurred for medical reasons, are also omitted from our dose estimates, as it is not possible to assess these on an individual basis. It would not be expected that doses from these other sources of radiation would be significantly correlated with those from the exposures that are included, so their omission should not lead to the introduction of bias.

This study has considerable advantages: it is of exceptional size and the inclusion of almost all records from an essentially complete population-based register of cases (with previously matched controls) means that participation bias, so often a problem for case–control studies, does not arise. Indeed, it is difficult to envisage how a study encompassing the 10–20 000 study subjects required to achieve enough statistical power to stand a reasonable chance of detecting the predicted effect of natural background radiation upon the risk of childhood leukaemia could be other than record-based.

However, the absence of individual contact in the study carries with it the unavoidable disadvantage that radiation levels and SES variables have been estimated as the mean for an area including the maternal residence at the child's birth rather than being directly assessed for the homes of those concerned; in the case of the radon estimates, the areas were small, but for gamma rays they were County Districts. Inevitably, this leads to uncertainty in the exposure estimates. Further, the degree of geographical matching on the place of birth registration of cases and controls resulted in a proportion of radiation exposure rate estimates for the two being the same; this arose rarely for radon estimates, but approaching half of the cases had the same gamma-ray dose rate

estimate as their controls. As the exposure period for controls was from birth to the date of diagnosis of the corresponding case, when a matched control is assigned the same dose rate as the case their cumulative doses will differ only because of small differences in the at-risk period arising from differences of up to 6 months in the dates of birth. This reduced the power of the study, but would not be expected to introduce bias. In this respect, it is reassuring that the effect of using higher resolution, rather than CD-averaged, radon measurements was to increase the RR for most endpoints, particularly for lymphoid leukaemia and all leukaemia (Tables 2, Table S17), suggesting that if there is any bias in the risks resulting from the use of CD-averaged gamma-ray measurements and consequent loss of case–control sets, it is towards the null. As indicated above, analyses using father's social class derived from his occupation as given on the birth certificate show very similar values of risk (Table S12) to those based on Carstairs index, if with slightly larger *P*-values; the larger *P*-values may arise, at least in part, because of the somewhat fewer records used.

A further consequence of the study design is that full residential histories for cases and controls were not available; address at birth was known for both cases and controls, but address at diagnosis only for cases. Consequently, cumulative radiation exposures were estimated on the basis of assessed exposure at the residential address at birth. About half the cases in this study had not moved between birth and diagnosis. This is broadly consistent with the findings of the UKCCS for controls[16] (no data for cases were given): 7629 families had lived at a total of 12 757 addresses (limited to addresses occupied for at least 6 months) so the mean number of addresses occupied was about 1.67, consistent with around half the controls not having moved, most of the remainder having moved once and a small proportion more often. The effect of study participants moving from the birth address will be to weaken the power of the study, but as it will introduce a Berkson-type error into the true dose, it would not be expected to introduce bias.[41] We note that the UKCCS set out to collect residential histories and conduct measurements at each address,[16] but finally analysed exposure data for the gamma-ray dose rate[13] and radon concentration[12] at a single address, that occupied at diagnosis. As we discuss in Supplementary Appendix 2, the sampling strategy for the gamma-ray survey is unlikely to appreciably bias results, and it seems unlikely that measurement error will result in significant dose-response bias.

The study has no information on potential confounders other than measures of SES, and the causes of the majority of cases of childhood leukaemia remain unknown. However, evidence is growing that infection has a major role in the aetiology of childhood leukaemia,[42,43] although it seems unlikely that such infections would be associated with higher naturally occurring gamma-ray exposures.

Ages at diagnosis are very similar for cases and their matched controls. However, if the distributions of these ages are considered for all cases and all controls then, on average, the controls are somewhat older than the cases (Table 1). This is due to the influence of the second controls (Table S2) and arises because cases born in, for example, 1990 can have a second control only if they are diagnosed at an age of 10 years or above. This will not affect the analysis, which is based on matched case–control sets. Nevertheless, we undertook a subsidiary analysis excluding second controls and this gave results very similar to the main analysis (Table S22), although the *P*-value for lymphoid leukaemia and gamma-ray dose is now below 0.01.

CONCLUSIONS

Many studies have tested for associations between childhood leukaemia and natural background radiation, but these generally lacked statistical power,[15] and many have suffered from other deficiencies. The present study is one of the few to have reasonable power of detecting the predicted risk of childhood leukaemia associated with natural background gamma-ray exposure. The statistically significant excess risk that is reported is around the level that would be predicted by recent analyses of moderate/high dose and high-dose rate data, and the study therefore supports the extrapolation of such risk models to protracted exposure to low doses or low dose rates. We found no strong evidence of excess risk of any other childhood cancer in relation to naturally occurring gamma radiation, nor for any childhood cancer with radon exposure. However, the statistical power of our study in relation to these other endpoints was low.

The possibility of confounding by some unidentified factor can never be entirely disproved, and is of particular concern when dealing, as here, with small RRs. However, we were unable to identify any mechanism whereby such confounding might plausibly account for the observed magnitude and specificity of effect in this study. Moreover, the study was of reasonable power and the findings conformed to prior predictions. Confirmation of our findings by similar studies in other countries where appropriately large cancer registration and dose databases are available would clearly be desirable, particularly in regions where natural background radiation levels are higher and more variable than in Great Britain.

We conclude that the significantly elevated RRs found in this study are likely to reflect a real effect on childhood leukaemia risk of exposure to natural background gamma radiation. Our study therefore provides support to the assumption that models of radiation-induced leukaemia risk derived from data observed at moderate and high doses and high dose rates may be appropriately applied to protracted RBM gamma-ray doses of about 1 mGy per annum. This is relevant to practical radiological protection in a number of situations, for example radiodiagnostic-imaging procedures.[44] The results of the study contradict the idea that there are no adverse radiation effects, or might even be beneficial effects, at these very low doses and dose-rates.

CONFLICT OF INTEREST

Dr Wakeford undertakes work as a paid consultant. All other authors declare no conflict of interest.

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Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study

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Summary

Background Although CT scans are very useful clinically, potential cancer risks exist from associated ionising radiation, in particular for children who are more radiosensitive than adults. We aimed to assess the excess risk of leukaemia and brain tumours after CT scans in a cohort of children and young adults.

Methods In our retrospective cohort study, we included patients without previous cancer diagnoses who were first examined with CT in National Health Service (NHS) centres in England, Wales, or Scotland (Great Britain) between 1985 and 2002, when they were younger than 22 years of age. We obtained data for cancer incidence, mortality, and loss to follow-up from the NHS Central Registry from Jan 1, 1985, to Dec 31, 2008. We estimated absorbed brain and red bone marrow doses per CT scan in mGy and assessed excess incidence of leukaemia and brain tumours cancer with Poisson relative risk models. To avoid inclusion of CT scans related to cancer diagnosis, follow-up for leukaemia began 2 years after the first CT and for brain tumours 5 years after the first CT.

