Third Analysis of the National Registry for Radiation Workers: Occupational Exposure to Ionising Radiation in Relation to Mortality and Cancer Incidence

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ABSTRACT

Mortality and cancer incidence have been studied in a cohort of about 175,000 persons on the National Registry for Radiation Workers (NRRW) who were followed until the end of 2001. This analysis is based on a larger cohort and nine years' further follow-up compared with the 2nd NRRW analysis, and includes cancer registration data for the first time. As in previous NRRW analyses, total mortality and mortality from major causes were less than would be expected based on rates for England and Wales; the Standardised Mortality Ratio (SMR) for all causes was 81, whilst the SMR for all malignant neoplasms was 84. This "healthy worker effect" was still present after adjustment for social class. The only cause for which mortality was statistically significantly greater than expected from national rates was pleural cancer, probably reflecting exposure to asbestos.

Within the cohort, there was borderline evidence of an increasing trend in total mortality with increasing external radiation dose. Much of the evidence for this trend related to cancer. Mortality and incidence from both leukaemia excluding chronic lymphatic leukaemia and the grouping of all malignant neoplasms other than leukaemia increased to a statistically significant extent with increasing dose. The corresponding central estimates of the trend in risk with dose were similar to those for the survivors of the atomic bombings of Hiroshima and Nagasaki, whilst the 90% confidence intervals for the NRRW trends excluded values more than about 2-3 times greater than the A-bomb risk estimates as well as values of zero or less. Whilst there was some evidence of an increasing trend with dose in mortality from all circulatory diseases combined, the irregular pattern in risk with dose and similarities with the corresponding pattern for lung cancer suggest that this finding may, at least in part, be due to confounding by smoking.

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In contrast, both for mortality and incidence, the trend with dose in the risk of all malignant neoplasms other than leukaemia was maintained when lung and pleural cancer were excluded from this disease grouping, so indicating that the trend is not an artefact due to smoking. Statistically significantly increasing trends with dose were seen for multiple myeloma (based on incidence data) and for cancers of the rectum (based on both mortality and incidence data), larynx (based solely on mortality data), all skin combined and non-melanoma skin specifically (based on incidence data) and uterus (based on mortality and - for endometrial cancer - incidence data); some of these results might be chance findings or artefacts.

This analysis provides the most precise estimates to date of the risks of mortality and cancer incidence following occupational radiation exposure and strengthens the evidence for raised risks due to these exposures. The cancer risk estimates obtained here are consistent with values used by national and international bodies in setting radiation protection standards. Continued follow-up of these workers should be valuable to see whether radiation-associated risks vary over time or by age, and to study specific cancers and causes of death in more detail.

CONTENTS

1 INTRODUCTION

Estimates of the long-term health risks from external exposure to ionising radiation are based largely on epidemiological studies of the survivors of the atomic bombings of Hiroshima and Nagasaki and from certain groups exposed for medical reasons (NRC, 2006; ICRP, 2007; UNSCEAR, 2008; Preston *et al*, 2003, 2004). Many of these people received high doses of radiation, in most cases over a short period of time. While there is extensive animal and other radiobiological evidence to indicate that the risks of cancer per sievert (Sv) for low doses received at low dose rates may be lower than those for high doses received at high dose rates (UNSCEAR, 1993; NRPB, 1993), there is no firmly established theoretical model for the extrapolation to low doses and low dose rates. Furthermore, most of the evidence relates to animals rather than humans. The derivation of the 'Dose and Dose Rate Effectiveness Factor' (DDREF) required to make the extrapolation to low doses and low dose rates has been discussed by, for example, the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 1993, 2000), the US BEIR VII Committee (NRC, 2006) and by the International Commission on Radiological Protection (ICRP, 2007).

The desirability of obtaining data directly concerning the risks from protracted or low dose radiation exposure has long been apparent. After extensive consultations with the nuclear industry and other interested parties, the National Radiological Protection Board (NRPB) started the National Registry for Radiation Workers (NRRW) in 1976, to form the largest study of UK radiation workers (Goodwin, 1975). The 1st analysis of the NRRW was published in 1992 (Kendall *et al*, 1992a,b). It examined mortality in a cohort of 95,217 radiation workers from five major employers in the nuclear industry: the Atomic Weapons Establishment (AWE); British Nuclear Fuels plc (BNFL, now the holding company for British Nuclear Group, Sellafield Ltd and Nexia Solutions); Ministry of Defence (MoD) employees monitored by the former Defence Radiological Protection Service (DRPS) and whose monitoring is now conducted by Dstl; Nuclear Electric (now split into British Energy Generation and Magnox Electric); and the then United Kingdom Atomic Energy Authority (UKAEA) [a]. The follow-up was up to the end of 1988 in most instances, but was terminated earlier for some groups of ex-workers at UKAEA, AWE and BNFL. The 1st NRRW analysis found a strong "Healthy Worker Effect", in that overall mortality rates were lower than expected from rates for the general population of England and Wales. Furthermore, within this cohort of workers, there was some evidence of an increasing trend in cancer risk with increasing external dose, particularly for leukaemia (excluding chronic lymphatic leukaemia, CLL, which does not appear to be radiation-inducible; UNSCEAR, 2008). However, the confidence intervals for these trends were wide, and encompassed the risks predicted by the International Commission on Radiological Protection (ICRP, 1991), as well as a range of other values both higher and lower.

[a] Where possible, the most recent name for each participating organisation has been used in this report. However, in situations where the historical name provides a more concise means of identifying the relevant group of workers (eg. for BNFL and UKAEA), this name has been retained here.

In order to obtain more information about mortality risks in relation to occupational radiation exposure, a 2nd analysis was undertaken (Muirhead *et al*, 1999a,b). This 2nd analysis was based on an enlarged cohort with about 30,000 extra workers, including additional workers at the organisations involved in the 1st analysis, plus radiation workers at the Daresbury and Rutherford Appleton Laboratories of the Council for the Central Laboratory of the Research Councils (now part of the Science and Technology Facilities Council, STFC); the Medical Research Council Radiobiology Unit (now MRC Harwell); NRPB (now the Health Protection Agency's Radiation Protection Division, HPA-RPD); Nycomed Amersham plc (now GE Healthcare), some groups of workers monitored by NRPB's Personal Monitoring Services (now the HPA Personal Dosimetry Service, PDS); Rolls-Royce and Associates (now Rolls-Royce Submarines); and Scottish Nuclear Ltd (now part of British Energy Generation or Magnox Electric). The analysis also incorporated updated dosimetry and personal data for those workers at UKAEA, AWE and BNFL Sellafield who were included in the Nuclear Industry Combined Epidemiological Analysis (NICEA) of Carpenter *et al* (1994), and involved follow-up to the end of 1992 for all workers. As in the 1st analysis, the 2nd NRRW analysis found a strong "Healthy Worker Effect", with mortality from all causes and for all cancers combined both being 82% of that expected from rates for the population of England and Wales. When cancer mortality was analysed in relation to external dose, the data were consistent both with existing radiation risk estimates and – for the most part – with the absence of an association between radiation and cancer risk. However, there was an increasing trend with dose in the risk of leukaemia other than CLL that was of borderline statistical significance.

Although the 2nd NRRW analysis was based on a larger cohort and a longer follow-up than the 1st analysis, the findings concerning mortality risks and radiation were still imprecise. Furthermore, neither analysis looked at cancer morbidity. Consequently, a 3rd analysis has now been conducted in order to provide more precise information on the risks of occupational radiation exposure, in terms of both mortality and cancer incidence. The key elements of this analysis are:

- a larger cohort, including both persons who recently commenced radiation work at many of the participating organisations, ex-workers at BNFL Capenhurst and Springfields (McGeoghegan and Binks, 2000a,b) and at MoD, and workers at Dungeness A and B power stations;
- another nine years of follow-up, to the end of 2001;
- data on cancer registrations, as well as mortality data.

This report describes in detail the design of and findings from the analysis and discusses the results. It complements a paper published in the peer-reviewed literature that summarises these findings (Muirhead *et al*, 2009).

2 STUDY DESIGN AND DATA COLLECTION

2.1 Introduction

The study population for the NRRW was originally defined, very widely, as all those exposed to ionising radiation in the course of their work and for whom radiation dose records were kept. This was intended to exclude workers who occasionally wore a dosemeter, but for whom no systematic dose record was maintained. It would, however, include workers who were monitored regularly and for whom dose records were kept, even if they were not 'classified radiation workers' and consequently subject to the detailed provisions of legislation. However, practical considerations meant that for some organisations, only classified radiation workers were considered for inclusion in the study.

For logistical reasons, the groups of workers first enrolled in the NRRW were those in the nuclear industry. Greater attention was given subsequently to including smaller organisations such as research laboratories and engineering firms. From the outset of the study, it was agreed that radiation workers at participating organisations should be given the opportunity to refuse to take part in the study. In practice, relatively few workers have exercised this option and, although refusal rates vary across organisations, overall the proportion who did not participate was only just over 1%.

When the NRRW was set up, it was realised that it would be easier to ensure the completeness and accuracy of data for those people who were still in radiation work than for those who ceased radiation work or had left employment with the relevant organisation. Consequently, and at the request of participating organisations, radiation workers at each site were divided into four categories, as follows:

A those who, as at 1 January 1976, were already working as radiation workers and who continued in this work;

B those continuing in employment with an NRRW participating organisation on 1 January 1976 and who had previously undertaken radiation work, but had stopped doing so before that date;

C those who had left employment before 1 January 1976 and who had previously undertaken radiation work;

D those who started radiation work after 1 January 1976.

During the early period of the study, particular attention was given to enrolling workers in categories A and D, as well as those in category B, based on a site-by-site judgement. Subsequently, attempts were made to collect data on category C workers. At the time of the 2nd analysis, this latter task had been achieved for many – although not all – of the participating organisations. However, an important advance for the current analysis has been the inclusion of category B and category C workers at MoD and at two additional BNFL sites (Capenhurst and Springfields). The definition of the study population for each employer/site and the inclusion of workers according to the above four categories are described in Appendix A.

Table 2.1 gives details of the numbers of employments that are eligible for the 3rd analysis, split by employer. In this table, people who were employed at more than one employer are counted for each of their employments. Thus the total number of employments (198,880) exceeds the total number of workers in the 3rd analysis, namely 174,541. Table 2.2 shows that most of the workers had only one NRRW employment, but that just over 20,000 people in the 3rd analysis had worked for two or more of the organisations that participate in the NRRW. For these people, employment and dose histories were unified across employers, even if some of the employers or sites were not included in this analysis (eg. non-classified workers at Naval dockyards).

TABLE 2.1 Numbers of employments and refusals by site

Employer/Site	Employments	Refusals
AWE	15809	76
British Energy Generation and Magnox Electric (England & Wales)	14130	616
Berkeley Centre	*1310*	54
Berkeley power station	*1318*	54
Bradwell	*1252*	29
Dungeness	*2292*	85
Hinkley Point	*2419*	143
Oldbury	*1293*	62
Sizewell-A	*1247*	46
Trawsfynydd	*1184*	79
Wylfa	*1094*	64
Non-power station staff	*721*	0
British Energy Generation and Magnox Electric (Scotland)	3757	66
Hunterston	*2267*	55
Torness	*1490*	11
BNFL	48183	407
Capenhurst	*3921*	75
Chapelcross	*2285*	4
Risley	*1854*	4
Sellafield	*23026*	128
Springfields	*17097*	196
GE Healthcare	4286	57
HPA-RPD	399	8
Chilton	*289*	7
Leeds	*69*	1
Glasgow	*41*	0
MRC Harwell	390	9
MoD	67112	209
Navy	*27508*	18
Army	*5828*	11
RAF	*13871*	16
Civilian	*19905*	164
PDS	587	7
CEC-Time	*191*	2
Honeywell Control Systems	*145*	2
Picker International	*251*	3
Rolls-Royce Submarines	3449	42
Main Site	*2443*	17
RR Power & Process (Hartlepool).	*103*	0
Manufacturing Division	*903*	25
STFC	3188	55
Daresbury	*789*	38

TABLE 2.1 Numbers of employments and refusals by site

Employer/Site	Employments	Refusals
Rutherford Appleton	*2399*	17
UKAEA	30668	636
Dounreay	*7218*	327
Harwell, Culham & London	*15525*	124
Risley & Culcheth	*3560*	61
Winfrith	*4365*	124
Other sites	6922	0
Total	198880	2188

TABLE 2.2 Number of employments per individual

Number of employments	Number of individuals
1	154399
2	17019
3	2468
4	455
5	110
6	38
7	21
8	11
9	8
10	3
11	6
12	2
13	0
14	1
Total Individuals	174541
Total Employments	198880

2.2 Collection of personal and dose information

Appendix B lists the data that are collected from participating organisations. The data fall into the following three categories, bearing in mind that some of these data (eg. date of birth) contribute to more than one category.

(a) Information used to identify the individual, in the course of communications with either the employer or organisations that provide follow-up information (see section 3), as well as to recognise successive employments by the worker at more than one NRRW employer. Examples of these data are name, date of birth and National Insurance Number.

(b) Information on factors that influence mortality and cancer incidence rates; eg. date of birth, gender and industrial classification (which is correlated with socio-economic status).

(c) Radiation dose history, which is limited here to recorded exposure to external radiation, with neutron and pro-rata notional dose components identified separately, together with flags of monitoring for internal emitters. (Notional doses are defined in Appendix D of Muirhead *et al*, 1999b.)

Data are notified to the NRRW on an annual basis. An electronic dataset, in a standard format, is securely transferred to the researchers and electronically processed. In this way new records are notified and annual dose exposures as well as other data items are updated within the NRRW database. Data anomalies are resolved by liaison between data providers and researchers.

Other data provision, for example the addition of historic workers or historic dose data, usually entails bespoke datasets and detailed electronic processing.

2.3 Characteristics of the study population

Table 2.3 lists the study population according to the worker's first employer, amongst those organisations that are included in the 3rd analysis. In contrast to Table 2.1, each worker is included only once in this table. There are wide differences in the numbers of employments between employers, from a few hundred up to tens of thousands.

TABLE 2.3 Number of employments by first employer

Employer/Site	Number of employments
AWE	14840
British Energy Generation and Magnox Electric (England & Wales)	13395
Berkeley Centre	*1205*
Berkeley power station	*1268*
Bradwell	*1191*
Dungeness	*2151*
Hinkley Point	*2264*
Oldbury	*1234*
Sizewell-A	*1206*
Trawsfynydd	*1142*
Wylfa	*1049*
Non-power station staff	*685*
British Energy Generation and Magnox Electric (Scotland)	3155
Hunterston	*2041*
Torness	*1114*
BNFL	40284
Capenhurst	*2826*
Chapelcross	*2024*
Risley	*1315*
Sellafield	*20631*
Springfields	*13488*
GE Healthcare	3893
HPA-RPD	281
Chilton	*191*
Leeds	*58*
Glasgow	*32*
MRC Harwell	364
MoD	64909
Navy	*26767*
Army	*5716*
RAF	*13755*
Civilian	*18671*
PDS	486
CEC-Time	*144*
Honeywell Control Systems	*114*

Employer/Site	Number of employments	
Picker International		*228*
Rolls Royce Submarines	2840	
Main Site		*2039*
RR Power & Process (Hartlepool)		*90*
Manufacturing Division		*711*
STFC	2428	
Daresbury		*662*
Rutherford Appleton		*1766*
UKAEA	27666	
Dounreay		*6610*
Harwell, Culham & London		*14555*
Risley & Culcheth		*2727*
Winfrith		*3774*
Total	174541	

As indicated in Table 2.4, 1241 workers (0.7% of the cohort) were excluded from the analysis. Most of these workers had incomplete follow-up information and/or insufficient personal or dose data. Many of them were within the group of pre-1977 MoD workers who were added to the NRRW in recent years. As described in Appendix A2.7, this analysis incorporates a much expanded cohort of MoD workers. Over 30,000 additional records were made available to the NRRW study, by adding information about workers who were monitored for occupational exposure to ionising radiation at MoD sites only before 1977. In general the data were of good quality. However, a small number of the records held by the dosimetry record holders had insufficient detail to enable the dose record to be matched to any other MoD personnel records or indeed to the records (described in section 3 and 4 below) that would provide vital status or follow-up information. These records form the majority (84%) of those excluded from the 3rd NRRW analysis on the basis of data completeness. The records did not generally seem to relate to long-term nor significantly exposed workers

TABLE 2.4 Reasons for exclusion from analysis

Reason	Number of individuals
Unflagged or untraced at NHSCRs	1039
Date of starting radiation work after date of stopping	130
Dose histories continue after date of death or emigration	35
Incomplete or inconsistent dates, including date of birth	36
Other	1
Total	1241

Note: Workers may have been excluded for more than one reason

Table 2.5 shows the distribution of the study population by period of birth and gender. As in the 2nd analysis, this distribution shows a peak for births between the late 1940s and the early 1960s. However, the 3rd analysis study population includes more workers born before then, owing to the inclusion here of additional category C workers, as well as more workers born in the 1970s. Just under 10% of all workers are female and they tend to have been born later than the male workers. In particular, the proportion of workers who are female is over 20% amongst those born in the 1970s or later, compared with a value of less than 10% for those born in the 1940s or earlier. In addition, mean lifetime doses for females are much lower than those for males.

TABLE 2.5 Study population by year of birth and gender

Period of birth	Male	Female	Total	Percentage by birth period
Before 1915	10108	332	10440	6%
1915-19	5011	213	5224	3%
1920-24	9136	468	9604	6%
1925-29	10256	568	10824	6%
1930-34	11427	818	12245	7%
1935-39	12971	1072	14043	8%
1940-44	14753	1243	15996	9%
1945-49	18299	1494	19793	11%
1950-54	15515	1697	17212	10%
1955-59	16261	2232	18493	11%
1960-64	15104	2387	17491	10%
1965-69	10923	2332	13255	8%
1970-74	5941	1695	7636	4%
1975-79	1578	444	2022	1%
1980 or later	222	41	263	0%
Total	157505	17036	174541	
Mean lifetime dose (mSv)	27.0	5.7	24.9	

Detailed information on social class is not available in general for workers on the NRRW. However, workers are classified as being either “industrial” or “non-industrial”. Historically, this classification appeared to be correlate well with a combination of social classes V, IV and III (manual) in the case of industrial workers and with social classes III (non-manual), II and I in the case of non-industrial workers. With the passage of time, the distinction between industrial and non-industrial workers (who tended to be classified on the basis of whether they were paid weekly or monthly) has become less clear. However, as will be shown later, industrial classification still appears to be correlated with social class. Table 2.6 shows the distribution of workers by industrial classification and by employer. Whilst there are more industrial workers than non-industrial workers overall, the ratio of these values varies between employers and sites. Information on industrial classification was available for 98.4% of workers. Many of the workers with unspecified industrial classification had first been employed by MoD, but

even here the percentage of workers whose industrial classification could be classified was 96.9%.