Findings During follow-up, 74 of 178 604 patients were diagnosed with leukaemia and 135 of 176 587 patients were diagnosed with brain tumours. We noted a positive association between radiation dose from CT scans and leukaemia (excess relative risk [ERR] per mGy 0·036, 95% CI 0·005–0·120; p=0·0097) and brain tumours (0·023, 0·010–0·049; p<0·0001). Compared with patients who received a dose of less than 5 mGy, the relative risk of leukaemia for patients who received a cumulative dose of at least 30 mGy (mean dose 51·13 mGy) was 3·18 (95% CI 1·46–6·94) and the relative risk of brain cancer for patients who received a cumulative dose of 50–74 mGy (mean dose 60·42 mGy) was 2·82 (1·33–6·03).

Interpretation Use of CT scans in children to deliver cumulative doses of about 50 mGy might almost triple the risk of leukaemia and doses of about 60 mGy might triple the risk of brain cancer. Because these cancers are relatively rare, the cumulative absolute risks are small: in the 10 years after the first scan for patients younger than 10 years, one excess case of leukaemia and one excess case of brain tumour per 10 000 head CT scans is estimated to occur. Nevertheless, although clinical benefits should outweigh the small absolute risks, radiation doses from CT scans ought to be kept as low as possible and alternative procedures, which do not involve ionising radiation, should be considered if appropriate.

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Introduction

CT imaging is a valuable diagnostic technique, and new clinical applications continue to be identified. As a result, the rates of CT use have increased rapidly in the USA and elsewhere, particularly in the past 10 years.[1] Although the immediate benefit to the individual patient can be substantial, the relatively high radiation doses associated with CT compared with conventional radiography have raised health concerns.[2–8] Potential increases in future cancer risk, attributable to the rapid expansion in CT use have been estimated with risk projection models, which are derived mainly from studies of survivors of the atomic bombs in Japan.[3,6,8] These studies have been criticised because of concerns about how applicable the findings from this group are to the relatively low doses of radiation exposure from CT scans and to non-Japanese populations. Some investigators claim that there are no risks, or even beneficial effects, associated with low-dose radiation.[9] No direct studies of cancer risk in patients who have undergone CT scans have been undertaken to date.

We did a study to directly assess the question of whether cancer risks are increased after CT scans in childhood and young adulthood. Here we assess the risks of leukaemia and brain tumours because they are the endpoints of greatest concern as the red bone marrow and brain are highly radiosensitive tissues, especially in childhood.[10] Furthermore, these tissues are also some of the most highly exposed from childhood CT scans,[11] and leukaemias and brain tumours are the most common childhood cancers.

Methods

Patients and study design

In our observational retrospective cohort study, we included patients without previous malignant disease who were first examined with CT between 1985 and

2002 when they were younger than 22 years of age. Patients were scanned at hospitals within 81 National Health Service (NHS) regional services in Great Britain (England, Wales, and Scotland). We assembled the cohort with historical data from electronic radiology information systems (RIS) from the participating hospitals or, for a small number of patients in five hospitals, from paper or film records. Retrieved data included date of birth, details of the CT examinations, sex, post code, and body parts scanned. We used the patient's identifiers to identify patients having scans in more than one hospital.

See Online for appendix

This study was approved by the Newcastle and North Tyneside Local Research Ethics Committee (Newcastle upon Tyne, UK) and by the UK National Information Governance Board, exempting the study from requiring individual patient's consent.

Procedures

Linkage with the NHS Central Registry (NHSCR) provided cancer incidence, mortality and loss-to-follow-up data (eg, notified emigrations) from Jan 1, 1985, to Dec 31, 2008. The NHSCR holds computerised records of everyone registered with an NHS general practitioner in Great Britain (most residents). It is continuously updated with births, deaths, marriages, name changes, and movements of patients, and records cancer incidence from the regional cancer registries. We excluded patients from the cohort who had an exit date of less than 2 years in the case of leukaemia or less than 5 years for brain tumours after the first scan to reduce the possibility of inclusion of patients who had CT scans because a cancer was suspected. We also excluded patients who could not be traced by NHSCR, and those who had missing information or inaccurate information on the date of CT scan.

The appendix shows details of the morphology codes used to define leukaemias. We examined four non-mutually exclusive leukaemia subgroups, which were acute lymphoblastic leukaemia, acute myeloid leukaemia, myelodysplastic syndromes, and leukaemia excluding myelodysplastic syndrome. We defined malignant and benign brain tumours with WHO's International Classification of Diseases for Oncology, 3rd edition topographic codes for meninges, brain, olfactory, and cranial nerves, and other parts of the CNS (spinal tumours were excluded). We examined two subgroups: glioma and meningioma plus schwannoma (appendix).

CT scans deliver very non-uniform radiation doses across the body. Therefore, we assessed the risk of leukaemia and brain tumours in relation to estimated radiation absorbed doses in the appropriate organ (red bone marrow or brain), which were estimated for each type of scan without knowledge of case status. The absorbed dose from a CT scan depends on factors including age, sex, examination type, and year of scan. Data for the machine settings that also influence dose, such as milliampere seconds and peak kilovoltage, were not available for every individual patient from the electronic databases during the study period. Therefore, we obtained typical machine settings for CT in young people from UK-wide surveys undertaken in 1989 and 2003.[11,12] We combined these data with those from a series of hybrid computational human phantoms[13] and Monte Carlo radiation transport techniques to estimate absorbed doses to the red bone marrow and brain for reference males and females for integer years of age between 0 and 22 years.[14,15] Table 1 shows estimated red bone marrow and brain doses from different CT examinations by age and sex after 2001. Dose estimates before 2001 were generally 2–3 times higher than were those after this date because age-specific technical settings were rarely used in earlier years.[12]

	Male patients		Female patients	
	Brain dose (mGy)	Red bone marrow dose (mGy)	Brain dose (mGy)	Red bone marrow dose (mGy)
Age at brain CT				
0 years	28	8	28	8
5 years	28	9	28	9
10 years	35	6	35	6
15 years	43	4	44	6
20 years	35	2	42	2
Age at chest CT				
0 years	0·4	4	0·4	4
5 years	0·3	3	0·3	3
10 years	0·3	3	0·3	3
15 years	0·2	4	0·3	4
20 years	0·2	4	0·3	4
Age at abdominal CT				
0 years	0·2	3	0·2	3
5 years	0·1	2	0·1	2
10 years	0·1	3	0·1	3
15 years	0·0	3	0·0	3
20 years	0·0	3	0·0	4
Age at extremity CT				
0 years	0·0	1	0·0	1
5 years	0·0	0·2	0·0	0·2
10 years	0·0	0·1	0·0	0·1
15 years	0·0	0·0	0·0	0·0
20 years	0·0	0·0	0·0	0·0

Table 1: **Estimated radiation doses to the brain and red bone marrow from one CT scan, by scan type, sex, and age at scan, as used in this study for scans after 2001**

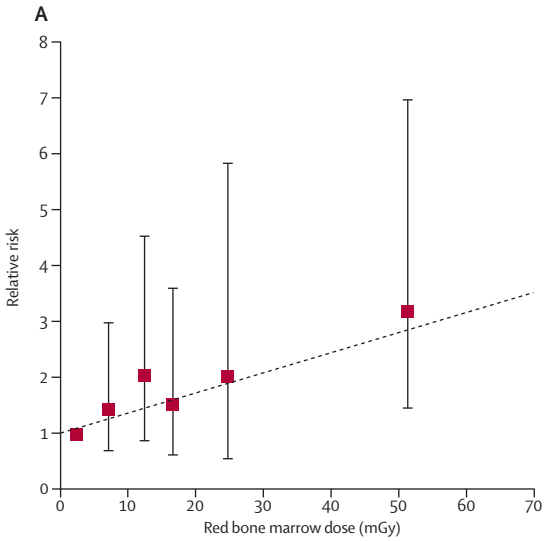
Statistical analysis

We assessed potential associations between radiation dose and cancer outcomes with Poisson relative risk models fitted by maximum likelihood (see appendix). To avoid inclusion of CT scans related to cancer diagnosis we began accrual of person-time for leukaemia incidence 2 years after the first CT scan and for brain tumours 5 years after the first CT scan. We continued

	Leukaemia*		Brain tumours†	
	Cases	Person-years	Cases	Person-years
Sex				
Male	42	953 634	65	657 169
Female	31	764 937	70	529 372
Unknown	1	2413	0	1666
Age at first exposure, years				
0	10	198 052	17	139 414
1–<5	17	262 437	18	185 942
5–<10	17	269 369	27	189 415
10–<15	10	345 320	30	236 891
≥15	20	645 807	43	436 545
Attained age, years				
0–<20	47	900 383	65	537 567
20–<30	23	689 274	53	519 313
30–<35	2	106 376	12	106 376
≥35	2	24 951	5	24 951
Years since first exposure				
0–<10	53	1 266 110	77	733 337
10–<15	15	347 786	45	347 786
15–<20	6	101 213	13	101 213
≥20	0	5871	0	5871
Number of CT scans				
1	45	1 239 170	72	862 661
2–4	22	429 324	50	291 192
≥5	7	52 493	13	34 354
Overall	74	1 720 984	135	1 188 207

Person-year data in the leukaemia group do not sum to the overall number because of rounding. *Follow-up starting 2 years after first CT scan. †Follow-up starting 5 years after first CT scan.

Table 2: **Cases of leukaemia and brain tumours and person-years for patients in the assessed cohort**



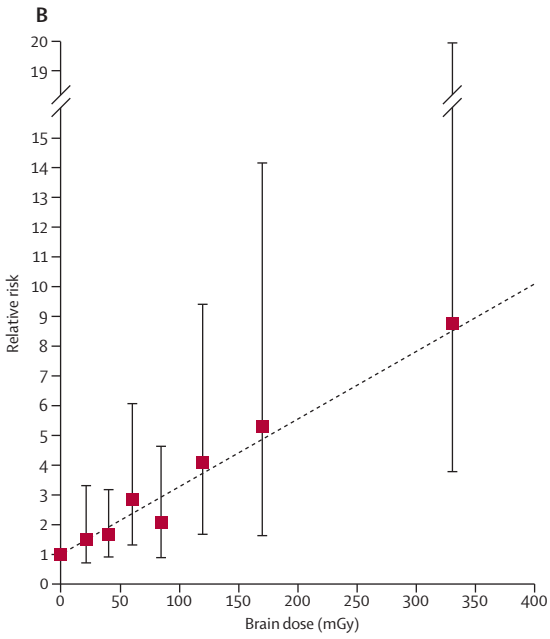


Figure: **Relative risk of leukaemia and brain tumours in relation to estimated radiation doses to the red bone marrow and brain from CT scans**
(A) Leukaemia and (B) brain tumours. Dotted line is the fitted linear dose-response model (excess relative risk per mGy). Bars show 95% CIs.

accrual of data until date of first cancer diagnosis or the earliest of death, loss-to-follow-up, or Dec 31, 2008. Because it typically takes at least 2 years for radiation-related leukaemia to develop and 5 years for a solid cancer to develop,[16] doses were lagged by 2 years for leukaemia and by 5 years for brain tumours. Application of the exclusions and lag periods are described in the appendix. We did sensitivity analyses in which the exclusion and lag periods were increased to 10 years for brain tumours, the follow-up period for leukaemia was decreased from 2008 to 2004, and the age at end of follow-up was restricted to patients younger than 25 years for leukaemia and younger than 28 years for brain tumours. We did significance tests on the basis of the likelihood-ratio test. Unless otherwise stated, we based CIs on the profile likelihood.[17] When the statistical software failed to produce a convergent profile likelihood bound we used the Wald-based (Fisher information-based) confidence bound. All p values are two-sided and $p<0·05$ was regarded as significant. We did all statistical analyses with the DATAB and AMFIT modules of the EPICURE programme.[18]

Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. MSP and ABdG had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

After exclusion of 33 372 patients who could not be traced by NHSCR because of incomplete names or dates of birth in the RIS databases (and 960 non-UK resident

	Cases	ERR per mGy (95% CI)	p value (test for dose-response)
Red bone marrow dose			
All leukaemia, including myelodysplastic syndromes	74	0·036 (0·005 to 0·120)	0·0097
Acute lymphoblastic leukaemia	26	1·719* (>0 to 17·73†)	0·0053
Acute myeloid leukaemia	18	0·021 (–0·042† to 0·155)	0·2653
Myelodysplastic syndromes	9	6·098* (>0 to 145·4†)	0·0032
Leukaemia excluding myelodysplastic syndromes	65	0·019 (–0·012† to 0·079)	0·1436
Brain dose			
All brain	135	0·023 (0·010 to 0·049)	<0·0001
Glioma	65	0·019 (0·003 to 0·070)	0·0033
Schwannoma and meningioma	20	0·033 (0·002 to 0·439)	0·0195

ERR=excess relative risk. *Iteratively reweighted least-squares algorithm failed to converge, so parameter estimates might be unreliable. †Calculated using Wald-based CI.

Table 3: **Excess relative risk per mGy for cancer subtypes in relation to organ-specific radiation doses received from CT scans**

patients) and those who were ineligible for follow-up because the exit date occurred less than 2 years in the case of leukaemia analyses or 5 years for brain tumours after the first scan (or when information, such as date of scan, was missing or obviously inaccurate), we included 178 604 individuals in the leukaemia analyses and 176 587 in the brain tumour analyses (table 2).

We included 283 919 CT scans in the analysis of leukaemia risk, of which 64% (182 337 scans) were of the head. The next most common CT scan types were of the abdomen and/or pelvis (9%, 25 695 scans) and chest CT (7%, 18 910 scans; appendix). The distribution of scan types was very similar for patients in the brain tumour analysis, but the total number of scans was slightly smaller than in the leukaemia analysis because of the longer exclusion period (279 824 scans). Table 2 lists the distributions of cases and overall person-years, by sex, age at first scan, attained age, years since first scan, and the number of scans.