TABLE 2.6 Study population by industrial/non-industrial classification and first employer

Employer/site	Industrial	Non-industrial	Unspecified	Total
AWE	5967	8848	25	14840
British Energy Generation and Magnox Electric (England and Wales)	8527	4652	216	13395
Berkeley Centre	*328*	*861*	*16*	*1205*
Berkeley power station	*874*	*372*	*22*	*1268*
Bradwell	*858*	*323*	*10*	*1191*
Dungeness	*1507*	*626*	*18*	*2151*
Hinkley Point	*1568*	*665*	*31*	*2264*
Oldbury	*880*	*325*	*29*	*1234*
Sizewell-A	*859*	*318*	*29*	*1206*
Trawsfynydd	*803*	*306*	*33*	*1142*
Wylfa	*759*	*267*	*23*	*1049*
Non-power station staff	*91*	*589*	*5*	*685*
British Energy Generation and Magnox Electric (Scotland)	1447	1705	3	3155
Hunterston	*1445*	*593*	*3*	*2041*
Torness	*2*	*1112*	*0*	*1114*
BNFL	23324	16774	186	40284
Capenhurst	*2053*	*683*	*90*	*2826*
Chapelcross	*1201*	*817*	*6*	*2024*
Risley	*78*	*1227*	*10*	*1315*
Sellafield	*10725*	*9892*	*14*	*20631*
Springfields	*9267*	*4155*	*66*	*13488*
GE Healthcare	838	2952	103	3893
HPA-RPD	5	272	4	281
Chilton	*3*	*185*	*3*	*191*
Leeds	*0*	*57*	*1*	*58*
Glasgow	*2*	*30*	*0*	*32*
MRC Harwell	26	338	0	364
MoD	44671	18255	1983	64909
Navy	*20711*	*5756*	*300*	*26767*
Army	*4173*	*1470*	*73*	*5716*
RAF	*11113*	*2342*	*300*	*13755*

TABLE 2.6 Study population by industrial/non-industrial classification and first employer

Employer/site	Industrial	Non-industrial	Unspecified	Total
Civilian	*8674*	*8687*	*1310*	*18671*
PDS	430	45	11	486
CEC-Time	*140*	*4*	*0*	*144*
Honeywell Control Systems	*67*	*36*	*11*	*114*
Picker International	*223*	*5*	*0*	*228*
Rolls-Royce Submarines	616	2110	114	2840
Main Site	*12*	*2027*	*0*	*2039*
RR Power & Process (Hartlepool).	*87*	*3*	*0*	*90*
Manufacturing Division	*517*	*80*	*114*	*711*
STFC	1027	1340	61	2428
Daresbury	*251*	*350*	*61*	*662*
Rutherford Appleton	*776*	*990*	*0*	*1766*
UKAEA	12076	15582	8	27666
Dounreay	*3573*	*3031*	*6*	*6610*
Harwell, Culham & London	*5880*	*8675*	*0*	*14555*
Risley & Culcheth	*660*	*2065*	*2*	*2727*
Winfrith	*1963*	*1811*	*0*	*3774*
Total	98954	72873	2714	174541

2.4 Radiation dose data

As in the previous two analyses, the 3rd analysis focuses on doses from penetrating radiation at the surface of the body that are estimated using personal dosemeters. Most of the doses are associated with x-rays and gamma rays, together – to a lesser extent – with beta particles and neutrons. Estimates of doses from internal emitters (ie. radionuclides which have been inhaled or ingested) were not generally available and consequently could not be used here. However, as described in Appendix B, workers who were monitored for potential exposure to internal emitters were identified.

Personal records of radiation exposure are maintained primarily to ensure compliance with legal or administrative dose limits, rather than for the purposes of epidemiological research and this is probably more the case for the more historical records. Accordingly, corrections have been applied to enable best possible data to be available for the epidemiological analysis. The corrections applied for this analysis are identical to those used for the 2nd NRRW analysis (Muirhead *et al*, 1999b).

The collective dose for the study population, after applying dose corrections, is estimated to be 4348 person Sv. Table 2.7 shows that about two-thirds of workers had a lifetime dose less than 10 mSv and that only 6% of workers had a lifetime doses in

excess of 100 mSv. Nevertheless, this latter group contributed nearly 60% of the collective dose in the study population.

TABLE 2.7 Study population by lifetime dose

Lifetime dose (mSv)	Number of individuals		Collective dose (person Sv)	
<10.0	118766	68%	245	6%
10.0-49.9	35402	20%	840	19%
50.0-99.9	9869	6%	692	16%
100.0 and above	10504	6%	2571	59%
Total	174541		4348	

Table 2.8 shows the distribution of lifetime dose and the collective and mean lifetime doses by site of first employment. The employers that form the main contributors to the collective external dose are BNFL, UKAEA, MoD and British Energy Generation and Magnox Electric (England and Wales), reflecting differing combinations of the numbers of workers and their dose distributions. The highest mean lifetime doses arise for PDS and BNFL, followed by UKAEA and GE Healthcare.

TABLE 2.8 Study population by lifetime dose and site of first employment

Employer/site	Dose range (mSv)				Total number of workers	Collective dose (person Sv)	Mean dose (mSv)
	<10.0	10.0-	50.0-	100.0+			
AWE	12240	2157	281	162	14840	122	8.2
British Energy Generation and Magnox Electric (England and Wales)	6313	5337	1132	613	13395	323	24.1
Berkeley Centre	*585*	*521*	*51*	*48*	*1205*	*26*	*21.9*
Berkeley power station	*377*	*481*	*206*	*204*	*1268*	*61*	*47.7*
Bradwell	*439*	*465*	*205*	*82*	*1191*	*40*	*33.2*
Dungeness	*1207*	*841*	*100*	*3*	*2151*	*31*	*26.7*
Hinkley Point	*633*	*1213*	*301*	*117*	*2264*	*71*	*31.4*
Oldbury	*718*	*448*	*61*	*7*	*1234*	*17*	*13.9*
Sizewell-A	*677*	*485*	*36*	*8*	*1206*	*16*	*13.6*
Trawsfynydd	*411*	*445*	*148*	*138*	*1142*	*45*	*39.5*
Wylfa	*664*	*362*	*21*	*2*	*1049*	*12*	*11.9*
Non-power station staff	*602*	*76*	*3*	*4*	*685*	*4*	*5.3*
British Energy Generation and Magnox Electric (Scotland)	1894	764	316	181	3155	71	22.7
Hunterston	*851*	*697*	*312*	*181*	*2041*	*68*	*33.5*
Torness	*1043*	*67*	*4*	*0*	*1114*	*3*	*3.0*
BNFL	19268	11343	3972	5701	40284	2160	53.6
Capenhurst	*2504*	*267*	*27*	*28*	*2826*	*18*	*13.8*
Chapelcross	*469*	*592*	*369*	*594*	*2024*	*177*	*87.5*
Risley	*1233*	*69*	*9*	*4*	*1315*	*5*	*3.9*
Sellafield	*7595*	*5886*	*2526*	*4624*	*20631*	*1687*	*81.8*
Springfields	*7467*	*4529*	*1041*	*451*	*13488*	*273*	*37.4*
GE Healthcare	2735	664	198	296	3893	122	31.4
HPA-RPD	207	51	15	8	281	4	14.2
Chilton	*147*	*27*	*11*	*6*	*191*	*2*	*12.7*
Leeds	*39*	*15*	*3*	*1*	*58*	*1*	*12.8*
Glasgow	*21*	*9*	*1*	*1*	*32*	*1*	*25.3*
MRC Harwell	348	14	2	0	364	1	2.1
MoD	56552	5878	1350	1129	64909	522	8.0
Navy	*24132*	*2321*	*238*	*76*	*26767*	*106*	*4.0*
Army	*5270*	*298*	*50*	*98*	*5716*	*43*	*7.5*
RAF	*13427*	*316*	*7*	*5*	*13755*	*25*	*1.8*

Employer/site	Dose range (mSv) <10.0	10.0-	50.0-	100.0+	Total number of workers	Collective dose (person Sv)	Mean dose (mSv)
Civilian	*13723*	*2943*	*1055*	*950*	*18671*	*348*	*18.6*
PDS	249	131	43	63	486	26	54.2
CEC-Time	*47*	*45*	*25*	*27*	*144*	*8*	*57.0*
Honeywell Control Systems	*96*	*9*	*5*	*4*	*114*	*1*	*11.6*
Picker International	*106*	*77*	*13*	*32*	*228*	*17*	*73.7*
Rolls-Royce Submarines	2213	497	115	15	2840	26	9.0
Main Site	*1825*	*183*	*23*	*8*	*2039*	*8*	*4.1*
RR Power & Process (Hartlepool).	*61*	*13*	*9*	*7*	*90*	*3*	*29.0*
Manufacturing Division	*327*	*301*	*83*	*0*	*711*	*15*	*20.5*
STFC	1709	600	83	36	2428	30	12.5
Daresbury	*556*	*89*	*10*	*7*	*662*	*6*	*9.1*
Rutherford Appleton	*1153*	*511*	*73*	*29*	*1766*	*24*	*13.7*
UKAEA	15038	7966	2362	2300	27666	940	34.0
Dounreay	*2865*	*2214*	*736*	*7955*	*6610*	*300*	*45.4*
Harwell, Culham & London	*7777*	*4545*	*1236*	*997*	*14555*	*450*	*30.9*
Risley & Culcheth	*2400*	*270*	*44*	*13*	*2727*	*15*	*11.9*
Winfrith	*1996*	*937*	*346*	*495*	*3774*	*175*	*46.3*
Total	118766	35402	9869	10504	174541	4348	24.9

Table 2.9 shows that mean doses tend to be higher for industrial than for non-industrial doses, although the ratio of these mean doses (some of which are based on relatively small numbers of workers) varies between employers.

TABLE 2.9 Breakdown of mean lifetime dose (in mSv) by industrial/non-industrial classification and first employer

Employer	Industrial	Non-industrial	Unspecified	**Total**
AWE	8.2	8.3	0.1	8.2
British Energy Generation and Magnox Electric (England and Wales)	27.5	18.0	23.4	24.1
British Energy Generation and Magnox Electric (Scotland)	36.5	11.1	8.5	22.7
BNFL	60.5	44.6	5.2	53.6
GE Healthcare	24.3	34.1	13.4	31.4
HPA-RPD	0.3	14.6	0.8	14.2
MRC Harwell	3.0	1.8	0.0	2.1
MoD	8.0	8.6	3.8	8.0
PDS	60.5	7.2	1.2	54.2
Rolls-Royce Submarines	25.0	4.6	4.2	9.0
STFC	9.9	14.4	12.4	12.5
UKAEA	40.6	28.8	1.4	34.0
Total	26.8	22.9	5.9	24.9

Table 2.10 shows the distribution of lifetime dose by the period of birth of the worker. Mean lifetime doses are larger for older than younger workers, reflecting both the longer period over which the former group could accumulate these doses and tightening of radiation protection standards over time.

TABLE 2.10 Study population by lifetime dose and period of birth

Period	Dose range (mSv)				Total number of workers	Collective dose (person Sv)	Mean dose (mSv)
	<10.0	10.0-	50.0-	100.0+			
Before 1915	4908	3494	942	1096	10440	462.2	44.3
1915-19	2391	1507	526	800	5224	324.4	62.1
1920-24	4608	2711	947	1338	9604	518.8	54.0
1925-29	5301	3001	1103	1419	10824	557.5	51.5
1930-34	6618	3207	1068	1352	12245	520.6	42.5
1935-39	8604	3394	962	1083	14043	414.4	29.5
1940-44	10843	3356	903	894	15996	365.7	22.9
1945-49	14231	3656	1007	899	19793	370.3	18.7
1950-54	12326	3290	812	784	17212	309.6	18.0
1955-59	13903	3198	815	577	18493	255.8	13.8
1960-64	14161	2576	525	229	17491	152.6	8.7
1965-69	11548	1453	222	32	13255	70.0	5.3
1970-74	7113	485	37	1	7636	22.4	2.9
1975 or later	2211	74	0	0	2285	3.6	1.6
Total	118766	35402	9869	10501	174541	4347.7	24.9

Table 2.11 shows the breakdown of lifetime dose by year of starting radiation work. The main contribution to the collective dose comes from those persons who started radiation work in the 1950s and – apart from a few pre-1945 workers – this group also had the highest lifetime doses. However, persons who started radiation work in the 1960s and 1970s also made a sizeable contribution to the collective dose.

TABLE 2.11 Study population by lifetime dose and period of starting radiation work

Period	Dose range (mSv)				Total number of workers	Collective dose (person Sv)	Mean dose (mSv)
	<10.0	10.0-	50.0-	100.0+			
1940-44	0	1	0	7	8	5.6	700.0
1945-49	998	1225	536	429	3188	165.3	51.9
1950-54	1925	2424	981	1704	7034	719.4	102.3
1955-59	4955	4597	1522	2275	13349	870.8	65.2
1960-64	8358	4791	1453	1600	16202	611.1	37.7
1965-69	15911	4477	1172	1198	22758	488.1	21.4
1970-74	13941	4104	1127	1275	20447	474.4	23.2
1975-79	15132	5665	1636	1447	23880	554.3	23.2
1980-84	15657	4022	918	437	21034	254.6	12.1
1985-89	16807	3031	438	130	20406	147.5	7.2
1990-94	15823	960	85	2	16870	48.7	2.9
1995-99	9257	105	1	0	9363	7.8	0.8
Total	118764	35402	9861	10504	174539	4347.6	24.9

Table 2.12 shows collective and mean annual doses according to the period of radiation monitoring. Other than for the sparse data prior to 1945, the mean annual dose was highest in the early 1950s and slightly lower during late 1950s through to the early 1970s. However, since then, mean annual doses have fallen steadily over time and – by the end of the 1990s – were less than 10% of the peak value. On the other hand, the numbers of workers monitored each year remained relatively constant from the 1970s through to the 1990s.

TABLE 2.12 Number of individuals monitored and collective and mean annual doses by period of monitoring

Period of monitoring	Number of workers monitored per year, summed over the relevant period	Collective dose (person Sv)	Mean annual dose (mSv)
Pre-1945	32	0.5	14.3
1945-49	5190	14.2	2.7
1950-54	30731	214.8	7.0
1955-59	62698	339.4	5.4
1960-64	117100	514.8	4.4
1965-69	152239	658.8	4.3
1970-74	176200	703.9	4.0
1975-79	197716	664.8	3.4
1980-84	229289	531.0	2.3
1985-89	242253	385.9	1.6
1990-94	226896	210.5	0.9
1995-99	184222	109.2	0.6
Total	1624566	4347.8	2.7

Table 2.13 shows the study population split by duration of radiation work and first employer. Overall, about 22% of workers were monitored for less than two years, whereas about 17% undertook radiation work for at least 20 years. This distribution varies somewhat by first employer.

TABLE 2.13 Study population by duration of radiation work and first employer

Employer	Duration of Radiation Work (years)									
	<2	2-4	5-9	10-14	15-19	20-24	25-29	30-39	40+	Total
AWE	3112	3250	2961	2048	1201	857	578	762	71	14840
British Energy Generation and Magnox Electric (England and Wales)	1285	1576	1810	1756	2152	2082	1566	1102	66	13395
British Energy Generation and Magnox Electric (Scotland)	409	259	456	745	440	421	306	119	0	3155
BNFL	7953	6326	6378	5232	4504	4148	2552	2825	366	40284
GE Healthcare	727	804	800	613	413	256	135	133	12	3893
HPA-RPD	33	53	57	47	23	23	37	8	0	281
MRC Harwell	76	121	67	34	21	17	13	14	1	364
MoD	17902	16700	13913	7882	4112	2511	1320	563	6	64909
PDS	21	61	90	78	85	62	36	40	13	486
Rolls-Royce Submarines	245	496	546	459	354	420	176	143	1	2840
STFC	490	489	432	277	199	147	136	239	19	2428
UKAEA	6946	5452	4482	2849	2436	1864	1473	1840	324	27666
Total	39199	35587	31992	22020	15940	12808	8328	7788	879	174541

3 METHOD OF FOLLOW-UP

3.1 Introduction

The method of following up the study population is similar to that used in previous NRRW analyses, with the exception that it has been expanded to cover cancer incidence as well as mortality. For occupational cohort studies in the UK such as the NRRW, it is not necessary to approach workers, their families or their GPs in order to study rates of mortality and cancer incidence in the workforce. Indeed, workers in the NRRW are routinely informed at the time of enrolment that the investigators would not be contacting either them or their families subsequently. As described below, the National Health Service Central Registers (NHSCRs) form the main source of information on deaths, cancer registrations and emigrations. Subject to ethical requirements and data protection provisions, the NHSCRs can pass such data to investigators who are undertaking approval Medical Research studies, such as the NRRW. The availability of such data on a national basis means that it is possible to ascertain these events in a relatively complete and uniform fashion. Nevertheless, as highlighted in section 4, other data sources are used to check the quality and completeness of the data provided by the NHSCRs.

3.2 Determination of deaths and emigrations

Work was undertaken to determine the vital status of all workers in the study population on 1 January 2002, and to identify as many as possible of those who had emigrated by that time. The methods employed were similar to those adopted in the previous two analyses. Members of the study have been "flagged" at the NHSCRs for England and Wales (situated at the General Register Office, GRO, of the Office for National Statistics, ONS, in Southport) and for Scotland (at the General Register Office for Scotland, GRO(S), in Dumfries). These offices routinely send details of deaths and emigrations among study members. Data have also been collected from regional offices covering Northern Ireland (namely, the Central Services Agency, CSA, Belfast and the General Register Office for Northern Ireland, GRO (NI)), the Isle of Man and the Channel Islands.

Information on mortality provided as by the NHSCRs as part of the flagging and follow-up process was supplemented by information collected in the course of validation checks (see section 4). In particular, based on the findings from vital status checks conducted at the Department of Work and Pensions (DWP), as well as cross-checks undertaken in conjunction with other research groups, attempts were made to trace additional death details at the NHSCRs.

For men who were found to have died, both the underlying and the contributory causes of death, as stated on the death certificate, were coded according to the 9th revision of the International Classification of Diseases (ICD-9). Deaths from 2000 onwards were supplied by the Scottish NHSCR based on the ICD 10th revision (ICD-10) and deaths provided by the NHSCR for England and Wales from 2001 were coded based on ICD

10th revision coding. For all ICD-10 coded events, causes of death were recoded to ICD-9 so as to make them compatible with the earlier deaths.

Table 3.1 shows the vital status of workers in the analysis at the end of follow-up, ie. 31 December 2001. As in previous analyses, the majority of workers were still alive at the end of follow-up. However, the number of deaths is more than double that in the 2nd analysis, reflecting both the longer follow-up and the expansion of the cohort.

TABLE 3.1 Status of workers in the 3rd analysis at the end of follow-up

Status	Number of individuals
Alive	140606
Dead	28320
Emigrated	4579
Untraced	1036
Total	174541

Table 3.2 gives the distribution of year of death for those study participants who died during the follow-up period. As in previous analyses, the numbers rise sharply with calendar period and approaching half of the deaths occurred from 1990 onwards. Nonetheless, relative to the previous analysis and reflecting the inclusion of additional groups of historical workers, there are additional deaths in earlier years, with almost 25% of the additional deaths having occurred in years before 1990.

TABLE 3.2 Distribution of deaths by year of death

Period	Number of individuals
1955-59	253
1960-64	601
1965-69	1111
1970-74	1824
1975-79	2676
1980-84	3608
1985-89	4270
1990-94	5197
1995-99	6164
2000-2001	2615
Total	28319

3.3 Determination of cancer incidence

Cases of cancer among workers in the study were determined by combining data on cancer registrations with mentions of cancer (either as underlying cause or as a

contributory cause) on death certificates. Cancer registration data are collected in regional cancer registries covering England, Wales and Scotland. Since 1971 these data have been passed to the NHSCRs. Under agreements reached with the participating organisations and with the British Medical Association Central Ethics Committee in 1981, data on cancer registrations among workers in the study are passed routinely to the investigators by the NHSCRs.

Cancer registrations supplied to the study team were coded to ICD-9, except for some pre-1979 cancers which were coded to ICD-8 and cancers with registration dates after 1994 from England and Wales, and with registration dates after 1996 from Scotland, which were coded to ICD-10.

The analysis of cancer incidence was based on the earliest cancer mentioned on either a cancer registration or a death certificate, with the following exceptions:

- leukaemia, multiple myeloma or lymphoma was selected in preference to other cancers, with the corresponding earliest date chosen;
- non-melanoma skin cancer was selected only if no other malignant cancers were listed or if a mentioned cause of death was either a tumour of unspecified site or a secondary cancer;
- malignancies were selected in preference to benign conditions.