The risk of leukaemia was positively associated with estimated doses delivered by CT scans to the red bone marrow (p=0·0097), as was the risk of brain tumours associated with estimated doses delivered by CT scans to the brain tissue (p<0·0001; figure).

Compared with doses of less than 5 mGy, the relative risk (RR) of leukaemia for patients who received doses of at least 30 mGy (mean dose in this group was 51·13 mGy) was 3·18 (95% CI 1·46–6·94; appendix). Compared with doses of less than 5 mGy, the RR of brain tumours for patients receiving 50–74 mGy (mean dose 60·42 mGy) was 2·82 (1·33–6·03; figure, appendix), and for patients receiving 50 mGy or more (mean dose 104·16 mGy) the brain tumour RR is 3·32 (95% CI 1·84–6·42; appendix). To put this into context, after 2001, 5–10 head CTs in children younger than 15 years result in the accumulation of about 50 mGy red bone marrow dose and 2–3 head CTs results in about a 60 mGy cumulative brain dose (table 1).

	Leukaemia		Brain tumours	
	ERR per mGy	p value	ERR per mGy	p value
Sex				
Male*	0·031	0·6300	0·016	0·0850
Female	0·042		0·028	
Years since first exposure				
0–<5	0·048	0·8061	0†	0·6468
5–<10	0·033		0·025	
≥10	0·026		0·021	
Years since last exposure				
0–<5	0·052	0·3004	0†	0·1976
5–<10	0·015		0·026	
≥10	0·014		0·016	
Number of CT scans				
1	0·013	0·8013	0·007	0·1213
2–4	0·028		0·021	
≥5	0·035		0·018	
Age at exposure (years)‡				
0–<5	0·030	0·5381	0·005	0·0003
5–<10	0·072		0·028	
10–<15	–0·002		0·037	
≥15	0·049		0·041	
Years since exposure‡				
2–<5	0·055	0·5357	··	0·2399
5–<10	0·021		0·026	
10–<15	0·005		0·023	
≥15	0·026		0·005	

ERR=excess relative risk. ··=not applicable (follow-up started at 5 years). *Includes individual of unknown sex. †Aliased parameter, set to zero. ‡Time-dependent variable.

Table 4: **Excess relative risk per mGy for leukaemia and brain tumours, by various personal characteristics**

We noted positive associations between CT scans and cancer subgroups of gliomas (p=0·0033), schwannoma and meningiomas (p=0·0195), acute lymphoblastic leukaemia (p=0·0053), and myelodysplastic syndromes (p=0·0032), but not acute myeloid leukaemia (p=0·2653) or leukaemia excluding myelodysplastic syndromes (p=0·1436; table 3). For leukaemia, the dose response did not vary between age at exposure, time since exposure, sex, or any other covariates examined (table 4). However, for brain tumours there was significant heterogeneity (p=0·0003) in estimated RR (ERR) across categories of age at exposure, with ERR increasing with increasing age.

We noted little evidence of non-linearity of the dose-response, using either linear-quadratic or linear-exponential forms of departure from linearity (leukaemia exponential p=0·2672 and quadratic p=0·4683, brain tumour exponential p=0·9203 and quadratic p=0·8993). In sensitivity analyses in which all scans 10 years before brain tumour diagnosis were excluded, the magnitude of the dose-responses was increased rather than decreased as might be expected if the association was driven by bias from CT scans related to the diagnosis (appendix). When

follow-up for leukaemia was restricted to 2004, the dose-response also increased, which was as expected given the short latency period for leukaemia and early peak in excess risk reported in previous studies.[10,16] To assess whether the missing exposure data after age 22 years resulted in underestimation of doses and hence overestimation of the relative risks, we restricted follow-up to individuals younger than 28 years for brain tumours and individuals younger than 25 years for leukaemia, but this did not change the dose-response estimates.

Discussion

In this retrospective cohort study, we show significant associations between the estimated radiation doses provided by CT scans to red bone marrow and brain and subsequent incidence of leukaemia and brain tumours. Assuming typical doses for scans done after 2001 in children aged younger than 15 years, cumulative ionising radiation doses from 2–3 head CTs (ie, ~60 mGy) could almost triple the risk of brain tumours and 5–10 head CTs (~50 mGy) could triple the risk of leukaemia.

Although no previous cohort studies have assessed the risk of cancer after CT, several studies have reported significantly increased cancer risks after radiation exposure in the range received from multiple CT scans (100 mGy).[19] Such studies include those of survivors of the atomic bombs in Japan,[20] nuclear workers,[21] and patients who received tens of diagnostic radiographs.[22] A few case-control studies have also assessed cancer risks from CT scans on the basis of self-reported history of diagnostic radiograph exposures.[23,24] These studies might be subject to recall bias whereby patients are more likely to recall previous medical radiation exposures than are unaffected controls, and also high levels of reporting error. We avoided such bias by taking a cohort approach and assessing more accurate exposure histories from medical records (panel).

In terms of the quantitative estimates of the risk, our primary comparison for leukaemias and brain tumours is with the Life Span Study[20] of Japanese atomic bomb survivors, which is the most comprehensive study of cancer after radiation exposure currently available.[10,16] The dose-response for leukaemia following childhood exposure and similar follow-up time (<15 years after exposure) in the Life Span Study was 0·045 per mSv (95% CI 0·016–0·188; appendix) which was much the same as our estimate (ERR of 0·036 per mGy [0·005–0·120]; 1 mSv=1 mGy). For brain tumours, our result (ERR 0·023 per mGy [0·010–0·049]) was about four times higher than was the Life Span Study estimate (0·0061 per mSv [0·0001–0·0639] <20 years after exposure; appendix), but the CIs are wide and overlapped. We had reduced power to examine risks by subtype of neoplasm, age, or time since exposure compared with the Life Span Study, partly because of the more restricted ranges of length of follow-up and age at exposure. The increased risks noted in our study compared with the Life Span Study might be because existing tumours in some patients were not detected at the time of their first CT. The relatively low-energy x-radiation from CT scans might also be about twice as biologically effective per unit dose as the mainly high-energy γ-rays that were the predominant exposure source from the atomic bombings in Hiroshima and Nagasaki.[16]

Our large study sample was collected from a wide range of hospitals in Great Britain. Because most medical attendances at hospitals in Great Britain, particularly for the age group in this study, are in public, free-to-access, NHS hospitals, the sample is probably representative of the childhood and young adult population in the country as a whole who undergo CT. Ascertainment of cancer diagnoses by NHSCR is estimated to be 97%[25] and therefore there is a low likelihood of losses to follow-up. Patients who were excluded because linkage to their records was not possible had similar characteristics to those who were linked and thus should not have biased conclusions. Because we assessed children and young adults, our results are directly applicable to a highly radiosensitive section of the population,[10] although whether the results can be generalised to adulthood CT scans has not been established. Moreover, because most (>80%) of the population assessed was white, whether the results are generalisable to other ethnic groups is unknown.

CT is often used as a diagnostic technique when a solid cancer is suspected. However, information about the reasons for CTs and other clinical variables were not available for this study. Instead, we excluded all scans undertaken in the 2 years before a leukaemia diagnosis and 5 years before a brain tumour diagnosis. Young

Panel: Research in context

Systematic review

We searched PubMed and Medline databases without date or language restriction for articles with the search terms "computed tomography", "ionizing radiation", "cancer", "radiation-induced neoplasms", "case-control", and "prospective". We reviewed reports from scientific committees such as the International Commission on Radiological Protection (ICRP), United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), and Biological Effects of Ionizing Radiations (BEIR), and also a broader range of publications and reports covering medical imaging and radiation exposure. We checked references from selected publications for relevance to this study including comments, correspondence, and editorials. Exposure to ionising radiation is an established risk factor for leukaemia and brain tumours.[10,16] Although CT has important clinical uses, concerns exist about the potential cancer risks from the associated ionising radiation, particularly for children. Rates of CT use have been rising rapidly in the developed world.

Interpretation

Increases that we noted in incidence rates of leukaemia and brain tumours after childhood exposure to CT scans are unlikely to be due to confounding factors. The evaluated risks per unit dose were consistent with those derived from recent analyses of cohorts exposed to higher average radiation doses and dose rates. The current study supports the extrapolation of such risk models to doses from CT scans.

patients with leukaemia are unlikely to have a CT because of their disease,[26] but we still used a cautious approach of applying an exclusion period. By contrast, patients with brain tumours will probably have a number of CT examinations during the diagnostic period, hence the longer exclusion period. Nevertheless, we noted much the same results in sensitivity analyses in which all scans in the 10 years before a brain tumour diagnosis were excluded. The absence of data for other exposures, such as radiographs, is unlikely to have introduced a major bias because the doses from these scans are typically ten-times smaller than those for CT scans. However, we cannot rule out this bias and the increased dose response noted for brain tumours compared with the survivors of the atomic bombs in Japan is also a possible indication of some residual bias despite the long exclusion period.

Previous dose estimates for CT typically provided effective dose rather than organ doses and were restricted in terms of the ages covered. In this study, a series of phantoms with a higher age resolution from newborn to adult was used for both males and females. We also used more realistic anatomy and bone marrow dosimetry models compared with previous computational phantoms. These advanced features allow more accurate and valid estimates of organ-specific doses. Despite these advanced methods, uncertainties exist for our dose estimates. However, such uncertainties are likely to be mainly Berksonian (resulting from applying group-averaged estimates), and thus would not be expected to bias the dose response.[27] Collection of detailed scan parameter data for individual patients was not possible. Instead, we used average CT machine settings from two national surveys and assumed that no technical adjustment was made for paediatric patients before 2001.[5]

Absolute excess risk estimates are necessary to put the risks into perspective with the benefits of the scans. Good evidence from the long-term study of the atomic bomb survivors in Japan suggests that cancer risk persists indefinitely after radiation exposure and most cancer types are inducible by radiation.[10,16] At present, we only have sufficient case numbers to assess brain tumours and leukaemia, and the maximum age of patients at the end of follow-up is 45 years, with a minimum age of 6 years and maximum follow-up time of 23 years. Provisional estimates of excess absolute risk for the end of follow-up at about 10 years after exposure suggest that, of 10 000 people between the ages of 0–20 years receiving 10 mGy from a CT scan, there would be about 0·83 (95% CI 0·12–2·77) excess leukaemia cases and 0·32 (0·14–0·69) excess brain tumours (appendix). Applying the dose estimates for one head CT scan before the age of 10 years (table 1) this estimate would translate into approximately one excess case of leukaemia and one excess brain tumour per 10 000 patients. Increased follow-up and analysis of other cancer types is needed to identify the lifetime excess cancer risk associated with CT scans. Some evidence[28] suggests that doses in the range delivered by several CT scans might increase the risk of cardiovascular disease. Investigating this feature would require not only the same long-term follow-up required for adulthood cancer outcomes, but also a new approach to obtain cardiovascular incidence data, which is not currently recorded on a registry rather than reliance on mortality data.

Various studies have estimated the potential lifetime excess cancer risks from CT scans from risk projection models, which are largely based on risk models from studies of survivors of the atomic bombs in Japan. Because our relative risk estimates are broadly consistent with the results from the Life Span Study, this study provides additional direct support for the existing life-time absolute cancer risk projections for paediatric patients.[3,7,8,29] The most recent risk projections[8] suggest that, for children with normal life expectancy, the lifetime excess risk of any incident cancer for a head CT scan (with typical dose levels used in the USA) is about one cancer per 1000 head CT scans for young children (<5 years), decreasing to about one cancer per 2000 scans for exposure at age 15 years. For an abdominal or pelvic CT scan, the lifetime risks for children are one cancer per 500 scans irrespective of age at exposure. These absolute excess lifetime cancer risks (to age 100 years) are very small compared with the lifetime risk of developing cancer in the general population, which is about one in three, and are also likely to be small compared with the benefits of the scan, providing it is clinically justified.[1]

We estimated doses for each scan that every patient received, obtained outcome data for the patients, and provided direct evidence that doses at the level children and young adults can receive from CT are associated with increased risks of leukaemia and brain tumours. The dose-response relation that we noted and relative risks of more than 2 for an exposure that is an established carcinogen at higher dose-levels[10,16] is evidence that this relation is unlikely to be entirely due to confounding factors. With the increasing use of CT worldwide, particularly within this young population,[8] knowledge of the risks based on empirical data will be crucial to assess safety in relation to the benefits that CT provides. Frequent calls have been made to decrease doses, following the as low as reasonably achievable (ALARA) principle, and only scan when justified as in the current image gently campaign.[30] In the UK, the Ionising Radiation (Medical Exposure) Regulations mean that a CT scan should only be done when clinically justified, which might explain the low levels of CT use in the UK compared with other countries that do not have such regulations. The immediate benefits of CT outweigh the long-term risks in many settings[31] and because of CT's diagnostic accuracy and speed of scanning, notably removing the need for anaesthesia and sedation in young patients, it will remain in widespread practice for the foreseeable future. Further refinements to allow reduction in CT doses should be a priority, not only for

the radiology community but also for manufacturers. Alternative diagnostic procedures that do not involve ionising radiation exposure, such as ultrasound and MRI might be appropriate in some clinical settings.

Contributors

LP and AWC conceived the study. MSP, LP, KM, AWC, CMR, ABdG organised funding or continued intramural funding. MSP, LP, AWC, and CMR designed the study. MSP, JAS, NLH, and PR did the data collection and processing. CL, KPK, ABdG, KM, and MSP did the dosimetry analysis. MPL, ABdG, and MSP did the statistical analysis. MSP and ABdG wrote the report, which was revised and approved by all authors. MSP and ABdG take overall responsibility for the integrity of the study. LP and ABdG were joint senior authors.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

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Leukaemia incidence statistics

Leukaemia incidence statistics are presented here, by sex, age and type. Trends over time and prevalence data are also presented.