The analysis includes all cancers registered during the period of the follow-up (ie. up to 1/1/2002) and which had been received from the NHSCRs by the time of the analysis.

4 VALIDATION

4.1 Personal and dose information

Checks on the accuracy and completeness of the data held by the NRRW have been made at the various participating sites. For organisations included in the first and second NRRW analyses, the outcomes of these audits has been described in Appendices E of Kendall *et al* (1992b) and Muirhead *et al* (1999b). Most dosimetry and personal data items are now transferred to the NRRW within a fixed format electronic dataset and on an annual basis. This strategy reduces the probability of transcription errors and provides more transparent data processing capability, thus providing better data quality assurance. The data processing software includes test on data matching, data completeness and the plausibility of the data content. Anomalous data are further inspected and assured by the researchers in conjunction with data providers.

For some groups, however, data transfer mechanisms were necessarily different and for those groups additional data audits were conducted in advance of this 3rd NRRW analysis. Further details are provided in Appendix C.

4.2 Ascertainment of deaths and emigrations

Work undertaken for previous NRRW analyses has demonstrated the high quality of data notification by the NHSCRs for England, Wales and Scotland. Nonetheless the size, duration and complexity of the work undertaken to flag workers at the NHSCRs is known to have caused a small degree of incompleteness in data notification. Accordingly, two specific data cross-checking exercises were undertaken to investigate and to improve the coverage of follow-up data held for the NRRW. These were carried out as discussed below.

4.2.1 Cross-study cross-checks of follow-up data

A number of workers included in the NRRW study are also members of ongoing 'industry cohort' studies such as that of AWE employees, of former BNFL employees and of former UKAEA employees. These industry studies are currently operated by researchers at Nuvia Limited (AWE and UKAEA worker studies) and at the Westlakes Research Institute (the BNFL worker studies).

At the time when these studies were being initiated and study participants were being flagged at the NHSCRs, a number of 'double-flagging' arrangements were agreed which were designed to reduce the tracing demands on NHSCR staff who were, at the time, working with paper-based registers. These arrangements generally worked well. However, investigation of various aspects of follow-up over the decades of the NRRW analyses had identified some instances of incomplete data notification. This was due to the way in which the double-flagging arrangements had been implemented and communicated across the different NHSCRs and over the years that the system had been in practice, particularly at the time that the registers were converted to electronic files. For example, it was noted in the 2nd NRRW analysis that there was a shortfall in the number of deaths among ex-workers at Dounreay (Muirhead *et al*, 1999b). This cross-study cross-check was conducted in order to assure that historic data provision issue were resolved and to enable the research projects to move forward with full understanding of the data completeness status.

This cross-study cross-check project proposal drawn up by the three research groups involved. It was presented to workforce representatives and was approved by NHSCR/ONS/GROS and by staff at the Medical Research Information Service (NHS-IC MRIS, now part of the NHS Information Centre, formerly NHSCR/ONS). The MRIS staff were subsequently able to provide invaluable support by resolving anomalies and, where appropriate, providing additional information.

The objectives of this project were:

- To provide reassurance that, for each individual person on more than one study, the same record had been flagged by NHSCR.
- To provide reassurance that each MR study had received satisfactory coverage of follow-up data.
- To identify, if necessary, why gaps in data provision had occurred and, if

appropriate, to identify strategies to complete coverage.

The cross-check was designed to inform HPA researchers operating the NRRW as well as researchers at Nuvia, operating the AWE and UKAEA worker studies and researchers at Westlakes operating the BNFL worker study. Comparisons only included records known to be common across a pair of datasets and data were not shared by all research groups.

A total of 80752 NRRW records were included in this cross-check. To simplify the cross-checking work, the cross-checks included a wider grouping than that applied for the 3rd NRRW analysis. Records for workers with an employment history involving more than one of the relevant organisations were included in each relevant cross-check.

Comparisons were made to see whether:

a) The same date of death, or absence of date of death was recorded by both partners.

b) In the event of a death being recorded, the same cause of death information was held by both partners.

c) The same cancer registration information was recorded by both partners.

Of the 80752 records compared, 2203 (3%) required investigation due to differences in the follow-up information recorded by the relevant researchers. Roughly 1% of the differences fell within each of the groups (a, b and c) outlined above

Less than 1% of the records had differences in either the date or fact of death information. In the largest group within this, it was found that only one of the parallel research studies had details of a death which should have been known to both. Following investigations by the NHSCR staff, who checked in each case whether the correct death trace had been made, details of just over 200 death events were additionally recorded for the NRRW and a similar number were also additionally reported for the other researchers combined. The majority of the NRRW records identified in this way did fall within the groups discussed in section 3.2 as being known to have incomplete NHSCR follow-up status, although there were a small number that had been matched to the wrong NHSCR record and whose status may not have been clarified without this cross-check.

Only a small number of discrepancies in date of death were identified and most were attributed to mis-entered dates – often as a result of handwritten death certificates where, for example, the difference between “thirteenth” and “thirtieth” can be difficult to differentiate from the ‘copperplate’ script. There were, however, 20 cases where a different death had been reported for the same individual. These events were all investigated by the NHSCRs who re-checked the matching and event notification to confirm the correct data to the researchers.

The final group identified from the fact of death checks was the group consisting of study participants who had died overseas and whose fact of death would not usually be known to the NHSCRs (because the individual was no longer living in the UK, for

example). Each research group had recorded fact of death information for some individuals whose deaths were not known to the parallel research study.

Differences in cause of death information were investigated at two levels. The first check was to see whether the underlying cause of death was identical. The second check was to ascertain whether relevant contributory cause of death had been provided to each relevant researcher. This latter cross-check was not as extensive as the check of the underlying cause of death, although for cancer as a contributory cause, full comparisons and investigations were undertaken. Just under 1% of the records in the cross-check raised a difference in data held but most were not significant. It was noted that time of flagging can make a difference to data ascertainment; for example, flagging a record well after the death of the individual may mean that researchers are notified of the cause of death following post-mortem, whereas a notification upon death will provide researchers with the originally recorded cause of death. However, late flagging may also make tracing and therefore ascertainment of death events more difficult, especially if the death had occurred before 1993 and the individual is therefore not included on electronic NHSCRs. There were also some differences identified from different coders' interpretation of the chain of causes of death recorded on the death certificate; these differences would have caused no significant differences for the NRRW analysis.

Just over 1% of the records examined were identified as having at least one difference in the cancer registration data held by the parallel studies. Investigation of these differences, by researchers and by the NHSCRs, identified that many differences could be attributed to reporting issues, especially where the cancer registries had revised details within a registration. There were also, however, a number of additional cancer events notified to all research groups as an outcome of this cross-check. Nonetheless, most of the issues noted also arose during the cancer registration data cross-checks undertaken by the HPA researchers and these are therefore discussed more fully in section 4.3.

The cross-study cross-checks were undertaken in parallel with other data verification work by both the HPA researchers and by the Nuvia and WRI researchers. It was therefore expected that some anomalies would be noted that would have been dealt with in the course of other ongoing work and this was, indeed, the case.

Overall the results of the work demonstrated a very satisfactory level of agreement across the datasets with only 3% of the records requiring investigation and a much smaller proportion being issues that would materially affect the analyses conducted by the researchers involved in the cross-study cross-checking work.

The discrepancies that were identified confirmed that the flagging and notification of events for some of the records submitted for flagging in the early years of the NRRW, AWE, BNFL and UKAEA studies was incomplete but affirmed that work being undertaken, by HPA researchers, separately from this particular cross-check would be largely likely to resolve these issues.

This work did, nonetheless, identify a number of issues for all of the research groups and certainly resulted in better coverage of mortality information and of cancer morbidity information being available for the 3rd NRRW analysis. Overall, however, the number of

issues raised were small and the work gives added confidence to the completeness of follow-up coverage for study participants.

The HPA researchers wish to acknowledge the assistance provided by the Medical Research teams who operate the NHSCRs at Southport and at Dumfries as well as the collaborating researchers at Nuvia Limited and at the Westlakes Research Institute.

4.2.2 Vital status checks at the Department of Work and Pensions (DWP)

A cross-check on follow-up was conducted at the Department of Work and Pensions (DWP). As an automated trace option was not available, the cross-check was targeted at those records with known follow-up issues following initial NHSCR follow-up. These records were identified, by the HPA researchers, based on outcomes of previous cross-checks with DWP for similar studies (eg. Muirhead *et al*, 1999b, 2003). A total of 5222 records were selected for investigation if there was reason to doubt the completeness of the follow-up information based on NHSCR flagging but also taking account of the current employment status of the worker; workers known to be in continuing work as radiation workers were not included in the DWP vital status checks.

An additional group of 769 records were submitted to DWP to test whether the researchers had adequately covered the groups likely to require additional review.

The results of the vital status checks by the DWP can be summarised as follows:-

(a) Not known to be dead: for records in this category, DWP had traced a record which did not indicate that the person had died.
(b) Known to be dead: for records in this category, DWP were able to provide the date of death (or a close approximation) and, in most cases, either the place of death or the place where a death grant had been claimed although sometimes it showed only the place where the person last had any 'contact' with the DWP (through salary for example). This information was helpful in enabling the NHSCR MRIS staff to identify the relevant entry in the death registers. A number of deaths reported by DWP had occurred outside the UK.
(c) Untraced: There were a number of records where the information that the researchers were able to provide to the DWP did not adequately give sufficient detail for the DWP to identify a match within their records.

Table 4.1 Third analysis DWP checks

	Alive	*(%)*	Dead	*(%)*	Untraced	*(%)*	TOTAL
Number	4746	*(79%)*	529	*(9%)*	716	*(12%)*	5991

Table 4.1 shows a summary of the results of the cross-checks by DWP. Overall, 716 records, 12% of those selected for investigation, were not traced to a recognised DWP record. The majority of these, 704, were those that had not been traced adequately by the NHSCRs and only 12 records were from the sample group.

The historic MOD records described in section 2.3 are a significant contributor to this component of the dataset and it is recognised that the data provided to the DWP were insufficient for them to adequately identify a unique record match. Records which could not be traced were excluded from the analysis.

Including events occurring both before the end of the analysis follow-up period and those occurring subsequently, the DWP cross-checks identified 529 reports of death not previously reported by the NHSCRs. NHSCR investigation of these reports enabled the identification of full death details in a number of cases although as a number of deaths had occurred outside the UK, full cause of death information was not available for all deaths reported in this way. For those cases where the NHSCRs had been able to confirm the fact of death, the deaths were included in the analysis with 'cause unknown' (799.9 in ICD-9).

The 1% sample, selected from records with no reports of death and where the records were thought to be adequately flagged at the NHSCRs, demonstrated that the targeted groupings had adequately identified the records requiring additional checks, with 98% of those submitted in the sample being reported by DWP as 'live' traces.

A number of the deaths identified through the DWP cross-checks and subsequently confirmed by the NHSCRs had occurred during the years prior to the period for which the NHSCRs have full electronic records. Unsurprisingly, the addition to the NRRW study group of additional historic worker records was largely responsible for this difficulty in identifying relevant records. It also became clear that a number of subsequently confirmed death events may not originally have been identified by the NHSCRs because the individuals concerned had migrated between the countries of England, Wales, Scotland and Northern Ireland. This was particularly pronounced in the case of ex-servicemen.

In summary, the outcome of the work with DWP demonstrated that this exercise was beneficial and that properly targeted cross-checks with agencies such as DWP enhance the completeness of vital status information, so allowing better completeness of the mortality and, where relevant, morbidity data. Such work is of particular benefit to a records based study such as the NRRW where workers may be identified at an early stage in a working life and are not in regular contact with researchers.

4.3 Ascertainment of cancer incidence

An investigation undertaken during 2001 and involving NRPB (now HPA) researchers and the NHSCRs at Southport (whose records cover patients in England and Wales) and Dumfries (whose records cover patients in Scotland) confirmed that there was a shortfall in the cancer registration data held by the researchers operating the NRRW study.

Previous NRRW analyses (Kendall *et al*, 1992a,b; Muirhead *et al*, 1999a,b) were mortality analyses only and thus cancer morbidity data had not been subjected to other cross-checks. For this 3rd NRRW analysis, therefore, work was undertaken to cross-

check data held for the NRRW study with records held by the NHSCRs and the cancer registries for patients in England, Wales and Scotland.

Data investigation/collection exercises were conducted between the HPA researchers and the NHSCR for England and Wales and the HPA researchers, the NHSCR for Scotland and the Scottish Cancer Registry at the Information and Statistics Division (ISD) of NHS Scotland. The cross-checks with the England and Wales records was undertaken between 2004 and 2005; the cross-checks with the Scottish records was undertaken later, in 2007, in order to allow time for data assimilation work that was already being undertaken between NHSCR Scotland and the ISD Scottish Cancer Registry.

The HPA researchers were very grateful for the support and for the approvals provided by the relevant NHSCRs and cancer registries for England, Wales and Scotland. The advice provided by the NHSCR and cancer registry staff was invaluable in resolving issues and resulted in much improved coverage of cancer incidence reporting for NRRW study participants.

A total of 642 additional cancer registrations were identified as a result of work with the National Cancer Intelligence Centre (NCIC) and the NHSCR at Southport. Most of these were associated with individuals who had died between 1971 and 1992, ie between the time that cancer registration data was collected on a national basis and the period when the NHSCR records were fully computerised.

A number of issues were identified as having contributed to the shortfall but all were related to issues which are no longer relevant and it is expected that data provision will be essentially complete for the future.

A total of 2194 workers from the NRRW were identified as matches with ISD records of cancer patients. As some of the matched patients had been diagnosed with more than one cancer registration, the number of cancers identified was 2508. Of the 2508 events detailed, 1410 were already known to the NRRW, 28 were known events but some detail required correction and 1070 events were previously unknown to the NRRW; this included 548 workers not previously reported as having had either a cancer death or a registration as a cancer patient.

Before the cross-checking work commenced, estimates of the completeness of notification of cancer morbidity data had been undertaken. This was based on the number of individuals who had been reported to have died and for whom cancer was recorded as either the underlying or a contributory cause of death (subsequently referred to as ‘cancer deaths’) and the number of those individuals for whom cancer registration data was, or was not, available. In 2002, the cancer registration data for workers that had died between 1974 and 1998 was judged to be 80% complete for the NRRW as a whole. Recent estimates, following the cancer cross-checks, now show a more satisfactory completeness rate of 95% for the same period. It is known that cancer registration reporting can take some time, but the NRRW database completeness is currently greater than 97% for all years 1991 to 2005. Also, the completness is more than 90% for years back to 1979.

It is clear that the cross-check exercise significantly improved the ascertainment of data. Investigation of the records involved revealed that various issues had contributed to the shortfall in data notification.

Historic issues such as the double-flagging arrangements as well as the dates at which each of those studies acquired approval to receive cancer data are believed to have affected the notification process historically. The current electronic flagging and record keeping system available to the NHSCRs now means that such issues are unlikely to significantly impact on future notifications.

Another issue recognised by the NHSCR Scotland and ISD staff who operate the Scottish Cancer Registry was the method by which the cancer registration event data is linked with NHSCR records and then subsequently made available to approved Medical Research projects. During the years 2000-2009 the NHSCR and ISD staff were able to implement a number of changes to the processing and notification processes such that the routine data notification process for researchers is now significantly improved.

5 METHOD OF ANALYSIS

5.1 General aspects

The methods of analysis were similar to those used in the two previous reports (Kendall *et al*, 1992a,b; Muirhead *et al*, 1999a,b). In particular, the analysis consisted of an "external analysis", in which the mortality of radiation workers was compared with that of the general population, and an "internal analysis", in which rates of mortality and cancer incidence were analysed for differences within the NRRW cohort; in particular, to see if there were any trends in rates with radiation dose.

The start of follow-up for each worker was taken to be the date of start of radiation work with a participating employer, the date from which full dose data were available, or 1st January 1955, whichever was later. Further details, split by employer, are given in Appendix A. As in the previous NRRW analyses, it was decided to exclude deaths prior to 1955, owing to indications of a substantial deficit in their number relative to national rates. Some of the analyses were based on a lag of, say, 2 or 10 years, in which case the follow-up commenced on the start of radiation work plus 2 / 10 years or on 1st January 1955, whichever was later. For the mortality analyses, workers were regarded as being at risk until their date of death or emigration, their 85th birthday, or 1st January 2002, whichever was earliest. For cancer incidence, workers were regarded as being at risk similarly, except that they were removed from the analyses on their date of cancer registration where appropriate. Deaths and cancers at ages of 85 years and over were excluded from the main analyses, because of problems of disease ascertainment at these ages. However, they were included in a subsidiary analysis (see Appendix D).

In addition to the types of analysis conducted in previous reports, some extra subsidiary analyses were conducted, in part to address points arising from the 15-country study of nuclear workers (Cardis *et al*, 2005, 2007; Vrijheid *et al*, 2007a,b). Furthermore, because of increased interest in the possible effects of radiation exposure on mortality from non-cancer diseases (Preston *et al*, 2003), these diseases were studied in more detail than was done previously.

5.2 External analysis

In this first part of the analysis, the mortality of the radiation workers was compared with that of the general population. In most instances the comparison was with the general population of England and Wales. However, in analyses by site of employment, data for workers at specific Scottish sites were also compared with rates for the general population of Scotland. Person-years at risk (ie. the length of time that each worker was in the study, summed over workers) were calculated for separately for men and women in each of fourteen, 5-year age groups (15–19, 20–24, … , 80–84 years) and in individual calendar years over the period 1955–2001. The person-years were multiplied by the corresponding age, gender and calendar year specific death rates for the general population and the resulting values were summed to give the expected number of deaths for each cause. Standardised Mortality Ratios (SMRs) were then calculated as the ratio of the observed to the expected number of deaths, multiplied by 100. These calculations were performed using the program PERSON YEARS (Coleman *et al*, 1986).

The statistical significance of the SMRs was calculated by assuming that the number of deaths observed from any cause had a Poisson distribution. Two-sided tests were used to assess whether the SMRs differed to a statistically significant extent from 100, ie. whether the observed mortality rates differed from national rates. Whilst there was a prior hypothesis linking radiation exposure to cancer, confounding factors could be expected to lead to a Healthy Worker Effect (Fox and Collier, 1976) - ie. lower mortality compared with national rates - which might dominate any effect of radiation. Consequently it was decided to test for both increases and decreases relative to national rates. Tests for trends and heterogeneity in SMRs according to factors such as age and gender were based on chi-squared statistics (Breslow and Day, 1987).

The external analysis was based on the underlying cause of death, coded according to the ninth revision of the ICD (WHO, 1977). Mortality rates for England and Wales since 1955 were calculated using computer tapes supplied by the Office for National Statistics (ONS). Where the analysis considered disease groupings whose ICD codes varied between revisions, these rates were bridge-coded to take account of the changes. This bridge-coding made use of information published in the statistical reviews of the Registrar General (1958, 1971a) and by the former Office of Population Censuses and Surveys (OPCS, 1982), which is now part of ONS. In view of the introduction of ICD-10 to code deaths in England and Wales towards the end of the study period, mortality rates for 1999 based on ICD-9 were also used for for 2000 and 2001. Mortality rates specific to social classes I and III (Registrar General, 1971b; OPCS, 1978, 1986) were used in an analysis of non-industrial and industrial workers, respectively. While the use

of these rates rather than those averaged over broader bands of social classes may lead to a small over-estimation of the adjusted SMRs for these two groups, the effect on differences and trends in these values should be small. For the years prior to 1968, national rates for subtypes of leukaemia were calculated using data published by Court-Brown and Doll (1959) and unpublished data based on a review of leukaemia death certificates for England and Wales from 1958 to 1967, made available by Professor LJ Kinlen (Kinlen, 1988). These rates for leukaemia subtypes have also been utilised in other studies, eg. of UK participants in the UK nuclear weapons test programme (Muirhead *et al*, 2003). Mortality rates for Scotland since 1955 were provided by the General Register Office (Scotland), and were used to derive SMRs for Scottish sites, both for all causes and all malignant neoplasms.