The term 'leukaemia' covers cancers of the white blood cells and bone marrow. The ICD codes for leukaemia are ICD-10 C91-95.

There are four main types of leukaemia: acute lymphoblastic leukaemia (ALL; ICD-10 C91.0), chronic lymphocytic leukaemia (CLL; ICD-10 91.1), acute myeloid leukaemia (AML; ICD-10 C92.0) and chronic myeloid leukaemia (CML; ICD-10 C92.1). These types differ substantially in their cellular origin and clinical behaviour. As such it is important to recognise this when interpreting statistics on the incidence of the group 'leukaemia' as a whole.

The latest incidence statistics available for leukaemia cancer in the UK are 2010. Please note that data in this section are for 2008 and that 2010 data are coming soon. Find out why more up to date statistics are not yet available.

On this page:

By sex

Grouped together leukaemia is the tenth most common cancer in the UK (2009), accounting for around 2.5% of all new cases. Overall leukaemia is more common in men than women, at a ratio of around 7:5 for males to females. Leukaemia is the tenth most common cancer in men (2009) and tenth in women (2009). In the UK in 2008 there were 7,659 new cases of leukaemia registered (**Table 1.1**). 1-4

Table 1.1: Leukaemia (C91-95), Number of New Cases, Crude and European Age-Standardised (AS) Incidence Rates per 100,000 Population, UK, 2008

		England	Wales	Scotland	Northern Ireland	United Kingdom
Male	**Cases**	**3,770**	**243**	**336**	**114**	**4,463**
	Crude Rate	14.9	16.7	13.4	13.1	14.8
	AS Rate	**12.5**	**13.2**	**11.4**	**12.2**	**12.4**
	AS Rate - 95% LCL*	12.1	11.5	10.2	9.9	12.0
	AS Rate - 95% UCL*	12.9	14.8	12.6	14.4	12.8
Female	**Cases**	**2,710**	**156**	**249**	**81**	**3,196**
	Crude Rate	10.4	10.2	9.3	9.0	10.2
	AS Rate	**7.3**	**7.1**	**7.1**	**7.5**	**7.3**

	AS Rate - 95% LCL*	7.1	6.0	6.2	5.9	7.0
	AS Rate - 95% UCL*	7.6	8.2	7.9	9.1	7.5
Persons	**Cases**	**6,480**	**399**	**585**	**195**	**7,659**
	Crude Rate	12.6	13.3	11.3	11.0	12.5
	AS Rate	**9.7**	**10.0**	**9.0**	**9.4**	**9.6**
	AS Rate - 95% LCL*	9.5	9.0	8.2	8.1	9.4
	AS Rate - 95% UCL*	9.9	10.9	9.7	10.7	9.9

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*95% LCL and 95% UCL are the 95% lower and upper confidence limits around the AS Rate

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By age

Figure 1.1 shows how incidence varies with age. The highest incidence in children is in the 0-4 age group mainly consisting ALL. Rates then decline and remain fairly stable until the 40s when they start to rise slowly to the early 50s. Leukaemia incidence then rises much more sharply and the rates reach their peak in the over 85s.

It has been estimated that the lifetime risk of developing leukaemia in 2008 is 1 in 71 for men and 1 in 105 for women in the UK. This was done using the AMP method.5

Figure 1.1: Leukaemia (C91-95), Average Number of New Cases per Year and Age-Specific Incidence Rates, UK, 2006-2008

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By type

The four main types of leukaemia make up over 80% of all leukaemia diagnoses. In 2008, there were 369 cases diagnosed of ALL in males, and 285 in females. The corresponding figures were 1,703 in males, 1,095 in females of CLL; 1,303 cases in males, 1,040 cases in females of AML; and 339 in males, 274 in females of CML.

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Trends over time

Incidence rates for leukaemia increased slowly until the end of the 1990s in Great Britain (**Figure 1.2**). Part of this increase will be due to better diagnostic tools and improvements in cancer registration. However, in the last couple of years there appears to be a fall in the incidence rates.

Figure 1.2: Leukaemia (C91-95), European Age-Standardised Incidence Rates, Great Britain, 1975-2008

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Figure 1.3 shows a similar pattern for the incidence trend in the UK for leukaemia.

Figure 1.3: Leukaemia (C91-95), European Age-Standardised Incidence Rates, UK, 1993-2008

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Lifetime risk

Lifetime risk is an estimation of the risk that a newborn child has of being diagnosed with cancer at some point during their life. It is a summary of risk in the population but genetic and lifestyle factors affect the risk of cancer and so the risk for every individual is different.

In 2010, in the UK, the lifetime risk of developing leukaemia is 1 in 66 for men and 1 in 96 for women.7

The lifetime risk for leukaemia cancer has been calculated by the Statistical Information Team using the 'Adjusted for Multiple Primaries' (AMP) method; this accounts for the possibility that someone can have more than one diagnosis of leukaemia cancer over the course of their lifetime.8

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Prevalence

Prevalence data relate to those people in the UK population who were alive on a specific date having previously been diagnosed with cancer. The latest analysis shows that on 31st December 2006, around 27,100 people were alive up to ten years after being diagnosed with leukaemia6. **Table 1.2** shows the one, five and ten year prevalence

by sex for leukaemia.

Table 1.2: Leukaemia prevalence in the UK, at 31st December 2006

	1 year prevalence	5 year prevalence	10 year prevalence
Males	2,668	10,053	15,738
Females	1,847	7,058	11,430
Persons	4,515	17,111	27,168

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- Leukaemia
- Incidence

References for leukaemia incidence

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2. Welsh Cancer Intelligence and Surveillance Unit. Cancer Incidence in Wales. 2010
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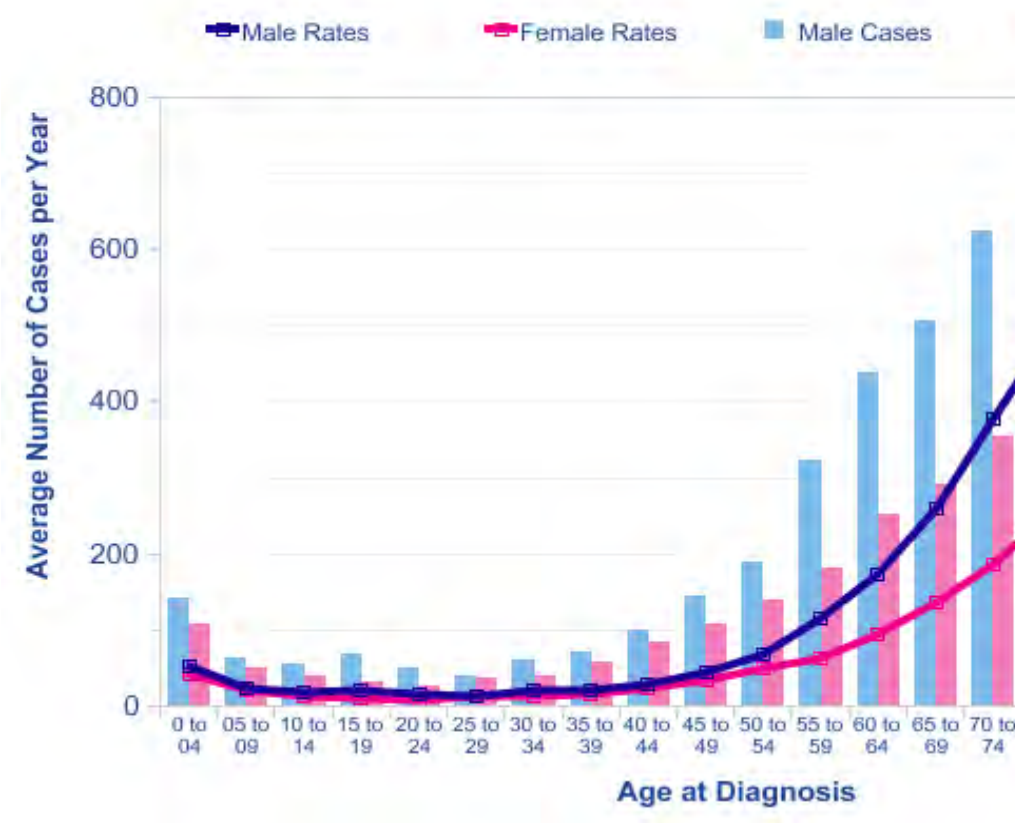
Leukaemia (C91-C95): 2006-2008

Average Number of New Cases Per Year and Age-Specific Incidenc

Age Range	Male Cases	Female Cases
0 to 04	142	108
05 to 09	64	51
10 to 14	55	39
15 to 19	68	30
20 to 24	49	27
25 to 29	40	37
30 to 34	61	40
35 to 39	71	58
40 to 44	100	85
45 to 49	143	107
50 to 54	189	139
55 to 59	322	181
60 to 64	438	252
65 to 69	506	291
70 to 74	624	354
75 to 79	634	419
80 to 84	503	427
85+	437	538
All Ages	4 447	3 182



Prepared by Cancer Research UK

Original data sources:

1. Office for National Statistics. Cancer Statistics: Registrations Series MB1. http://www.statistic
2. Welsh Cancer Intelligence and Surveillance Unit. http://www.wcisu.wales.nhs.uk.
3. Information Services Division Scotland. Cancer Information Programme. www.isdscotland.or
4. N. Ireland Cancer Registry. www.qub.ac.uk/nicr.

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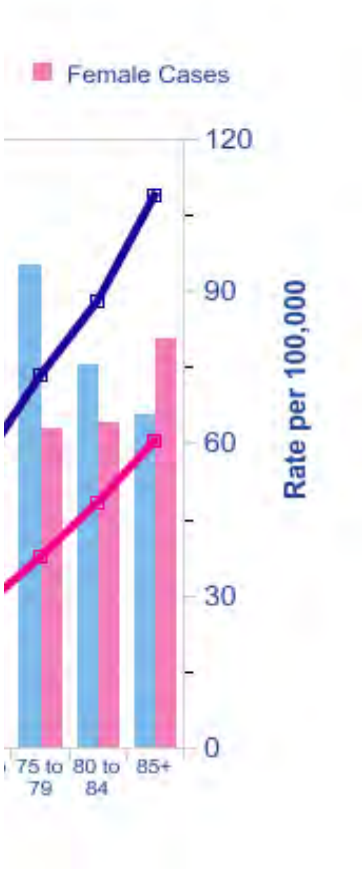
:e Rates per 100,000 Population, UK

Male Rates	Female Rates
7,7	6,2
3,6	3
2,9	2,1
3,3	1,6
2,3	1,3
2	1,9
3,1	2
3,2	2,5
4,3	3,6
6,8	5
10,2	7,3
17,4	9,5
25,9	14,3
38,8	20,6
56,5	28
73,6	37,7
88,1	48,4
109	60,4
14,9	10,2



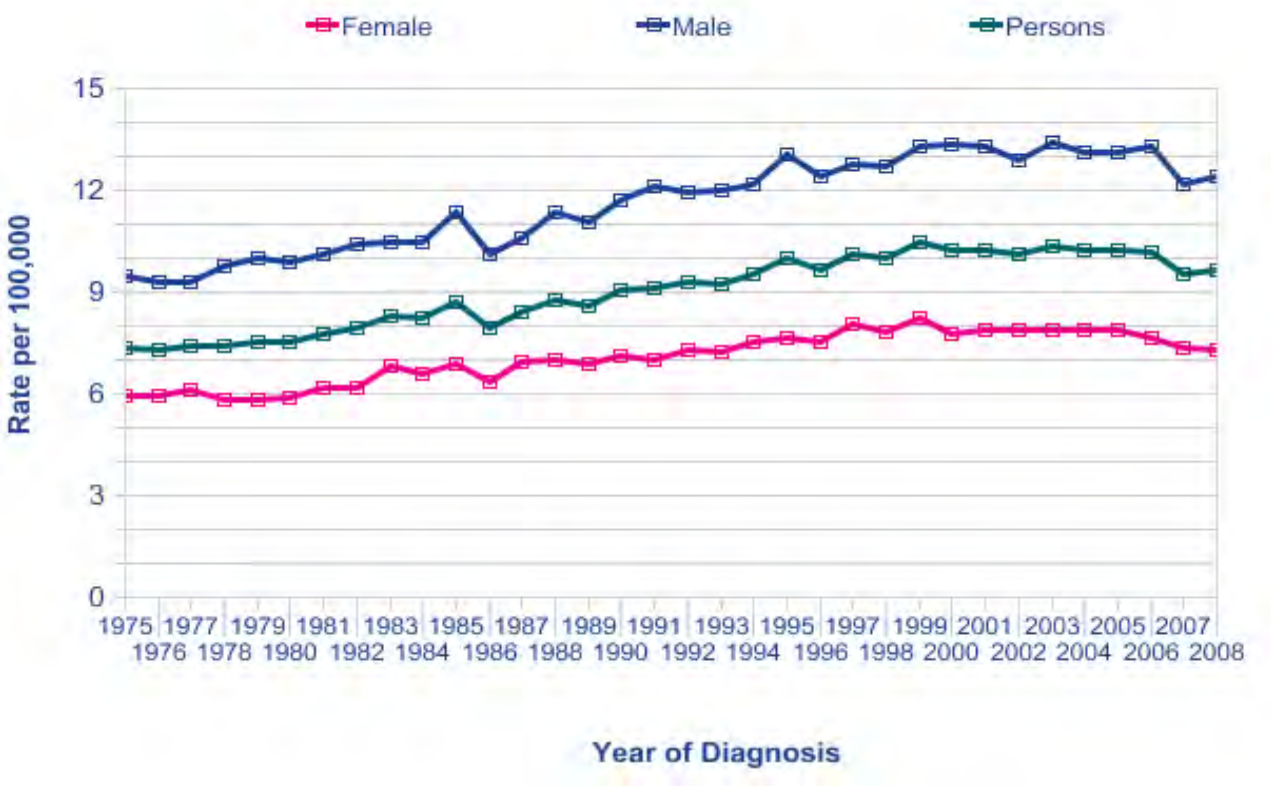
s.gov.uk/statbase/Product.asp?vlnk=8843.

g/cancer.