The external analysis was performed using solely data on mortality. This is because cancer incidence was assessed in this study using a combination of registration and mortality data (see section 3.3). Consequently, these rates cannot be compared with national rates that are based solely on cancer registrations.

5.3 Internal analysis

In view of the difficulty in interpreting the results of the external analysis owing to the "Healthy Worker Effect" described in section 5.2, greater emphasis is placed on the "internal analysis". This involved examining mortality in relation to radiation dose, after adjusting for other factors. The format of the analysis based on the full cohort was the same as in the first two NRRW analyses (Kendall *et al*, 1992a,b; Muirhead *et al*, 1999a,b), with amendments solely to allow for a longer period of follow-up and additional employers. In particular, the numbers of deaths and person-years were stratified by: age in 5-year groups (as described earlier); gender; calendar period (as 1955–, 1960–,…, 1995–, 2000–2001); industrial classification (industrial/non-industrial/unknown); and first employer as follows (see Appendix A):

(a) AWE;
(b) BNFL Sellafield;
(c) BNFL Chapelcross;
(d) other BNFL sites;
(e) British Energy Generation and Magnox Electric sites in England and Wales;
(f) British Energy Generation and Magnox Electric sites in Scotland;
(g) GE Healthcare;
(h) MoD workers monitored by DRPS;
(i) Rolls-Royce Submarines, together with workers monitored by PDS (other than those at HPA-RPD);
(j) STFC, HPA-RPD and MRC Harwell;
(k) UKAEA Dounreay;
(l) UKAEA Winfrith;
(m) UKAEA Risley/Culcheth;
(n) UKAEA Harwell/Culham/London.

For some of the subsidiary analyses, the data were also stratified according to time since starting radiation work, duration of radiation work or on the basis of whether the worker had ever been monitored for exposure to internal emitters (see Appendix D).

The strata were further subdivided by cumulative external dose, categorised as 0–, 10–, 20–, 50–, 100–, 200–, 400+ mSv. This stratification was performed using the program ARFAR (At Risk For Any Reason), which was developed at NRPB (Barry, 1986) and subsequently expanded here for analyses of the NRRW. This program subdivides the follow-up period according to how doses are accumulated over time. To allow for a latent period, the doses were 'lagged' in the internal analysis, ie. rather than seeking correlations between death rates and lifetime dose to the year in question, lifetime doses were summed up to a specified number of years before this year. This 'lag' period was taken to be 2 years when analysing leukaemia rates and 10 years for other cancers and other causes of death. Similarly, the first 2 years of follow-up following initial exposure were excluded when analysing leukaemia whilst the first 10 years were excluded for other cancers and death cases, in order to allow both for a latent period and for the possibility that the Healthy Worker Effect may be particularly strong soon after starting work. Within each stratum defined on the basis of non-radiation factors, a calculation was made of the number of deaths that would be expected in each dose category, given the total number of deaths over all dose categories and presuming no effect of dose.

Inference was based on a model under which, following the latent period, the excess relative risk (ERR) varies as a linear function of dose. The test for a trend in risk with dose, as described by Darby and Reissland (1981) and Little *et al* (1993), was then performed by:

(a) comparing the observed and expected numbers of deaths or cancers across dose categories to form a test statistic within each 'informative' stratum (ie. each stratum for which person-years were accrued in more than one dose category);

(b) pooling the stratum-specific test statistics in order to form an overall test statistic.

In particular, if O_{si} and E_{si} denote the observed and expected numbers respectively in stratum s and dose group i, then the test statistic is:

$$S = \sum_{s,i} d_i (O_{si} - E_{si})$$

where d_i is the lagged median dose (in Sv) in dose group i. To assess statistical significance, the standardised form of this 'score' statistic (Cox and Hinkley, 1974) – as given in Tables 6.9 and 6.10 - was generally compared with the standardised normal distribution. However, comparison with the normal distribution may not be appropriate when the data are sparse, and therefore the significance level was calculated using 100,000 simulations when the total number of strata was 100 or fewer. A one-sided significance test was performed of any increase in mortality or cancer incidence rates, since there was prior interest in any increase in cancer rates with increasing dose.

However, Tables 6.9-6.11 also list significance levels for two-sided tests, ie. based on looking for either an increasing or a decreasing trend in rates with increasing dose.

The ERR per Sv was estimated by fitting a linear relative model using the method of maximum likelihood (Breslow and Day, 1987; Cox and Hinkley, 1974), and confidence intervals were calculated on the basis of the score statistic *S*. Tables 6.9-6.11 list 90% confidence intervals for the ERR per Sv, together with 95% confidence intervals for selected cancer and causes of death. Occasionally all the person-years and deaths or cancer cases within a stratum fell in a single dose category, in which case this stratum was uninformative about any trend in risk with dose. However, these uninformative strata arose predominantly in the lowest dose group and only very rarely at higher doses.

As in previous analyses of the NRRW, particular attention was given in the internal analysis to diseases such as leukaemia for which there is a prior hypothesis of a link to radiation exposure. Accordingly, the cause of death was taken to be leukaemia, non-Hodgkin lymphoma or multiple myeloma if this was coded anywhere on the death certificate, even if it was not the primary cause. If there was no leukaemia, non-Hodgkin lymphoma or multiple myeloma, then neoplasms were selected in preference to non-neoplastic diseases. The inclusion of these extra cancer deaths should increase the power of the internal analysis. There should be no intrinsic tendency to bias estimates of risk since the internal analysis does not involve a comparison with national rates and the extra deaths may fall in any of the dose groups. However, as a check, a subsidiary analysis was performed that examined deaths classified solely on the basis of underlying cause (see Appendix D).

The disease categories studied here are mostly the same as those considered in the previous analysis (Muirhead *et al*, 1999a,b). However, some additional categories have been included here, such as the following.

(i) Many cancers of the liver are secondary cancers originating in other sites. Consequently, in addition to the standard definition of liver cancer (ICD 9th revision code 155), primary liver cancer has been studied in the analyses of specific types of cancer.

(ii) It is known that the registration of skin cancers other than melanoma is substantially incomplete. Whilst there is no particular reason to think that the completeness of registration would vary according to occupational radiation exposure, these cancers form a sizeable component of the total number of cancers registered in the UK. Consequently, in addition to analyses of the incidence of cancers of all types, results are presented for the incidence of all cancers combined excluding non-melanoma skin cancer, as a check as to whether the non-melanoma skin cancer findings affected the results for total cancer incidence. Since non-melanoma skin cancer is very rarely fatal, the impact of this category on analyses of total cancer mortality was minimal (see section 6.2).

5.4 Allowing for possible effects of age and time on radiation risks

The internal analysis described in section 5.3 is based upon a statistical model under which, following a lag period, the relative risk is constant over time. Studies of populations exposed to high radiation doses, such as the Japanese atomic bomb survivors (Preston *et al*, 2003, 2007; UNSCEAR, 2008), indicate that this is a fairly reasonable model for the risk of most solid cancers following exposure in adulthood, although the ERR per Sv may vary by attained age. On the other hand, these studies do indicate that the relative risk of leukaemia (other than CLL) varies with time since exposure (Preston *et al*, 1994, 2003; UNSCEAR, 2008). In particular, the risk model derived by the US BEIR VII Committee based on A-bomb data (NRC, 2006) incorporated age and temporal variations in the ERR.

Since the follow-up period in the first NRRW analysis was less than 25 years in most instances, potential time-variation in the relative risk was not modelled explicitly in that analysis (Kendall *et al*, 1992a,b). In the second NRRW analysis (Muirhead *et al*, 1999a,b), this issue was studied in more detail through a nested case-control analysis that aimed to fit risk models of the type previously proposed for leukaemia by the BEIR V Committee (NRC, 1990). However, the data lacked the precision required to draw inferences on possible temporal effects. As described in Appendix D, a similar analysis has been undertaken based on NRRW-3 data for leukaemia excluding CLL, in which the updated risk model proposed by the BEIR VII Committee (NRC, 2006) was considered. Again this involved a nested case-control analysis. In particular, rather than analysing data for the entire cohort and sub-dividing the person-years on the basis of cumulative dose, data on cases of leukaemia excluding CLL and on matched controls sampled from the cohort were utilised. In contrast to the 2nd NRRW analysis, incident cases as well as deaths from leukaemia were considered here. Information on how radiation doses were received over time for the cases and their controls was then used to allow for possible effects of time since exposure and age at exposure on any radiation-associated risk. The principal advantage of this nested case-control analysis is that it allows data on potential time variations in risk following chronic exposure to be handled in a relatively simple fashion. Furthermore, by choosing a large number of controls per case, the statistical power of the nested case-control analysis should be reasonably close to that of the full cohort analysis.

A similar analysis was performed for cancers other than leukaemia, in view of evidence that the risk of these cancers varies with attained age (Preston *et al*, 2003, 2007). Appendix D describes the analysis of nested case-control data for these cancers, using BEIR VII–type models that allow for possible effects of attained age and age at exposure on any radiation-associated risk.

6 RESULTS

6.1 Mortality - external analysis

Table 6.1 shows SMRs by broad cause of death in the study population. There is a strong Healthy Worker Effect. Without adjustment for social class, mortality from all causes is 81% of that expected in the general population of England and Wales (95% CI 80-82), while mortality from all malignant neoplasms is 84% of that expected in the general population (95% CI 82-86). Compared with rates for England and Wales as a whole, the SMR for industrial workers is nearly 50% higher than that for non-industrial workers, both for all causes and all malignant neoplasms. However, when compared with rates for social classes that equate approximately to these two groups of workers, the SMR for non-industrial workers is roughly 10% higher that for industrial workers, both for all causes and all malignant neoplasms. Nevertheless, even after adjusting for social class, mortality by broad cause in the study population is still lower than expected from England and Wales rates; namely an SMR of 84 (95% CI 83-85) for all causes and 82 (95% CI 81-84) for all malignant neoplasms.

TABLE 6.1 Standardised mortality ratios (SMRs)[a] by broad cause, gender and industrial classification

Gender	Industrial Classification	Number of Deaths		Unadjusted		Social-class adjusted	
		Observed	Expected	SMR	95% CI [b]	SMR	95% CI
All Causes							
Both	All	26731	33014	81	80-82	84	83-85
	Industrial	18285	19660.37	93	92-94	82	80-83
	Non-industrial	8146	12950.43	63	62-64	90	88-92
Males	All	25841	31852.94	81	80-82	84	83-85
Females	All	890	1161.06	77	72-82	84	79-90
χ^2 for heterogeneity in SMR between males and females				*2.77*		*0.01*	
All malignant neoplasms							
Both	All	8107	9666.63	84	82-86	82	81-84
	Industrial	5394	5640.72	96	93-98	80	78-82
	Non-industrial	2622	3905.75	67	65-70	88	85-91
Males	All	7752	9229.92	84	82-86	82	80-84
Females	All	355	436.71	81	73-90	84	76-93
χ^2 for heterogeneity in SMR between males and females				*0.36*		*0.17*	

Notes

(a) Based on the general population of England and Wales.

(b) Confidence interval.

Analyses conducted separately for males and females show a Healthy Worker Effect for both genders (see Table 6.1). Both for all causes and all malignant neoplasms, the

SMR for males based on mortality rates for England and Wales as a whole is greater that that for females, although the differences are not statistically significant**.** Since the proportion of females who are non-industrial workers is greater than the corresponding proportion for males, Table 6.1 also shows gender-specific SMRs based on social-class adjusted rates. Both for all causes and all malignant neoplasms, the social-class adjusted SMRs are very similar among males and females.

TABLE 6.2 Standardised mortality ratios (SMRs)[a] by broad cause and time since start of radiation work

		Unadjusted		Social class adjusted	
Years since start of radiation work	Observed deaths	SMR	95% CI [b]	SMR	95% CI
All Causes					
0-1	388	60	54-66	68	61-75
2-4	816	67	62-72	74	69-80
5-9	2059	75	72-78	81	78-85
10-14	2825	78	75-81	82	79-86
15-19	3653	82	80-85	85	82-88
20-24	4152	84	82-87	86	83-89
25-29	4129	85	82-87	86	84-89
30-34	3667	84	82-87	85	83-88
35+	5042	81	79-83	84	81-86
χ^2 for heterogeneity in SMR		*103.36****		*39.72****	
χ^2 for trend		*46.7****		*14.79****	
All malignant neoplasms					
0-1	97	64	52-79	66	54-81
2-4	219	72	63-83	74	65-85
5-9	644	89	82-96	90	83-97
10-14	833	83	77-89	83	77-89
15-19	1086	85	80-91	84	79-89
20-24	1236	85	81-90	83	79-88
25-29	1289	87	82-92	85	80-89
30-34	1134	84	79-89	81	76-86
35+	1569	81	77-85	79	76-83
χ^2 for heterogeneity in SMR		*17.93**		*16.02**	
χ^2 for trend		*0.13*		*0.67*	

Notes

(a) Based on the general population of England and Wales.

(b) Confidence interval.

*** p<0.001, ** p<0.001, * p<0.05, + 0.05<p<0.1

Table 6.2 shows SMRs by time since start of radiation work. For mortality from all causes, there is strong evidence of an increasing trend over time in the SMR that is unadjusted for social class. Part of this evidence appears to be due to particularly low

SMRs within the first five years after starting radiation work. The SMRs during this period are higher once adjustment is made for social class, but there is still evidence of an increasing trend over time in these adjusted all-cause SMRs. In contrast, there is no evidence of a time trend and in the SMRs for all malignant neoplasms, either with or without adjustment for social class. Whilst there is evidence of heterogeneity over time in the SMRs for all malignant neoplasms, much of this heterogeneity (as for all causes) appears to arise within five years of starting radiation work.

Table 6.3 indicates that SMRs for all causes of death and for all malignant neoplasms increase with increasing age at death in the absence of a social class adjustment, but are more stable once such an adjustment is made.

TABLE 6.3 Standardised mortality ratios (SMRs)[a] by broad cause and age at death

		Unadjusted		Social class adjusted	
Age group (years)	Observed deaths	SMR	95% CI [b]	SMR	95% CI
All Causes					
<25	189	84	73-97	112	96-129
25-34	583	69	64-75	93	86-101
35-39	460	64	58-70	76	69-84
40-44	762	69	64-74	83	77-89
45-49	1244	72	68-76	81	76-86
50-54	1956	75	72-78	84	77-81
55-64	6401	77	75-79	79	77-81
65-74	9017	84	83-86	85	84-87
75-84	6119	91	88-93	88	86-90
χ^2 for heterogeneity in SMR		*202.1****		*70.21****	
χ^2 for trend		*155.46****		*2.75+*	
All malignant neoplasms					
<25	11	49	24-87	52	26-92
25-34	102	77	63-94	80	65-97
35-39	122	82	68-98	86	71-103
40-44	202	76	66-87	79	69-91
45-49	373	78	70-86	83	74-91
50-54	657	80	74-86	84	78-91
55-64	2200	79	75-82	78	75-81
65-74	2883	86	83-89	83	80-87
75-84	1557	94	89-99	87	83-92
χ^2 for heterogeneity in SMR		*41.76****		*15.84**	
χ^2 for trend		*25.79****		*3.54+*	

Notes

(a) Based on the general population of England and Wales.

(b) Confidence interval.

*** p<0.001, ** p<0.001, * p<0.05, + 0.05<p<0.1

Table 6.4 shows strong heterogeneity with calendar period of death in the SMRs for all causes and all malignant neoplasms, either with a social class adjustment or – in the case of all causes – without such an adjustment.

TABLE 6.4 Standardised mortality ratios (SMRs)[a] by broad cause and calendar period

		Unadjusted		Social class adjusted	
Calendar period	Observed deaths	SMR	95% CI [b]	SMR	95% CI
All Causes					
1955-59	252	73	65-83	77	68-87
1960-64	598	76	70-82	81	74-87
1965-69	1106	78	73-83	82	77-86
1970-74	1810	81	78-85	85	81-89
1975-79	2632	84	81-88	89	86-93
1980-84	3518	86	83-89	92	89-95
1985-89	4096	80	78-83	84	81-87
1990-94	4886	81	78-83	83	80-85
1995-99	5557	80	78-82	82	79-84
2000-01	2276	77	74-80	78	74-81
χ^2 for heterogeneity in SMR		*30.27****		*63.14****	
χ^2 for trend		*1.21*		*12.36****	
All malignant neoplasms					
1955-59	70	84	66-107	85	66-108
1960-64	163	84	72-98	85	73-100
1965-69	287	80	71-90	81	72-91
1970-74	477	83	76-91	85	77-93
1975-79	721	87	81-94	90	84-97
1980-84	1007	88	83-94	92	86-97
1985-89	1179	78	74-83	78	74-83
1990-94	1568	83	79-87	80	76-85
1995-99	1863	86	83-90	82	78-85
2000-01	772	83	77-89	76	71-82
χ^2 for heterogeneity in SMR		*12.63*		*26.78***	
χ^2 for trend		*0.01*		*8.42***	

Notes

(a) Based on the general population of England and Wales.

(b) Confidence interval.

*** p<0.001, ** p<0.001, * p<0.05, + 0.05<p<0.1

TABLE 6.5 Standardised mortality ratios (SMRs)[a] by broad cause and duration of radiation work

		Unadjusted		Social class adjusted	
Length of radiation work	Observed deaths	SMR	95% CI [b]	SMR	95% CI
All Causes					
<5	11307	83	81-84	85	83-86
5-9	4943	83	80-85	85	83-88
10-14	3322	80	77-82	81	78-84
15-19	2638	82	79-85	84	81-87
20-24	1994	81	77-85	85	81-89
25-29	1407	77	73-81	84	79-88
30+	1120	68	64-72	77	73-82
χ^2 for heterogeneity		*48.31****		*14.45**	
χ^2 for trend		*28.66****		*5.2**	
All malignant neoplasms					
<5	3399	86	83-89	83	80-86
5-9	1507	88	84-93	86	82-90
10-14	926	78	73-83	76	71-81
15-19	770	83	77-89	81	76-87
20-24	619	84	77-90	83	77-90
25-29	481	84	76-91	86	78-94
30+	405	73	66-81	78	71-86
χ^2 for heterogeneity		*17.22***		*11.28*+*	
χ^2 for trend		*7.26***		*0.55*	

Notes

(a) Based on the general population of England and Wales.

(b) Confidence interval.

*** p<0.001, ** p<0.001, * p<0.05, + 0.05<p<0.1

There is strong evidence of a decrease in the all-cause SMR with increasing duration of radiation work, either without or (to a lesser extent) with adjustment for social class (see Table 6.5). The social class-unadjusted SMR for all malignant neoplasms also decreases with increasing duration of radiation work, whereas there is less evidence of such a trend in the corresponding SMR that is adjusted for social class. A general finding from Table 6.5 is that the SMRs for those involved in radiation work for more than 30 years are relatively low.

Table 6.6 shows all-cause SMRs (unadjusted for social class) by first employer and by site of first employment. There is wide variation in the SMRs, part of which is likely to represent random variation due to small numbers; for example, for some of the smaller employers or sites. Aside from HPA-RPD, MRC Harwell and PDS, all-cause SMRs by first employer vary between 63 and 90 when based on a comparison with mortality rates for England and Wales. The corresponding range based on social-class adjusted rates is narrower, between 72 and 90 (see Appendix E). It can also be seen in Appendix E

that the pattern in SMRs for all malignant neoplasms by employer is similar to that for all-cause SMRs. For sites in Scotland (Dounreay, Chapelcross, Hunterston and Torness), the all-cause SMRs shown in Table 6.6 are lower when calculated using Scottish rates (rather than rates for England and Wales) and they mostly fall within the range of SMRs for comparably-sized sites in England and Wales.

An important addition to the cohort for this 3rd analysis is a group of MoD radiation workers who were monitored by DRPS up to (but not after) the end of 1976. Workers who were monitored from 1977 onwards had been included in previous NRRW analyses. As mentioned in section 2.3, it was not possible to include all of these pre-1977 workers in the 3rd analysis, owing to a lack of identifying data or service details in some instances, although the proportion of workers so excluded was judged to be small enough to allow this group of early workers to be included here. This judgement is backed up by examination of SMRs for the group of MoD workers who were monitored by DRPS up to the end of 1976. (This group was considered in preference to those workers who ceased monitoring by DRPS prior in 1977, so as to reduce any selection effect.) The all-cause SMRs for this group, both taken as a whole (ie. 79) and for each service (Navy - 83, Army - 80, RAF - 74, civilians - 79), are compatible with the corresponding values for all MoD workers given in Table 6.6.

TABLE 6.6 Standardised mortality ratios (SMRs) for all causes by first employer

Employer/Site	Number of deaths		SMR	95% CI [b]
	Observed	Expected [a]		
AWE	2746	3537.34	78***	75-81
BNFL	9216	10211.99	90***	88-92
Capenhurst	655	741.96	88**	82-95
Chapelcross	534	566.01	94	87-103
- based on Scottish rates		*686.3*	*78****	*71-85*
Risley	52	106.28	49***	37-64
Sellafield	3904	4136.37	94***	91-97
Springfields	4071	4661.37	87***	85-90
STFC	373	506.13	74***	66-82
Daresbury	103	142.34	72***	59-88
Rutherford Appleton	270	363.79	74***	66-84
MoD	4790	6131.4	78***	76-80
Navy	1552	1893.41	82***	78-86
Army	252	333.67	76***	66-85
RAF	987	1387.94	71***	67-76
Civilian	1999	2516.38	79***	76-83
MRC Harwell	19	31.51	60	36-94
HPA-RPD	5	14.42	35**	11-81
British Energy Generation and Magnox Electric (England & Wales)	2281	3063.87	74***	71-78
Berkeley Centre	167	230.8	72***	62-84
Berkeley power station	281	340.83	82***	73-93
Bradwell	257	360.62	71***	63-81
Dungeness	276	398.91	69***	61-78
Hinkley Point	349	445.33	78***	70-87
Oldbury	184	263.49	70***	60-81
Sizewell	209	307.44	68***	59-78
Trawsfyndd	231	273.75	84**	74-96
Wylfa	165	203.9	81**	69-94
Non-power station staff	162	238.78	68***	58-79
GE Healthcare	204	322.87	63***	55-72
PDS	24	37.31	64	41-96
CEC-Time	5	6.65	75	24-176
Honeywell Control Systems	1	4.76	21	1-117
Picker International	18	25.9	69	41-110
Rolls-Royce Submarines	220	305.52	72***	63-82
British Energy Generation and Magnox Electric (Scotland)	277	316.84	87	77-98
- based on Scottish rates	*277*	*396.29*	*70****	*62-79*
Hunterston	246	268.12	92	81-104

TABLE 6.6 Standardised mortality ratios (SMRs) for all causes by first employer

Employer/Site	Number of deaths: Observed	Expected [a]	SMR	95% CI [b]
- based on Scottish rates		*332.42*	*74****	*65-84*
Torness	31	48.72	64**	43-90
- based on Scottish rates		*63.87*	*49****	*33-69*
UKAEA	6575	8533.83	77***	75-79
Dounreay	1494	1431.56	104	99-110
- based on Scottish rates		*1738.07*	*86****	*82-90*
Harwell-Culham etc	3774	5294.68	71***	69-74
Risley	643	899.64	71***	66-77
Winfrith	664	907.95	73***	68-79

Notes

(a) England and Wales rates used, except where stated.

(b) Confidence interval.

*** p<0.001, ** p<0.05, + 0.05<p<0.1

Table 6.7 lists SMRs for specific causes of death. These values are unadjusted for social class, since it is not possible to derive social class adjustments for individual causes. However, in order to take account of any latency effects or weakening over time in the health worker effect, results are presented both including and excluding the first 10 years after starting radiation work. (For leukaemia, a two-year lag was used.) For most causes of death, mortality rates are lower than expected in the general population of England and Wales. In some instances, particularly for causes with relatively small numbers of deaths, the findings are consistent with England and Wales mortality rates. However, for more common causes – particularly those related to smoking such as lung cancer – the SMR is statistically significantly lower than 100. There are only a few causes of death for which the SMR is greater than 100. For thyroid cancer the SMR is slightly greater than 100 in both unlagged and lagged analyses (SMRs of 110 and 123 respectively), but in both analyses the findings are consistent with national rates. Both the unlagged and the lagged SMRs for testicular cancer (ie. 103 and 65 respectively) are consistent with national rates, as are the corresponding SMRs for all uterine cancers combined (ie. 85 and 102 respectively). In contrast, the SMR for pleural cancer is considerably greater than 100 in both unlagged and lagged analysis (SMRs of 209 and 207 respectively) and these increases relative to national rates are statistically significant.

TABLE 6.7 Standardised mortality ratios (SMRs) [a] for different causes of death

		Unlagged analysis				Lagged analysis			
	ICD 9th revision	Number of deaths				Number of deaths			
Disease	codes	Obs	Exp [b]	SMR	95% CI [c]	Obs	Exp	SMR	95% CI
All causes	000-999	26731	33014	81	80-82	23441	28404.41	83	81-84
All known causes excluding malignant neoplasms	000-139 209-799.8 800-999.8	18097	23313.43	78	76-79	15874	19889.15	80	79-81
All malignant neoplasms	140-208	8107	9666.63	84	82-86	7136	8486.91	84	82-86

		Unlagged analysis				Lagged analysis			
	ICD 9th revision	Number of deaths				Number of deaths			
Disease	codes	Obs	Exp [b]	SMR	95% CI[c]	Obs	Exp	SMR	95% CI
All neoplasms	140-239	8209	9779.55	84	82-86	7227	8580.18	84	82-86
Specific Malignancies									
Mouth, tongue and pharynx	141, 143-148, 149.0	97	142.15	68	55-83	85	124.01	69	55-85
Oesophagus	150	349	414.38	84	76-94	331	378.75	87	78-97
Stomach	151	594	703.19	84	78-92	498	598.91	83	76-91
Large intestine	153, 159.0	616	690.56	89	82-97	548	619.67	88	81-96
Rectum	154.0-154.2 154.4-154.9	321	397.62	81	72-90	275	350.35	78	69-88
Liver	155	94	120.22	78	63-96	83	108.87	76	61-95
Primary liver	155.0	44	66.77	66	48-88	39	58.23	67	48-92
Gall bladder	156	27	41.09	66	43-96	27	34.77	78	51-113
Pancreas	157	355	410.94	86	78-96	320	363.86	88	79-98
Larynx	161	65	89.03	73	56-93	60	78.68	76	58-98
Trachea, bronchus and lung	162	2433	3192.97	76	73-79	2130	2790.19	76	73-80
Pleura	163	112	53.68	209	172-251	102	49.39	207	168-251
Bone	170	14	23.7	59	32-99	7	15.21	46	18-95
Connective and soft tissue	171	35	42.37	83	58-115	30	34.26	88	59-125
All skin	172-173	113	123.5	91	75-110	90	103.02	87	70-107
Female breast	174	76	106.02	72	56-90	61	85.51	71	55-92
Uterus	179-182	23	26.95	85	54-128	21	20.61	102	63-156
Ovary	183	23	33.66	68	43,103	18	27.47	66	39-104
Prostate	185	629	641.26	98	91-106	605	613.79	99	91-107
Testis	186	33	31.9	103	71-145	10	15.28	65	31-120
Bladder	188, 189.3-189.9	291	341.52	85	76-96	261	310.41	84	74-95
Kidney	189.0-189.2	195	215.13	91	78-104	170	190.24	89	76-104
Brain	191-192, 224-225, 239.6	316	343.72	92	82-103	261	275.07	95	84-107
Thyroid	193	18	16.35	110	65-174	17	13.81	123	72-197
Ill defined and secondary cancers	195-196	634	677.46	94	86-101	588	626.72	94	86-102
All lymphatic and haematopoietic	200-208, 238.6	597	703.47	85	78-92	508[d]	584.51	87	80-95
Non-Hodgkin lymphoma	200, 202.2-202.3, 202.5-202.9	237	258.34	92	80-104	206	222.47	93	80-106
Hodgkin lymphoma	201	38	58.65	65	46-89	28	34.45	81	54-117
Multiple myeloma	203.0, 203.2-203.9, 238.6	106	129.43	82	67-99	97	117.54	83	67-101

Disease	ICD 9th revision codes	Unlagged analysis				Lagged analysis			
		Number of deaths				Number of deaths			
		Obs	Exp [b]	SMR	95% CI [c]	Obs	Exp	SMR	95% CI
All leukaemia	202.4, 203.1, 204-208	216	256.96	84	73-96	215	248.99	86	75-99
Leukaemia excluding chronic lymphatic	202.4, 203.1, 204.0, 204.2-207.7, 207.9-208.9	177	205.06	86	74-100	176	197.58	89	76-103
All malignant neoplasms excluding leukaemia	140-202.3, 202.5-203, 203.2-203.9	7891	9409.5	84	82-86	6959	8276.81	84	82-86
All malignant neoplasms excluding leukaemia, lung and pleura	140-161.9, 164-202.3, 202.5-203, 203.2-203.9	5346	6162.98	87	84-89	4727	5437.27	87	84-89
Malignant neoplasms strongly related to smoking	141, 143.0-149.0, 150.0-150.9, 157.0-157.9, 161.0-163.9, 188.0-189.9	3897	4859.33	80	78-83	3459	4285.41	81	78-83
Non-malignant diseases									
Infectious and parasitic diseases	000-139	114	238.24	48	39-57	99	175.26	56	46-69
Benign and ill-defined neoplasms	209-239	102	112.84	90	74-110	91	93.22	98	79-120
Nervous system diseases	320-389	376	526.22	71	64-79	356	434.99	82	74-91
Coronary heart disease	410-414	8405	9974.11	84	82-86	7447	8765.96	85	83-87
Bronchitis, emphysema and chronic obstructive disease	491-492, 496, 519	1089	1763.94	62	58-66	1015	1577.3	64	60-68
Aortic aneurysm	441	505	551.31	92	84-100	478	517.26	92	84-101
Non-malignant diseases strongly related to smoking	410-414, 441, 491-492, 496, 519	9999	12289.39	81	80-83	8940	10860.6	82	81-84
Circulatory diseases not strongly related to smoking	390-409, 415-440, 442-459	12265	14762.38	83	82-85	10961	12968.53	85	83-86
Cerebrovascular diseases	430-438	2077	2594.49	80	77-84	1905	2162.78	88	84-92
All circulatory diseases	390-459	12265	14762.38	83	82-85	10961	12968.53	85	83-86

		Unlagged analysis				Lagged analysis			
	ICD 9th revision	Number of deaths				Number of deaths			
Disease	codes	Obs	Exp [b]	SMR	95% CI[c]	Obs	Exp	SMR	95% CI
Respiratory diseases (not smoking related)	460-490, 493-495, 497-518	1028	1718.41	60	56-64	960	1522.37	63	59-67
Digestive disease	520-579	777	1051.3	74	69-79	696	909.11	77	71-82
Genitourinary diseases	580-629	221	316.94	70	61-80	186	262.39	71	61-82
All accidents and violence	800-999.8	1459	1825.77	80	76-84	912	1106.62	82	77-88
Unknown causes	799.9, 999.9	527				431			

Notes

(a) Excluding the first 10 years after the start of radiation work (2 years for leukaemia).

(b) Number expected based on England and Wales rates (not adjusted for social class)

(c) Confidence interval

(d) Based on a 10 year lag

*** p<0.001, ** p<0.001, * p<0.05, + 0.05<p<0.1

SMRs for various sub-types of leukaemia are given in Table 6.8, based on either including or excluding the first two years after the start of radiation work. Some of the variation in the SMRs appears to reflect the small numbers of deaths for rare leukaemia sub-types. However, for the more common sub-types (chronic lymphatic, acute myeloid and chronic myeloid), mortality is lower than expected from national rates, although the SMRs are also mostly statistically consistent with these rates. The SMRs for all leukaemias combined are statistically significantly lower than 100, but are just consistent with this value for the grouping of all leukaemias excluding chronic lymphatic leukaemia (CLL).

TABLE 6.8 Standardised mortality ratios (SMRs) by leukaemia subtype (including pre-1967 deaths)

Leukaemia subtype	ICD 9th revision codes	Unlagged analysis				Lagged analysis [a]			
		Number of deaths				Number of deaths			
		Obs	Exp [b]	SMR	95% CI [c]	Obs	Exp	SMR	95% CI
Acute lymphatic	204.0 204.2	12	20.39	59	30-103	12	18.66	64	33-112
Chronic lymphatic	204.1 207.8	39	52.17	75	53-102	39	51.66	75	54-103
Unspecified lymphatic	204.8 204.9	3	3.07	98	20-286	3	2.98	101	21-294
Acute myeloid	202.4, 205.0, 205.2, 206.0, 207.0	95	116.82	81	66-99	94	113.37	83	67-101
Chronic myeloid	205.1, 205.3, 206.1	39	43.32	90	64-123	39	42.01	93	66-127
Unspecified myeloid	205.8, 205.9, 206.8, 206.9	4	4.34	92	25-236	4	4.11	97	27-249
Unspecified acute	203.1, 208.0, 208.2	17	11.43	149	87-238	17	10.87	156	91-250
Unspecified chronic	207.1, 207.2, 208.1	0	1.12	0	0-331	0	1.1	0	0-335
Unspecified	208.8, 208.9	7	5.43	129	52-266	7	5.29	132	53-273
All leukaemia	202.4, 203.1, 204-208	216	256.96	84	73-96	215	248.99	86	75-99
All leukaemia (except chronic lymphatic)	202.4, 203.1, 204.0, 204.2-207.7 207.9-208.9	177	205.06	86	74-100	176	197.58	89	76-103

Notes:

(a) Excluding the first 2 years after the start of radiation work.

(b) Number expected based on England and Wales rates (not adjusted for social class).

(c) Confidence interval.

6.2 Mortality - internal analysis

Table 6.9 shows results from an analysis that looks for any trend in mortality with external radiation dose. For each cause of death, the observed number of deaths within each group for cumulative dose (based on a 10-year lag) is given, together with the number of deaths that would be expected if there were no association between the risk of mortality and dose. In contrast to the expected numbers cited earlier in the External Analysis, the expected numbers here have been calculated internally to the cohort. In particular, the sum across dose groups of the expected numbers of deaths equals the corresponding sum of the observed deaths. Also presented in this table are the estimated ERR per Sv, ie. the trend in the relative risk per unit dose, and its 90% confidence interval (CI), together with the results of tests for trend, looking for an increasing trend only (using a one-sided test) or for a trend in risk that is either increasing or decreasing with dose (using a two-sided test).

It can be seen from Table 6.9 that there is borderline evidence of an increasing trend in the risk of total mortality with increasing dose from a one-sided test (p=0.049), although the corresponding evidence from a two-sided test is weak (p=0.098). Most of the evidence for this trend relates to cancer mortality; there is no statistically significant trend with dose in total mortality from known causes other than malignancies, and the associated estimate of the ERR per Sv is lower than that for mortality from all causes combined. There is evidence of an increasing trend in mortality from all malignancies combined with increasing radiation dose from a one-sided test (p=0.036), although the corresponding evidence from a two-sided test is weaker (p=0.073); similar results arise when leukaemia is omitted from this disease category.

Of the 28 non-overlapping groupings of cancers in Table 6.9 (and considering all liver cancer rather than primary liver cancer), the estimate of the ERR per Sv is positive in 19 instances and negative in 9 instances. There are four types of cancer for which there is an increasing trend in mortality with dose that is statistically significant at the 5% level, based on a one-sided test, namely: rectal cancer (p=0.027), laryngeal cancer (p=0.026), all uterine cancers (p=0.016, due mainly to results for endometrial cancer with p=0.012) and leukaemia excluding CLL (p=0.042). The last of these disease categories – which was analysed using a two-year lag - was considered because of information from other studies suggesting that CLL may not be radiation-inducible (UNSCEAR, 2008). In contrast to the findings for leukaemia excluding CLL, there is no evidence of a trend with dose in the risk of all leukaemias combined (one-sided p=0.225). Amongst the four disease categories highlighted, only for all uterine cancers (p=0.03) is the estimated trend in risk with dose statistically significant at the 5% level when based on a two-sided test. There is no cancer for which there is evidence of a decreasing trend in risk with increasing dose, based either on a one-sided test for a decreasing trend or on a two-sided test.

Table 6.11 shows the results of tests for trend with dose in the risk of mortality from the main leukaemia sub-types, based on a two-year lag. There is evidence from a one-sided test (p=0.027) of an increasing trend with increasing dose in mortality from chronic myeloid leukaemia; the corresponding evidence from a two-sided test is of borderline statistical significance (p=0.054). Whilst the corresponding trends for the other leukaemia sub-types are not statistically significant, the estimated ERR per Sv is greater than zero for acute myeloid and acute lymphatic leukaemia but is less than zero for CLL. The estimated ERR for CLL is still less than zero if – as in a recent analysis of US workers (Schubauer-Berigan *et al*, 2007a) - a 10-year lag rather than a two-year lag is used (ERR per Sv <-1.929, 90% CI <-1.93,1.83).

Turning to mortality from specific non-malignant causes, it can be seen from Table 6.9 that there is a statistically significant increasing trend with dose in deaths from all circulatory diseases combined based on a one-sided test (p=0.03), whereas a two-sided test gives p=0.059. Much of the evidence for this trend relates to coronary heart disease (CHD) (one-sided p=0.053, two-sided p=0.105), which forms the majority of deaths from circulatory disease. In contrast, when CHD is analysed in combination with other non-malignant diseases that are strongly related to smoking, there is no evidence of an increasing trend in risk with dose. Indeed, there is very strong evidence from a two-sided test (p=0.001) that mortality from bronchitis, emphysema and chronic obstructive disease decreases with increasing dose. The only other notable finding from

Table 6.9 concerns the grouping of respiratory diseases that are not related to smoking, for which there is evidence from a one-sided test of an increasing trend in risk with increasing dose (p=0.04), although the corresponding evidence from a two-sided test is weaker (p=0.079).