Leukaemia (C91-C95): 1975-2008

European Age-Standardised Incidence Rates per 100,000 Population, by Sex, Great E

Sex	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988
Female	5,9	5,9	6,1	5,8	5,8	5,9	6,2	6,2	6,8	6,6	6,9	6,4	6,9	7
Male	9,5	9,3	9,3	9,8	10	9,9	10,1	10,4	10,5	10,5	11,3	10,1	10,6	11,4
Persons	7,4	7,3	7,4	7,4	7,5	7,5	7,8	7,9	8,3	8,2	8,7	7,9	8,4	8,8



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2. Welsh Cancer Intelligence and Surveillance Unit. http://www.wcisu.wales.nhs.uk.
3. Information Services Division Scotland. Cancer Information Programme. www.isdscotland.org/cancer.
4. N. Ireland Cancer Registry. www.qub.ac.uk/nicr.

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Britain

1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
6,9	7,1	7	7,3	7,2	7,5	7,6	7,5	8,1	7,8	8,2	7,8	7,9	7,9	7,9
11,1	11,7	12,1	11,9	12	12,2	13,1	12,4	12,8	12,7	13,3	13,3	13,3	12,9	13,4
8,6	9	9,1	9,3	9,3	9,5	10	9,7	10,1	10	10,4	10,2	10,3	10,1	10,3

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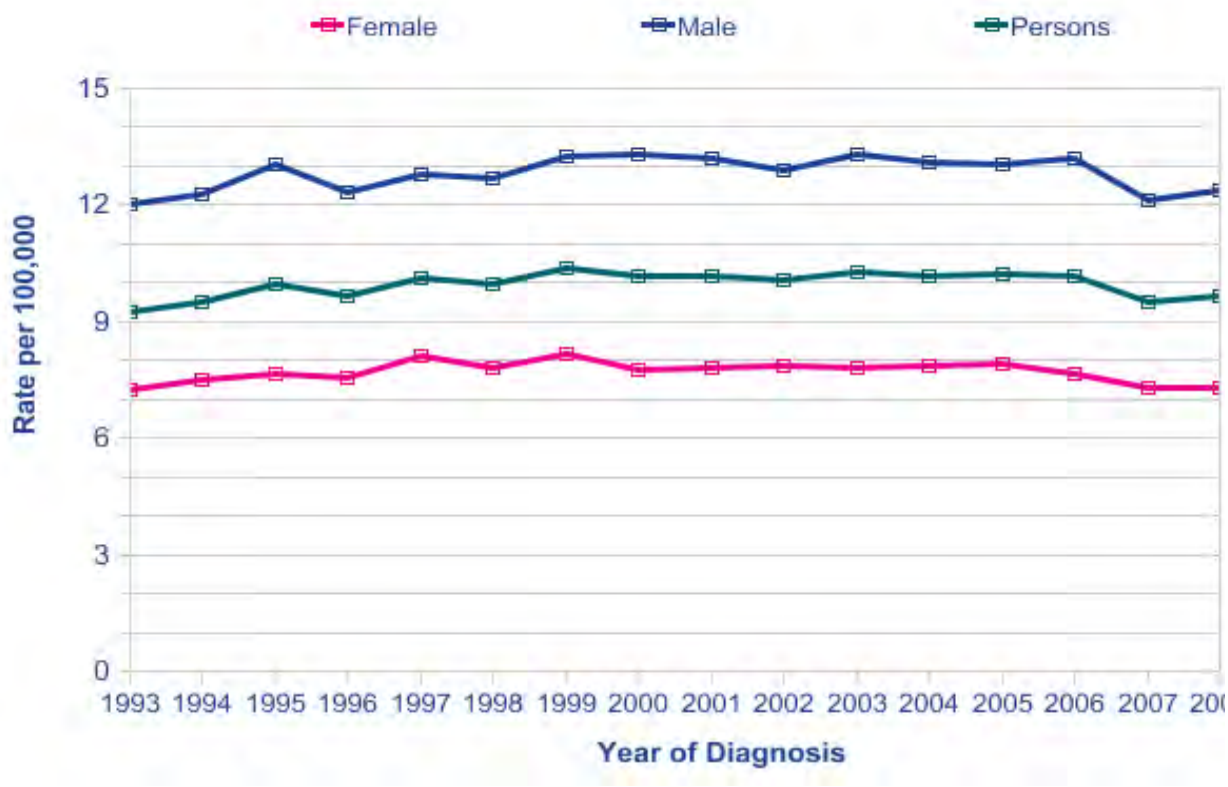
2004	2005	2006	2007	2008
7,9	7,9	7,7	7,3	7,3
13,1	13,1	13,3	12,2	12,4
10,2	10,3	10,2	9,5	9,6

Leukaemia (C91-C95): 1993-2008

European Age-Standardised Incidence Rates per 100,000 Population, by Sex, UK

Sex	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Female	7,2	7,5	7,6	7,5	8,1	7,8	8,2	7,7	7,8	7,9	7,8	7,9	7,9
Male	12	12,3	13,1	12,4	12,8	12,7	13,2	13,3	13,2	12,9	13,3	13,1	13,1
Persons	9,3	9,5	10	9,6	10,1	10	10,4	10,2	10,2	10,1	10,3	10,2	10,2



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3. Information Services Division Scotland. Cancer Information Programme. www.isdscotland.org/cancer.
4. N. Ireland Cancer Registry. www.qub.ac.uk/nicr.

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2006	2007	2008
7,7	7,3	7,3
13,2	12,1	12,4
10,2	9,5	9,6

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	distance km	Coef surface marginale	dose efficace	dose/secteur rad	cumul rad
	1		1210		
0,21	1,1	0,21	685	198,975	198,975
0,44	1,2	0,23	389,1	123,5215	322,4965
0,69	1,3	0,25	220,7	76,225	398,7215
0,96	1,4	0,27	125,7	46,764	445,4855
1,25	1,5	0,29	72,1	28,681	474,1665
1,56	1,6	0,31	41,2	17,5615	491,728
2,24	1,8	0,68	13,5	18,598	510,326
3	2	0,76	4,4	6,802	517,128

dose moyenne gamma rad		neutron
rad	rad	rad
	255	191
	155	106
	94,6	58,9
	57,7	32,6
	35,2	18,1
	21,6	10,1
	13,2	5,6
	5	1,7
172,376	1,9	0,5