TABLE 6.9 Test for trend in mortality with dose by cause of death (lagged by 10 years, except for leukaemia where a 2-year lag is used)

					Malignant neoplasms						
Dose (mSv)	*Number of deaths*	All Causes	All known causes excluding malignant neoplasms	All neoplasms	All malignant neoplasms	All malignant neoplasms excluding leukaemia	All malignant neoplasms excluding lung, pleura and leukaemia	Mouth, tongue and pharynx	Oesophagus	Stomach	Large intestine
<10	*Obs*	11836	7643	3982	3917	3803	2626	60	186	229	310
	Exp	11877.37	7653.89	4036.13	3969.54	3854.81	2655.18	53.09	176.98	243.38	300.33
10-	*Obs*	2920	1908	981	967	940	662	16	40	70	79
	Exp	2937.61	1935.59	972.91	955.77	926.13	635.46	11.81	39.89	67.43	72.89
20-	*Obs*	3693	2454	1211	1182	1142	777	5	53	89	79
	Exp	3726.4	2459.39	1228.2	1208.08	1169.99	800.64	14.74	52.1	87.37	92.02
50-	*Obs*	2082	1360	711	703	682	450	7	20	62	55
	Exp	2067.73	1362.25	683.15	672.26	650.98	446.16	8.08	30.15	50.2	52.56
100-	*Obs*	1380	912	461	454	442	294	4	13	30	31
	Exp	1365.53	903.08	448.53	441.33	428.29	293.74	5.33	20.82	34.08	36.19
200-	*Obs*	914	614	291	288	277	187	4	21	24	20
	Exp	855.01	568.77	278.85	274.78	267.02	179.99	3.3	12.86	22.02	21.3
400+	*Obs*	501	320	175	173	169	122	2	8	14	14
	Exp	496.34	328.03	164.23	162.23	157.79	106.84	1.64	8.19	13.52	12.71
Total deaths in informative strata		23326	15211	7812	7684	7455	5118	98	341	518	588
Score statistic		1.66	0.86	1.74	1.8	1.75	1.75	-0.16	0.23	0.58	-0.27
1-sided p-value		0.049	0.194	0.041	0.036	0.04	0.04	0.536	0.407	0.282	0.606
2-sided p-value		0.098	0.388	0.081	0.073	0.08	0.081	0.928	0.815	0.564	0.788
ERR Sv^{-1}		0.145	0.093	0.268	0.279	0.275	0.323	-0.162	0.146	0.336	-0.126
90% CI		(0.00, 0.3)	(-0.08, 0.28)	(0.01, 0.55)	(0.02, 0.56)	(0.02, 0.56)	(0.02, 0.67)	(-1.26, 2.22)	(-0.72, 1.42)	(-0.51, 1.58)	(-0.75, 0.77)
95% CI		(-0.03, 0.33)	(-0.11, 0.32)	(-0.03, 0.61)	(-0.02, 0.62)	(-0.03, 0.62)	(-0.04, 0.74)	(-1.38, 2.86)	(-0.84, 1.72)	(-0.63, 1.88)	(-0.84, 0.98)

TABLE 6.9 Test for trend in mortality with dose by cause of death (lagged by 10 years, except for leukaemia where a 2-year lag is used) (cont.)

		Malignant neoplasms *continued*									
Dose (mSv)	*Number of deaths*	Rectum	Liver	Primary Liver	Gallbladder	Pancreas	Larynx	Trachea, bronchus and lung	Pleura	Bone	Connective and soft tissue
<10	*Obs*	130	46	25	14	171	33	1125	52	5	21
	Exp	150.51	48.61	22.42	15.11	175.88	35.84	1146.93	52.69	4.51	19.18
10-	*Obs*	41	10	3	5	43	9	270	8	1	3
	Exp	36.87	11.69	5.23	3.81	40.46	8.41	278.71	11.96	1.07	3.31
20-	*Obs*	59	16	5	8	47	12	349	16	1	2
	Exp	47.59	13.33	5.68	4.93	50.27	9.97	353.4	15.95	1.06	3.63
50-	*Obs*	28	5	3	0	34	1	224	8	1	3
	Exp	28.48	7.49	3.22	2.52	27.56	5.15	194.86	9.96	0.53	2.35
100-	*Obs*	20	8	3	1	19	5	136	12	0	2
	Exp	19.42	4.61	1.99	1.47	18.03	3.63	127.12	7.43	0.35	1.47
200-	*Obs*	14	3	1	1	10	3	82	8	0	0
	Exp	13.07	2.13	0.98	0.74	11.39	2.4	81.71	5.32	0.3	0.67
400+	*Obs*	11	1	0	0	6	4	44	3	0	0
	Exp	7.05	1.13	0.47	0.42	6.42	1.59	47.28	3.68	0.19	0.39
Total deaths in informative Strata		303	89	40	29	330	67	2230	107	8	31
Score statistic		1.93	0.8	-0.4	-0.76	-0.06	2.13	0.35	0.81	-0.93	-0.87
1-sided p-value		0.027	0.208	0.619	0.75	0.525	0.026	0.363	0.209	0.811	0.787
2-sided p-value		0.054	0.415	0.761	0.499	0.95	0.052	0.726	0.417	0.377	0.426
ERR Sv^{-1}		1.687	0.800	-1.500	<-1.929	-0.049	4.071	0.106	1.311	<-1.929	<-1.929
90% CI		(0.19, 4.12)	(-1.19, 8.28)	(<-1.93, 6.3)	(<-1.93, 4.69)	(-1.00, 1.64)	(0.57, 12.02)	(-0.35, 0.67)	(-0.87, 5.69)	(<-1.93, 12.1)	(<-1.93, 4.76)
95% CI		(-0.02, 4.73)	(-1.43, 10)	(<-1.93, 8.56)	(<-1.93, 7.6)	(-1.11, 2.07)	(0.18, 14.46)	(-0.43, 0.79)	(-1.09, 6.87)	(<-1.93, 28.51)	(<-1.93, 7.49)

TABLE 6.9 Tests for trend in mortality with dose by cause of death (lagged by 10 years, except for leukaemia where a 2-year lag is used) (cont.)

		Malignant neoplasms *continued*									
Dose (mSv)	*Number of deaths*	All skin	Female breast	Uterus	Ovary	Prostate	Testis	Bladder	Kidney	All Brain	Thyroid
<10	*Obs*	57	41	13	12	348	7	148	100	154	8
	Exp	55.12	42.08	13.36	13.25	347.66	7.33	148.22	99.28	156.67	9.46
10-	*Obs*	7	7	3	2	90	1	42	32	40	2
	Exp	9.81	7.12	2.78	2.16	88.84	1.32	38.93	22.65	35.33	1.71
20-	*Obs*	12	5	1	4	108	1	45	25	46	4
	Exp	12.58	5.03	2.23	2.01	116.26	1.71	49.84	28.8	39.19	2.67
50-	*Obs*	8	3	1	0	69	2	27	19	15	1
	Exp	6.7	1.14	0.45	0.33	66.09	1.13	27.14	16.09	21.87	1.38
100-	*Obs*	4	0	0	0	42	1	17	5	16	1
	Exp	4.51	0.53	0.15	0.16	41.5	0.85	17.81	10.44	13.56	0.94
200-	*Obs*	3	0	1	0	25	1	14	3	6	0
	Exp	2.86	0.1	0.01	0.09	25.37	0.49	11.82	6.3	7.61	0.58
400+	*Obs*	2	0	0	0	20	0	8	3	1	1
	Exp	1.43	0	0.01	0	16.28	0.18	7.24	3.44	3.75	0.26
Total deaths in informative strata		93	56	19	18	702	13	301	187	278	17
Score statistic		0.44	0.18	2.76	-0.11	0.88	0.38	0.54	-1.56	-1.54	0.91
1-sided p-value		0.316	0.37	0.016	0.418	0.191	0.301	0.296	0.941	0.938	0.177
2-sided p-value		0.632	0.736	0.03	0.818	0.381	0.602	0.591	0.118	0.125	0.352
ERR Sv^{-1}		0.637	2.285	17.805	<-1.929	0.416	3.291	0.400	-1.028	-1.362	3.124
90% CI		(-1.07, 4.78)	(<-1.93, 30.37)	(<-1.93, 72.27)	(<-1.93, 89.13)	(-0.31, 1.41)	(<-1.93, 42.71)	(-0.64, 2.07)	(-1.52, 0.08)	(-1.82, 0.13)	(-0.88, 44.89)
95% CI		(-1.23, 5.98)	(<-1.93, 38.21)	(<-1.93, 91.96)	(<-1.93, 121.76)	(-0.42, 1.64)	(<-1.93, 59.25)	(-0.78, 2.48)	(-1.57, 0.39)	(-1.85, 0.55)	(-1.09, 68.13)

TABLE 6.9 Tests for trend in mortality with dose by cause of death (lagged by 10 years, except for leukaemia where a 2-year lag is used) (cont.)

		Malignant neoplasms *continued*								Non-Malignant Diseases	
Dose (mSv)	*Number of deaths*	Ill-defined and secondary cancers	Lymphatic or haematopoietic	Non-Hodgkin lymphoma	Hodgkin lymphoma	Multiple myeloma	All leukaemia	Leukaemia excluding chronic lymphatic	Malignant neoplasms strongly related to smoking	Coronary heart disease	Bronchitis, emphysema & chronic obstructive disease
<10	*Obs*	326	308	118	18	58	143	115	1875	3526	495
	Exp	320.58	318.26	122.36	19.67	61.5	135.12	106.45	1888.9	3540.69	472.02
10-	*Obs*	60	83	40	3	13	26	18	460	920	130
	Exp	75.76	79.19	31.07	4.19	14.28	33.98	24.11	452.84	908.49	128.78
20-	*Obs*	94	103	36	7	20	43	25	552	1112	172
	Exp	99.46	97.71	37.28	4.7	17.64	43.32	29.87	575.06	1169.91	163.66
50-	*Obs*	56	46	11	2	12	21	13	340	664	77
	Exp	54.22	52.8	20.33	2.02	9.16	24.86	17.24	318.99	662.64	88.35
100-	*Obs*	49	36	17	3	4	15	11	211	467	54
	Exp	34.75	33.95	13.72	1.29	5.89	15.48	10.59	210.62	446.07	58.17
200-	*Obs*	18	24	9	0	4	13	10	145	322	30
	Exp	20.88	19.52	7.86	0.79	3.12	8.76	6.04	135.11	280.54	37.12
400+	*Obs*	16	12	6	0	2	6	6	78	157	14
	Exp	13.35	10.57	4.38	0.33	1.41	5.48	3.69	79.47	159.66	23.9
Total deaths in informative strata		619	612	237	33	113	267	198	3661	7168	972
Score statistic		1.17	1.08	0.89	-0.31	0.75	0.76	1.73	0.58	1.62	-3.19
1-sided p-value		0.121	0.14	0.186	0.58	0.221	0.225	0.042	0.282	0.053	0.999
2-sided p-value		0.242	0.28	0.372	0.839	0.442	0.45	0.084	0.565	0.105	0.001
ERR Sv^{-1}		0.689	0.655	0.777	<-1.929	1.195	0.63	1.712	0.128	0.259	-1.041
90% CI		(-0.23, 1.99)	(-0.28, 1.97)	(-0.50, 2.88)	(<-1.93, 24.24)	(-0.88, 5.96)	(-0.57,2.53)	(0.06, 4.29)	(-0.22, 0.53)	(0.00, 0.55)	(-1.35, -0.59)
95% CI		(-0.37, 2.29)	(-0.43, 2.28)	(-0.66, 3.4)	(<-1.93, 32.73)	(-1.08, 7.31)	(-0.74,2.98)	(-0.17, 4.92)	(-0.28, 0.62)	(-0.05, 0.61)	(-1.40, -0.48)

TABLE 6.9 Tests for trend in mortality with dose by cause of death (lagged by 10 years, except for leukaemia where a 2-year lag is used) (cont.)

		Non-Malignant Diseases *continued*									
Dose (mSv)	*Number of deaths*	Aortic aneurysm	Non-malignant diseases strongly related to smoking	Circulatory diseases not strongly related to smoking	All circulatory diseases	Cerebrovascular disease	Respiratory diseases not strongly related to smoking	Digestive	Genito-urinary	All accidents and violence	Unknown causes
<10	*Obs*	219	4240	1395	5140	846	446	353	78	541	276
	Exp	237.35	4250.06	1399.19	5177.23	861.44	441.08	361.14	78.93	545.57	253.94
10-	*Obs*	50	1100	359	1329	234	105	86	28	107	45
	Exp	58.3	1095.57	380.38	1347.17	241.29	113.15	76.79	22.92	102.3	46.24
20-	*Obs*	93	1377	493	1698	318	138	106	32	121	57
	Exp	73.8	1407.37	483.91	1727.62	312.39	146.01	95.22	30.97	116.07	58.93
50-	*Obs*	47	788	258	969	169	80	43	14	69	19
	Exp	41.52	792.51	261.54	965.7	169.19	78.55	52.06	16.93	60.63	33.22
100-	*Obs*	28	549	181	676	127	50	28	9	28	14
	Exp	27.64	531.88	173.18	646.89	113.63	50.44	33.9	11.11	37.59	21.12
200-	*Obs*	24	376	122	468	84	35	19	6	19	12
	Exp	16.17	333.82	112.55	409.26	75.42	31.07	19.92	7.31	20.94	11.47
400+	*Obs*	5	176	67	229	39	24	15	6	7	8
	Exp	11.23	194.79	64.25	235.13	43.64	17.7	10.96	4.84	8.9	6.08
Total deaths in informative strata		466	8606	2875	10509	1817	878	650	173	892	431
Score statistic		-0.132	0.35	1.12	1.88	0.49	1.76	0.49	-0.11	-1.13	-0.6
1-sided p-value		0.563	0.364	0.132	0.03	0.31	0.04	0.314	0.544	0.871	0.727
2-sided p-value		0.874	0.729	0.265	0.059	0.621	0.079	0.627	0.912	0.258	0.546
ERR Sv^{-1}		-0.132	0.050	0.280	0.251	0.161	0.799	0.237	-0.082	-0.593	-0.305
90% CI		(-1.17, 1.53)	(-0.18, 0.3)	(-0.12, 0.75)	(0.03, 0.49)	(-0.34, 0.77)	(0.04, 1.79)	(-0.47, 1.25)	(-0.96, 1.54)	(-1.18, 0.33)	(-0.93, 0.64)
95% CI		(-1.29, 1.92)	(-0.22, 0.35)	(-0.19, 0.85)	(-0.01, 0.54)	(-0.42, 0.91)	(-0.08, 2.01)	(-0.58, 1.48)	(-1.07, 1.97)	(-1.26, 0.55)	(-1.02, 0.87)

6.3 Cancer incidence - internal analysis

Table 6.10 is similar in format to Table 6.9, but gives results for cancer incidence rather than from malignant and non-malignant causes of death. In total, there are 11165 cases of malignancy included in the incidence analysis, compared with 7684 deaths from malignancies in the mortality analysis, based on a 10-year lag. There is strong evidence of an increasing trend in the incidence of all malignancies combined with increasing radiation dose from both one-sided (p=0.018) and two-sided (p=0.036) tests. Similar results are obtained when either leukaemia or non-melanoma skin cancers are omitted from this disease category.

Of the 29 non-overlapping groupings of cancers in Table 6.10 (and considering all liver cancer rather than primary liver cancer), the estimate of the ERR per Sv is positive in 19 instances and negative in 10 instances. There are five types of cancer listed in this Table for which there is an increasing trend in incidence with dose that is statistically significant at the 5% level, based on a one-sided test, namely: rectal cancer (p=0.02), all skin cancers (p=0.01), non-melanoma skin cancer (p=0.02), multiple myeloma (p=0.008) and leukaemia excluding CLL (p=0.03). Other than for the last of these disease categories, the trend findings are also statistically significant at the 5% level if a two-sided rather than a one-sided test is used. The trends for all uterine cancers (p=0.057), thyroid cancer (p=0.079) and non-Hodgkin lymphoma (p=0.081) approach statistical significance based on a one-sided (but not a two-sided) test. In particular, within the grouping of uterine cancers, there is a statistically significant increasing trend with dose in the incidence of endometrial cancer (one-sided p=0.01). There is no cancer for which there is a statistically significantly decreasing trend in risk with increasing dose, based either on a one-sided test for a decreasing trend or on a two-sided test.

Table 6.11 shows the results of tests for trend with dose in the incidence of the main leukaemia sub-types, based on a two-year lag. There is evidence from both one-sided (p=0.011) and two-sided (p=0.022) tests of an increasing trend with increasing dose in the incidence of chronic myeloid leukaemia. The corresponding trends for the other leukaemia sub-types are not statistically significant. In particular, the estimated ERR per Sv is greater than zero for acute myeloid and acute lymphatic leukaemia but is less than zero for CLL. Furthermore, the estimated ERR for CLL is still less than zero if a 10-year lag rather than a two-year lag is used (ERR per Sv-0.337, 90% CI -1.72, 3.1)

For all leukaemias combined (which total 362 cases included in the incidence analysis compared with 267 deaths in the mortality analysis), there is no evidence for an increasing trend in the incidence risk with increasing dose. However, as mentioned above, there is evidence of such a trend when CLL is omitted from the grouping of all leukaemias.

TABLE 6.10 Tests for trend in cancer incidence with dose by diagnosis (lagged by 10 years, except for leukaemia where a 2-year lag is used)

Dose (mSv)	*Number of cases*	All neoplasms	All malignant neoplasms	All malignant neoplasms excluding leukaemia	All malignant neoplasms excluding lung, pleura and leukaemia	Mouth, tongue and pharynx	Oesophagus	Stomach	Large intestine	Rectum	Liver
<10	*Obs*	6411	5918	5756	4521	104	159	305	472	295	46
	Exp	6504.56	5993.79	5832.14	4580.49	100.2	158.08	306.97	469.91	312.72	47.44
10-	*Obs*	1463	1377	1346	1066	23	36	82	120	69	7
	Exp	1443.48	1357.39	1318.99	1019.79	19.55	36.11	78.79	109.56	68.35	10.89
20-	*Obs*	1786	1665	1612	1238	13	49	95	122	95	16
	Exp	1806.81	1703.95	1654.42	1273.93	23.18	45.49	102.77	136.88	89.52	12.98
50-	*Obs*	1029	976	950	709	18	22	66	90	54	8
	Exp	990.96	932.93	906.18	697.01	12.57	25.49	57.01	78.96	50.94	7.49
100-	*Obs*	682	640	623	474	7	14	33	50	33	7
	Exp	643.8	605.18	587.83	450.97	8.19	17.56	37.12	53.6	32.53	4.17
200-	*Obs*	382	364	349	259	6	13	21	22	24	2
	Exp	389.07	367.05	356.33	269.83	4.96	10.95	22.7	31.97	20.6	2.08
400+	*Obs*	243	225	219	176	0	7	16	23	16	0
	Exp	217.32	204.71	199.11	150.98	2.36	6.31	12.65	18.11	11.34	0.94
Total cases in informative strata		11996	11165	10855	8443	171	300	618	899	586	86
Score statistic		2.33	2.09	1.96	2.01	-1.11	0.22	0.6	-0.07	2.05	-0.09
1-sided p-value		0.01	0.018	0.025	0.022	0.866	0.414	0.274	0.527	0.02	0.513
2-sided p-value		0.02	0.036	0.05	0.045	0.268	0.828	0.549	0.947	0.041	0.973
ERR Sv^{-1}		0.302	0.281	0.266	0.305	-1.756	0.154	0.305	-0.026	1.307	-0.09
90% CI		(0.08, 0.54)	(0.06, 0.53)	(0.04, 0.51)	(0.05, 0.58)	(<-1.93, 0.98)	(-0.79, 1.68)	(-0.44, 1.37)	(-0.56, 0.71)	(0.21, 2.85)	(<-1.93, 6.58)
95% CI		(0.05, 0.59)	(0.02, 0.57)	(0.00, 0.56)	(0.01, 0.64)	(<-1.93, 1.63)	(-0.91, 2.06)	(-0.55, 1.62)	(-0.65, 0.88)	(0.04, 3.2)	(<-1.93, 8.39)

TABLE 6.10 Tests for trend in cancer incidence with dose by diagnosis (lagged by 10 years, except for leukaemia where a 2-year lag is used) (cont.)

Dose (mSv)	*Number of cases*	Primary Liver	Gallbladder	Pancreas	Larynx	Trachea, bronchus and lung	Pleura	Bone	Connective and soft tissue	All skin	Malignant melanoma
<10	*Obs*	35	22	164	93	1148	87	7	38	313	160
	Exp	30.81	23.42	172.34	85.53	1149.49	102.15	8.72	34.73	328.03	166.09
10-	*Obs*	2	8	44	16	255	25	3	5	71	26
	Exp	7.11	5.67	39.93	19.61	278.17	21.04	2.38	6.29	68.78	28.93
20-	*Obs*	8	11	44	22	343	31	3	6	91	37
	Exp	8.45	7.12	48.84	24.92	352.4	28.08	2.61	7.51	85.77	31.97
50-	*Obs*	5	0	37	9	223	18	2	6	47	18
	Exp	4.91	3.99	26.32	14.09	193.01	16.16	1.55	4.01	47.18	16.33
100-	*Obs*	4	1	18	12	131	18	1	3	29	11
	Exp	2.6	2.57	16.58	10.29	125.42	11.44	0.89	2.87	29.65	10.01
200-	*Obs*	2	2	7	7	83	7	1	0	19	5
	Exp	1.39	1.41	10.38	6.89	79.76	6.73	0.6	1.75	17.45	5.11
400+	*Obs*	0	1	6	6	39	4	0	0	17	4
	Exp	0.73	0.81	5.62	3.67	43.74	4.39	0.25	0.83	10.14	2.56
Total cases in informative Strata		56	45	320	165	2222	190	17	58	587	261
Score statistic		-0.2	-0.15	0.09	0.95	0.16	0.91	0.14	-1.55	2.34	1.13
1-sided p-value		0.548	0.513	0.463	0.172	0.434	0.182	0.4	0.955	0.01	0.128
2-sided p-value		0.905	0.973	0.926	0.343	0.869	0.363	0.799	0.09	0.019	0.257
ERR Sv^{-1}		-0.651	-0.226	0.078	0.839	0.051	1.354	1.177	<-1.934	1.466	1.390
90% CI		(<-1.93, 5.96)	(-1.50, 3.88)	(-0.95, 2)	(-0.46, 3.05)	(-0.41, 0.62)	(-0.71, 5.51)	(<-1.93, 36.34)	(<-1.93, 0.3)	(0.36, 3.03)	(-0.43, 4.74)
95% CI		(<-1.93, 7.73)	(-1.59, 5.29)	(-1.07, 2.51)	(-0.63, 3.61)	(-0.49, 0.74)	(-0.94, 6.61)	(<-1.93, 52.16)	(<-1.93, 1.42)	(0.19, 3.39)	(-0.65, 5.6)

TABLE 6.10 Tests for trend in cancer incidence with dose by diagnosis (lagged by 10 years, except for leukaemia where a 2-year lag is used) (cont.)

Dose (mSv)	*Number of cases*	Non-melanoma skin cancer	Female breast	Uterus	Ovary	Prostate	Testis	Bladder	Kidney	All Brain	Thyroid
<10	*Obs*	153	110	46	10	758	84	399	163	199	34
	Exp	161.94	114.38	47.02	10.48	774.09	79.37	392.51	164.58	197.85	35.4
10-	*Obs*	45	16	5	2	213	7	89	48	48	7
	Exp	39.85	17.51	5.81	1.94	187.54	11.95	92.03	35.11	40.38	5.71
20-	*Obs*	54	20	4	3	239	10	106	32	45	6
	Exp	53.8	13.46	3.7	1.9	248.92	12.64	116.53	44.1	45.15	6.29
50-	*Obs*	29	3	2	0	135	8	63	29	21	2
	Exp	30.85	3.23	0.9	0.43	137.45	6.41	64.63	23.79	25.11	3.25
100-	*Obs*	18	2	0	0	97	3	43	12	14	3
	Exp	19.64	1.8	0.46	0.2	87.09	3.26	42.14	15.13	15.49	1.88
200-	*Obs*	14	0	1	0	47	4	30	8	7	0
	Exp	12.34	0.49	0.11	0.05	50.15	1.71	25.76	9.09	8.7	1
400+	*Obs*	13	0	0	0	27	0	18	4	3	2
	Exp	7.58	0.12	0	0	30.77	0.66	14.4	4.21	4.32	0.47
Total cases in informative strata		326	151	58	15	1516	116	748	296	337	54
Score statistic		2.05	-0.03	1.74	-0.39	-0.53	0.37	1.28	-0.55	-1.25	1.48
1-sided p-value		0.02	0.511	0.057	0.587	0.701	0.33	0.1	0.708	0.895	0.079
2-sided p-value		0.04	0.978	0.112	0.826	0.599	0.66	0.199	0.584	0.21	0.157
ERR Sv^{-1}		1.497	-0.228	10.523	<-1.934	-0.180	1.018	0.646	-0.411	-0.882	3.236
90% CI		(0.23, 3.4)	(<-1.93, 14.49)	(0.27, 39.4)	(<-1.93, 61.13)	(-0.65, 0.43)	(<-1.93, 7.21)	(-0.15, 1.72)	(-1.22, 1.09)	(-1.49, 0.36)	(-0.19, 13.9)
95% CI		(0.05, 3.85)	(<-1.93, 18.09)	(-0.50, 48.02)	(<-1.93, 88.75)	(-0.73, 0.57)	(<-1.93, 8.85)	(-0.28, 1.96)	(-1.32, 1.48)	(-1.56, 0.69)	(-0.48, 17.51)

TABLE 6.10 Tests for trend in cancer incidence with dose by diagnosis (lagged by 10 years, except for leukaemia where a 2-year lag is used) (cont.)

Dose (mSv)	*Number of cases*	Ill-defined and secondary cancers	Lymphatic or haematopoietic	Non-Hodgkin lymphoma	Hodgkin lymphoma	Multiple myeloma	All leukaemia	Leukaemia excluding chronic lymphatic	All malignant neoplasms excluding non-melanoma skin cancer	Malignant neoplasms strongly related to smoking
<10	*Obs*	299	442	166	43	71	198	135	5758	2317
	Exp	287.91	456.33	169.03	42.88	82.76	190.46	130.74	5828.11	2324.88
10-	*Obs*	57	97	42	3	21	32	20	1351	536
	Exp	69.83	102.02	38.46	7.16	17.99	44.48	27.73	1328.66	541.54
20-	*Obs*	88	138	46	12	27	55	35	1628	640
	Exp	90.36	126.62	45.86	7.89	23.35	56.19	34.49	1672.3	683.56
50-	*Obs*	44	56	14	2	14	31	16	959	419
	Exp	50.92	66.21	23.51	4.01	11.94	31.43	18.74	916.67	376.06
100-	*Obs*	51	49	19	6	7	21	12	629	255
	Exp	35.03	42.64	15.27	2.63	7.39	20.37	11.67	595.18	246.74
200-	*Obs*	17	32	12	1	4	16	9	359	161
	Exp	22.94	24.62	8.44	1.68	3.78	12.08	6.89	361.94	154.52
400+	*Obs*	15	17	6	0	5	9	7	221	84
	Exp	14.01	12.57	4.43	0.76	1.78	6.99	3.74	202.14	84.7
Total cases in informative strata		571	831	305	67	149	362	234	10905	4412
Score statistic		0.19	2.33	1.4	-0.39	2.43	1.34	1.88	1.98	0.8
1-sided p-value		0.425	0.01	0.081	0.626	0.008	0.09	0.03	0.024	0.213
2-sided p-value		0.849	0.02	0.162	0.748	0.015	0.18	0.06	0.048	0.426
ERR Sv^{-1}		0.100	1.344	1.284	<-1.934	3.597	1.011	1.782	0.267	0.170
90% CI		(-0.63, 1.17)	(0.34, 2.67)	(-0.18, 3.53)	(<-1.93, 9.08)	(0.77, 8.94)	(-0.18, 2.79)	(0.17, 4.36)	(0.04, 0.51)	(-0.17, 0.56)
95% CI		(-0.74, 1.42)	(0.18, 2.97)	(-0.38, 4.06)	(<-1.93, 12.55)	(0.43, 10.37)	(-0.36, 3.21)	(-0.06, 4.99)	(0.00, 0.56)	(-0.23, 0.64)

TABLE 6.11 Excess relative risk (ERR) per Sv estimates for the main leukaemia subtypes

	Mortality					Incidence				
				p-value					p-value	
Leukaemia subtype	Deaths	ERR Sv^{-1}	(90%CI)	1-sided	2-sided	Cases	ERR Sv^{-1}	(90%CI)	1-sided	2-sided
Acute myeloid	102	1.215	(-1.23, 5.69)	0.239	0.479	109	0.616	(-1.45, 4.83)	0.362	0.724
Chronic myeloid	44	3.266	(0.44, 9.28)	0.027	0.054	59	4.079	(0.88, 11.24)	0.011	0.022
Acute lymphatic	15	7.786	(<-1.92, 89.52)	0.303	0.606	19	8.801	(<-1.92, 61.8)	0.203	0.405
Chronic lymphatic	69	<-1.919	(<-1.92, 1.23)	0.884	0.232	128	-0.117	(-1.42, 2.71)	0.538	0.925
All leukaemias excluding chronic lymphatic	198	1.712	(0.06, 4.29)	0.042	0.084	234	1.782	(0.17, 4.36)	0.03	0.06
All leukaemias	267	0.63	(-0.57, 2.53)	0.225	0.45	362	1.011	(-0.18, 2.79)	0.09	0.18

6.4 Subsidiary analyses

Appendix D gives details of various analyses that were conducted in order to examine whether the findings vary greatly if the format of the main analysis is changed. The key findings from these analyses are as follows:

(i) Excluding workers who were monitored for internal exposure leads to changes in the central estimate of the ERR per Sv and widens the associated confidence interval, as well as weakening the evidence of a trend in risk with dose in several instances. In contrast, retaining internally-monitored workers in the analysis but stratifying on the basis of whether a worker was ever monitored for internal exposure tends to give similar results to those from the main analysis, at least for the large disease groupings.

(ii) Stratifying by time since exposure generally has little effect, although the evidence for a trend with dose in mortality from all circulatory diseases combined is weaker after this adjustment.

(iii) Attempting to adjust for any "healthy worker survivor effect" by stratifying on the basis of whether or not the duration of radiation work was at least 10 years tends to diminish estimates of trends in risk with dose and to increase p-values. Inferences are generally similar to those in the main analysis, except for multiple myeloma incidence, thyroid cancer incidence and mortality from circulatory diseases where the evidence for trends in risk with dose is greatly diminished. Stratifying on the basis of whether or not the duration of radiation work was at least 30 years has little effect.

(iv) As expected, omitting the adjustment for industrial classification leads to an upward bias in risk estimates for major groupings of mortality and cancer incidence. Similarly, adjustment by country (England & Wales vs. Scotland) rather than by employer/site leads to an upward bias in the risk estimates for causes of death that are related strongly to socio-economic status, reflecting the effects of SES that are missed by this alternative adjustment.

(v) The central estimate of the ERR per Sv for cancer tends to increase with increasing lag period, but the p-value from the test for trend in risk with dose is relatively stable.

(vi) For leukaemia excluding CLL, the central ERR estimate is higher at ages 70 years or more than at younger ages for the oldest age group and – for mortality but not for incidence – the variation in the ERR per Sv by attained age is statistically significant. However, for the grouping of all malignant neoplasms excluding leukaemia and for the corresponding grouping that also excludes lung and pleural cancer, the data are consistent with the ERR per Sv being constant across age groups.

(vii) Omitting various adjustments to the recorded external doses has very little impact on analyses of disease risk in relation to dose.

(viii) Using mean rather than median doses has very little effect on estimates of the ERR per Sv or on associated significance tests.

(ix) Restricting the cohort to that used in the 2nd NRRW analysis, but following them over the period of the 3rd analysis, gives similar results to those from the full cohort when analysing trends in risk with dose.

(x) Restricting the cohort to that used in the 15-country nuclear worker study (Cardis *et al*, 2005, 2007; Vrijheid *et al*, 2007), but following them over the period of the 3rd analysis, gives much less precise results than in the main analysis. This reflects the exclusion of about half of the workers who are in the main analysis, including a substantial proportion of the workers with relatively high external doses. Within this restricted cohort, there is generally no evidence of trends with dose in the risk of cancer or of circulatory disease mortality. Similar inferences are drawn if, as in the 15-country study, these data are also stratified according to whether or not the duration of radiation work was at least 10 years.

(xi) Omitting cancers listed as contributory cause on death certificates leads to a slight weakening of the evidence for an association between solid cancer mortality and external dose, but has very little impact on analyses of cancer incidence.

(xii) Analysing cancer incidence on the basis of registration data alone tends to increase the central estimate of the ERR per Sv and to decrease the p-value from the test for trend in risk with dose, particularly for thyroid cancer.

(xiii) Classifying workers on the basis of their longest or last NRRW employer, rather than on the basis of their first NRRW employer, generally has little impact on the results.

(xiv) Including deaths and cancers at ages of 85 years or more has very little effect on inferences.

(xv) Having adjusting for possible age and temporal variations in the ERR per Sv on the basis of models derived by the BEIR VII Committee (NRC, 2006), the estimates of the ERR per Sv from the NRRW are consistent with the corresponding values for the Japanese atomic bomb survivors. However, the NRRW data are not sufficiently powerful to detect age and temporal effects of the magnitude seen in the Japanese A-bomb data.

7 DISCUSSION

7.1 General patterns in mortality

As in the two previous analyses of the NRRW, overall rates of mortality were lower than expected from rates for England and Wales. This "healthy worker effect" (HWE) has been seen not only in the NRRW, but also among radiation workers in the nuclear industry in many other countries (Vrijheid *et al*, 2007a), among non-radiation workers at nuclear facilities (eg. McGeoghegan and Binks, 2000b; Atkinson *et al*, 2004) and in various other industries (Baillargeon, 2001).

As in the previous NRRW analysis (Muirhead *et al*, 1999a,b), mortality rates for all causes and for all malignant neoplasms combined differ considerably between workers classified as industrial and those classified as non-industrial. Whilst social-class-adjusted SMRs for industrial and non-industrial workers were similar to each other in the 2nd analyses, the same is not true in this analysis, although this adjustment does reduce the difference between these SMRs. The remaining disparity may partly reflect the fact that, whilst in the past there was a clear distinction between industrial workers (who were usually paid weekly) and non-industrial workers (who usually paid monthly), this distinction has become blurred over time. Consequently, the assignment of these groups to specific social classes (ie. I for non-industrial workers and III for industrial workers), which appeared to be valid previously, may be in error for more recent workers. Nevertheless, the substantial difference between these two groups in overall mortality and mortality from all malignant neoplasms combined (see Table 6.1) highlights the importance of adjusting for this social class effect in the internal analyses and in some of the external analyses, and of continuing to collect data on industrial classification for use in future analyses.

The SMRs for all causes and all malignant neoplasms combined from the 3rd NRRW analyses are similar to the corresponding values in the previous two analyses (Kendall *et al*, 1992a,b; Muirhead *et al*, 1999a,b). However, whilst the overall magnitude of the HWE has changed little, SMRs have varied over the period of follow-up, with increases up to the early 1980s followed by a decrease. There was a slight suggestion in the 2nd NRRW analysis (Muirhead *et al*, 1999a,b) of a decrease in SMRs after the early 1980s, but this pattern has become clearer with the longer follow-up. Adjustment for social class did not alter these findings. Whereas unadjusted SMRs for males were higher than those for females, there did not appear to be differences in SMRs between males and females after allowing for social class. Furthermore, such an adjustment also reduced variations in all-cause SMRs with age, both for all causes and for all malignant neoplasms.

As in the previous NRRW analyses, there was variation in all-cause mortality by employer and/or site of first employment. Some of this is likely to reflect random variation owing to relatively small numbers of deaths for some sites or employers. However, there is also likely to be some contribution from geographical variation in mortality rates. For example, SMRs calculated for sites in Scotland using Scottish rates tended to be closer to SMRs for sites in England and Wales than was the case when

England and Wales rates were used to calculate SMRs for sites throughout Great Britain. This highlights the importance of including an adjustment for employer and (in some instances) site in the internal analysis, so as to allow for geographical variations in mortality. In addition, there is no indication from examination of SMRs for MoD workers first monitored before 1977 that mortality among these workers – many of whom have been included in the NRRW for the first time – has been under-ascertained. Although many of the MoD workers in this analysis were first monitored after 1976, the early group tended to be older and hence made a greater contribution to the deaths observed among MoD workers as a whole.

In considering the fall in SMRs in recent years, it is worth looking at trends in SMRs with time since start of radiation work and duration of radiation work. Various studies have indicated the HWE is often particularly strong soon after starting employment, probably because of the criteria used in selecting people into work. Similarly, individuals selected into radiation work are likely to have general good health. Consequently, the low SMRs soon after starting radiation work that were seen both in previous NRRW analyses and in this one (Table 6.2) are not surprising. However, although SMRs for all causes and all malignant neoplasms subsequently increase and remain fairly constant over the period 10-29 years after start of radiation work, there is evidence of a subsequent decrease in SMRs, even after adjusting for social class. Again the 3rd NRRW analysis provides more information on the period 30 or more years after start of radiation work than was available from previous analyses of the NRRW.

This fall in the SMRs 30 or more years after start of radiation work is matched in the analysis by duration of radiation work, which indicates lower SMRs among those involved in radiation work for 30 or more years than for those involved for a shorter time. However, the evidence for such a difference is considerably weaker after allowance is made for social class. In the 15-country study of radiation workers in the nuclear industry (Cardis *et al*, 2005, 2007; Vrijheid *et al*, 2007a,b), it was decided to allow for duration of radiation work (or duration of employment) when looking at mortality trends in relation to radiation dose, so as to allow for the "healthy worker survivor effect" (HWSE). In particular, epidemiological studies of various occupational groups have sometimes indicated that mortality among long-term workers is lower than that of short-term workers (Arrighi and Hertz-Picciotto, 1994; Richardson *et al*, 2004). Within the current analysis, a stratification along the lines of that used in the 15-country study – namely, according to whether or not the duration of radiation work was at least 10 years – tended, if anything, to reduce estimates of the ERR per Sv. In contrast, use of this stratification in the 15-country study led to a sizeable increase in the estimated ERR per Sv for the grouping of all cancers other than leukaemia (Cardis *et al*, 2007). Stratifying on the basis of duration of radiation work being greater than or less than 30 years had little impact on the main results within the 3rd NRRW analysis.

7.2 Cancer mortality and incidence

7.2.1 Leukaemia

Epidemiological studies of the survivors of the atomic bombings of Hiroshima and Nagasaki and of patients who received radiotherapy for various conditions have shown

raised risks of leukaemia excluding CLL (AGIR, 2003; UNSCEAR 2000, 2008). Associations with radiation exposure have also been reported in several analyses of large groups of radiation workers, including the first two analyses of the NRRW (Kendall *et al*, 1992a,b; Muirhead *et al*, 1999a,b), international studies coordinated by the International Agency for Research on Cancer (IARC) (Cardis *et al*, 1995, 2005, 2007), as well as an analysis of US workers that also adjusted for benzene exposure (Schubauer-Berigan *et al*, 2007b). It is therefore not surprising that the 3rd NRRW analysis has also shown an increasing trend in the risk of leukaemia other than CLL with external dose. It should be acknowledged that the afore-mentioned analyses of radiation workers are based on overlapping populations. In particular, the current analysis includes workers who were included in previous NRRW analyses, many of whom in turn were included in the IARC 15-country study (Cardis *et al*, 2005, 2007). Nevertheless, the number of deaths from leukaemia excluding CLL in this analysis is more than double the corresponding number in the 2nd NRRW analysis. Furthermore, the number of cases of leukaemia excluding CLL in the incidence analysis is nearly two and half times the corresponding number of deaths in the 2nd analysis. As a consequence, relative to the 2nd analysis, the 90% CI for the ERR per Sv is about 40% narrower than before.

Figure 7.1 Trends with dose in relative risk (and 90% CI) for mortality from leukaemia excluding CLL

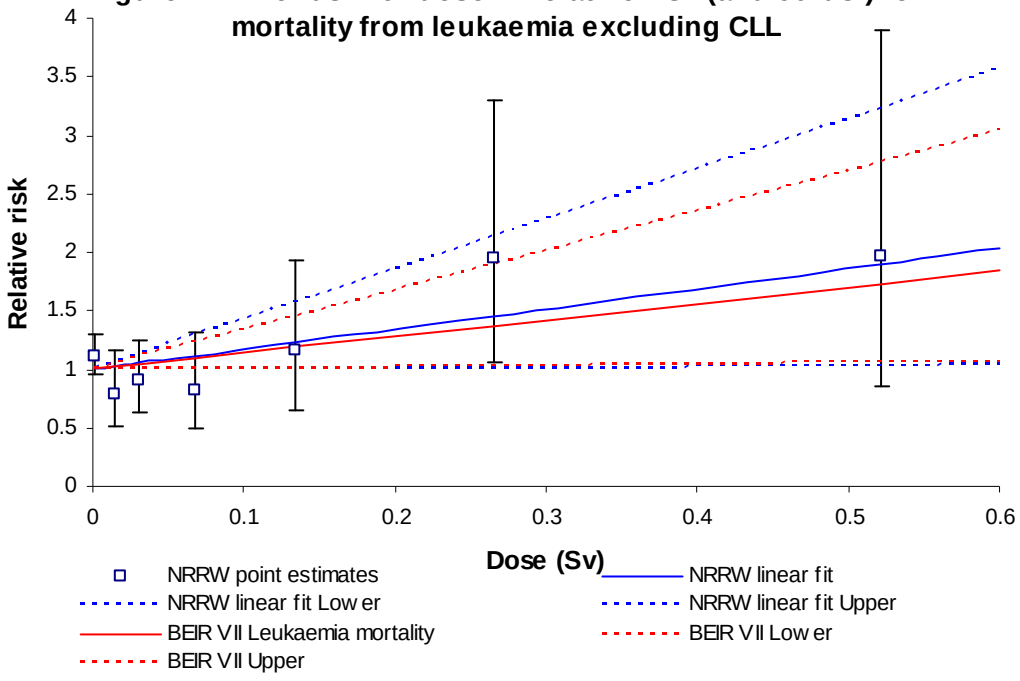


Table 7.1 shows good agreement across the 3rd NRRW analysis (based on both mortality and incidence data), the 2nd NRRW analysis, the 15-country worker study and the Japanese A-bomb study in the estimated ERR per Sv. The ERR estimates cited for the Japanese atomic bomb survivors are based on the low dose component of a linear-

quadratic dose-response model, such the risk per unit dose is smaller at lower doses than it is at higher doses. Figure 7.1 shows the trends in leukaemia mortality with dose for the 3rd NRRW analysis (NRRW-3) and the A-bomb study (the latter based on the BEIR VII estimate, as given in Table 7.1). The corresponding graph based on the NRRW incidence data would be similar. Whilst the A-bomb and the NRRW-3 risk estimates are subject to some uncertainty, the findings from the current analysis are consistent with the dose reduction factor of 2 that is commonly used when extrapolating leukaemia risks among the Japanese A-bomb survivors down to low doses (eg. ICRP, 2007), as well as values that are smaller or larger than this. In particular, the 90% confidence interval for the ERR estimate from NRRW-3 ranges from just above zero to just over three times the central estimate from the A-bomb data at low doses (see Table 7.1). This range would be greater if uncertainties in the A-bomb data – including uncertainties in the modifying effects of age, gender and time – were taken into account. Nevertheless, the NRRW-3 data are valuable in indicating that the risk of leukaemia other than CLL following occupational radiation exposure is greater than zero but is unlikely to be more than three times greater than that estimated by bodies such as the BEIR VII Committee (NRC, 2006).

The subsidiary analyses showed that the leukaemia findings are relatively robust to changes to the format of the analysis. For example, stratifying on the basis of internal monitoring led to a change in the estimated ERR per Sv, but there was still a statistically significant trend in risk with external dose, based on either the incidence or the mortality data. Adjusting for time since exposure by fitting a BEIR VII-type model had little effect of inferences. Indeed, the similar degree of goodness-of-fit between this model and the simple linear dose-response model with no modifying effect of age or time highlights the low power of this analysis to detect effects of the magnitude seen among the Japanese A-bomb survivors. In particular, whilst the A-bomb data point to a strong decrease in the ERR per Sv with increasing time since exposure for exposures that arose in childhood, this trend is less marked following exposure in adulthood (Preston *et al*, 1994). Low statistical power probably explains the lack of evidence from the 15-country study for any temporal variation in the ERR per Sv (Cardis *et al*, 2007). In a study of workers at the Savannah River Site in the USA, Richardson and Wing (2007) reported that leukaemia mortality was more strongly related to radiation doses received 3-15 years previously than to earlier doses, although there were fewer deaths in that analysis than in NRRW-3. Whilst there is little evidence from NRRW-3 of variations in the ERR with time since exposure, the mortality data in particular suggest that the ERR per Sv may be greater for attained ages of 70 years or more when compared with younger ages.

The sub-type of leukaemia for which there is strongest evidence of an association with radiation dose in this analysis – based on both mortality and incidence data – is chronic myeloid leukaemia. This finding was also reported in previous NRRW analyses (Little *et al*, 1993; Muirhead *et al*, 1999a,b). Furthermore, studies of the Japanese atomic bomb survivors and of some medically-exposed groups have also shown an association between chronic myeloid leukaemia and radiation exposure (Little *et al*, 1999). For acute lymphatic leukaemia and acute myeloid leukaemia, this analysis did not show statistically significant trends in either mortality or incidence with dose, although the central estimate of the ERR was greater than zero. Studies of the Japanese atomic

bomb survivors and of some medically-exposed groups indicate that these leukaemia sub-types are also radiation-inducible (Little *et al*, 1999). A notable finding here was the absence of evidence for an association between CLL (using either mortality or incidence data) and radiation dose, even when based on a 10-year rather than a 2-year lag as in Schubauer-Berigan *et al* (2007a)'s analysis of US workers. Indeed, adding CLL to the grouping of leukaemia excluding CLL removes the evidence for a trend in leukaemia risk with dose. Studies of radiation-exposed groups have generally not shown raised risks of CLL (AGIR, 2003; UNSCEAR, 2008); the 3rd NRRW analysis supports this conclusion. In contrast, this analysis did provide some weak evidence of a raised incidence of non-Hodgkin lymphoma (NHL), within which B-cell CLL is sometimes classified (Hartge *et al*, 2006). Taking together the results for CLL and NHL, there is little evidence of a trend in incidence with dose from this analysis.

7.2.2 All cancers other than leukaemia combined

Since the aetiologies of specific solid cancers are diverse and their radiation sensitivities may vary, some caution might be attached to studying malignant neoplasms other than leukaemia as a whole. Nevertheless, analyses of data for the Japanese atomic bomb survivors have indicated that whilst there is some evidence of heterogeneity between cancers in the ERR per Sv, the variation in ERR across cancers and the modifying effects of factors such as age and time are not greatly different (Preston *et al*, 2003). Given also that the statistical power available in occupational studies such as the NRRW to examine radiation in relation to specific cancers is low, in view of the generally low doses received by workers, it is worth examining the findings derived here for the grouping of malignant neoplasms other than leukaemia. Specific cancers are considered later.

Unlike the previous two NRRW analyses, the 3rd NRRW analysis does show a statistically significant trend with external dose in the risk of all malignant neoplasms other than leukaemia, based both on mortality and incidence data. It should be stressed that the width of the 90% CI for the ERR per Sv has decreased in successive analyses. In particular, relative to that in the 2nd analysis, this CI is about 30% narrower based on mortality data and about 40% narrower based on incidence data. The findings from the three NRRW analyses to date are mutually consistent, but the results have become progressively more precise.

The NRRW-3 results are also consistent with those from the 15-country worker study, although the central estimate obtained here for the ERR is towards the lower end of the 90% CI from the international study. This latter CI is considerably wider than that for NRRW-3, reflecting in part the higher ERR estimate in the 15-country study and the exclusion from that study of some groups of workers with relatively high external doses, on the basis that they also had potential for internal exposure (Cardis *et al*, 2005, 2007). As shown in Appendix D, restricting the NRRW-3 cohort to those UK workers who were included in the 15-country study leads to much less precise results. Such a restriction not only halves the number of workers, but also excludes a substantial proportion of the workers with higher external doses, because many of them were monitored for internal exposure. Simply excluding workers monitored for internal exposure from NRRW-3 leads to increases in both the ERR estimate and the width of the corresponding 90% CI,

although the p-value for a trend in the risk of either mortality or incidence with external dose does not change greatly. On the other hand, stratifying the data on the basis of whether a worker was ever internally monitored has little impact on the NRRW-3 results.

TABLE 7.1 Comparison of estimates of ERR per Sv (and 90% CI) for cancer in the NRRW, the IARC 15-country study and the Japanese A-bomb survivors

	Leukaemia excluding CLL	All malignant neoplasms excluding leukaemia	All malignant neoplasms excluding leukaemia, lung and pleura cancer
3rd NRRW analysis			
- mortality	1.712 (0.06, 4.29)	0.275 (0.02, 0.56)	0.323 (0.02, 0.67)
- incidence	1.782 (0.17, 4.36)	0.266 (0.04, 0.51)	0.305 (0.05, 0.58)
2nd NRRW analysis (Muirhead *et al*, 1999a,b): mortality	2.55 (-0.03, 7.16)	0.09 (-0.28, 0.52)	0.17 (-0.26, 0.70) [a]
IARC 15-country study (Cardis *et al*, 2005, 2007): mortality	1.93 (<0, 7.14)	0.97 (0.27, 1.80)	0.59 (-0.16, 1.51)
Japanese A-bomb survivors			
- BEIR VII (NRC, 2006): mortality	1.4 (0.1, 3.4) [b]	0.26 (0.12, 0.41) [c]	-
- BEIR VII (NRC, 2006): incidence	-	0.43 [d]	-
- IARC (Cardis *et al*, 2005): mortality	1.54 (-0.76, 4.61) [e]	0.32 (0.07, 0.47) [f]	-

a Based on data for all malignant neoplasms excluding leukaemia and lung cancer.

b Based on the low dose component of a linear-quadratic dose-response model fitted to A-bomb data on mortality during 1950-2000. The ERR estimate cited applies to males exposed at ages of 30 years or more, at 15 years following exposure. Values as given by Cardis et al (2007).

c Based on fitting a linear dose-response model to A-bomb data on solid cancer mortality during 1950-2000. The ERR estimate cited applies to males exposed at ages of 30 years or more, at an attained age of 50 years. Values as given by Cardis et al (2007).

d Based on fitting a linear dose-response model to A-bomb data on the incidence of all solid cancers other than thyroid and non-melanoma skin cancers during 1958-98. The ERR estimate cited applies to males exposed at ages of 30 years or more, at an attained age of 50 years.

e Based on the low dose component of a linear-quadratic dose-response model fitted to A-bomb data on mortality during 1950-1990 among males exposed at ages 20-60 years.

f Based on fitting a linear dose-response model to A-bomb data on mortality during 1950-1997. The ERR estimate cited applies to males exposed at age 35 years.

Within the 15-country worker study, the ERR estimate appeared to be particularly influenced by findings for lung cancer, specifically in the data from Canada (Cardis *et al*, 2005, 2007). The authors of that study suggested that confounding by smoking might have partly, but not entirely accounted for their ERR estimate for all cancers other than leukaemia. Like the 15-country study, the NRRW does not hold information on individual smoking habits, so it is not possible to examine directly the possibility of confounding by smoking. However, as in the 2nd NRRW analysis, the grouping of all malignant neoplasms other than leukaemia and lung cancer has been studied, so as to reduce any impact of smoking. (Pleural cancer has also been omitted on this occasion, in order to minimise any effect of asbestos exposure – see section 7.2.5.) Table 7.1 shows that the ERR estimate for this grouping in NRRW-3 is slightly greater than that for the grouping of all malignant neoplasms other than leukaemia, based both on mortality and incidence data. Furthermore, the 15-country study results are closer to the NRRW-3 mortality results when based on the former, rather than on the latter disease grouping. In particular, the 90% CI from NRRW-3 is entirely contained within the corresponding CI from the 15-country study.

Figure 7.2 Trends with dose in relative risk (and 90%CI) for mortality from all malignant neoplasms excluding leukaemia

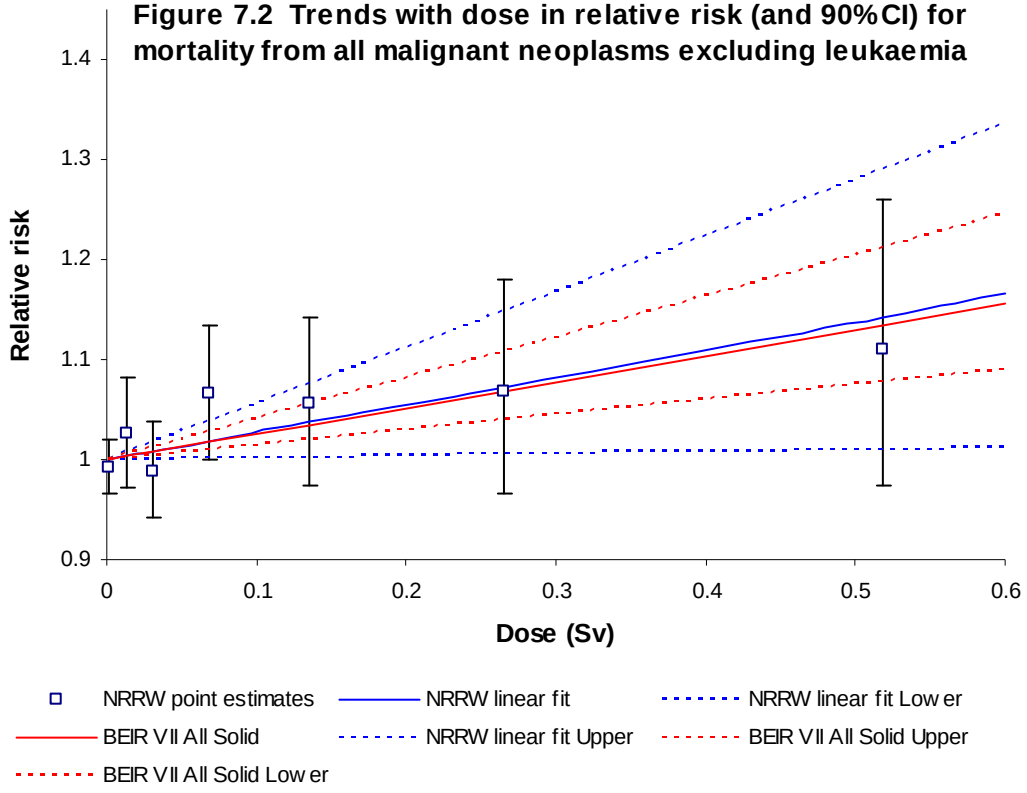


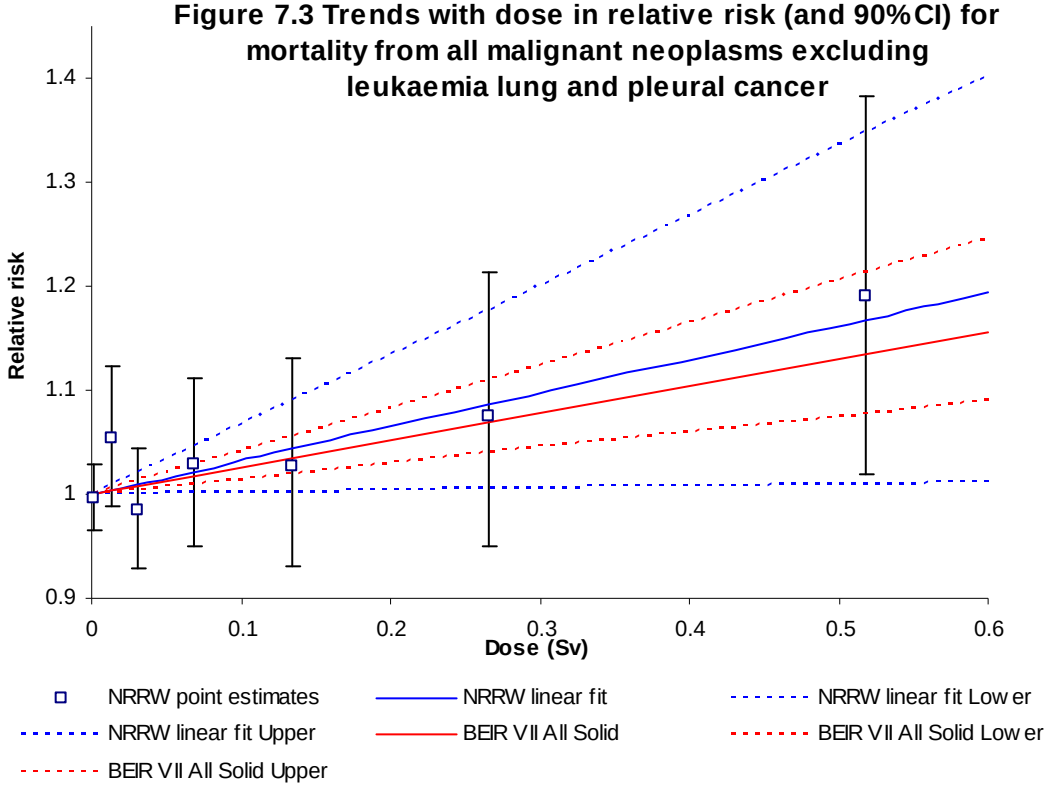
Figure 7.2 shows good agreement between the ERR mortality estimates for the grouping of all malignant neoplasms other than leukaemia from NRRW-3 and from the Japanese A-bomb study (the latter based on the BEIR VII model), although the associated CIs are wider for the NRRW than for the atomic bomb survivors. An important theme in radiation protection is the means by which cancer risks at low doses and low dose rates might be estimated based on results from the Japanese atomic

bomb survivors, who received a wide range of doses but acutely rather than in a protracted or chronic manner. ICRP (1990, 2007) has recommended a DDREF of 2 when extrapolating from high doses and high dose rates down to low doses and/or low dose rates. Based on a joint analysis of the Japanese A-bomb data and of radiobiological data, the BEIR VII Committee (NRC, 2006) derived a range for a low dose extrapolation factor of (1.1, 2.3) with a central estimate of 1.5. (It should be stressed that the BEIR VII risks cited in Table 7.1 and in Figures 7.2 and 7.3 for cancers other than leukaemia are based on a linear dose-response model and do not include this low dose extrapolation factor.) An analysis of the A-bomb data based on the recently revised dosimetry system does indicate curvature in the dose-response for solid cancer mortality over the range 0 – 2 Sv, such that the risk per unit dose is lower at lower doses than at higher doses (Preston *et al*, 2004). However, the estimate of the ERR per Sv at low doses from that analysis was about one-third lower than the corresponding estimate based on the range 0 – 1 Sv among the A-bomb survivors. Preston *et al* (2004) concluded that most of the evidence for curvature in the A-bomb dose-response for solid cancer mortality arises at doses of about 0.5 - 2 Sv, which are greater than most of the doses received in the NRRW. For the incidence of solid cancers among the A-bomb survivors, the BEIR VII Committee (NRC, 2006) estimated a DDREF of 1.3 (95% CI 0.8, 2.6) based on an analysis over the range 0 - 1.5 Sv.

Whilst there is some uncertainty associated with making comparisons, the results for cancers other than leukaemia taken as a whole in NRRW-3 are consistent with those from a linear dose-response analysis of the Japanese A-bomb data, as well as with risks that are both higher and lower than this. In particular, the 90% confidence interval for the ERR estimate from NRRW-3 ranges from just above zero to just over two times the central estimate from the A-bomb data in the case of mortality, and from just above zero to less than twice the central estimate from the A-bomb data in the case of incidence (see Table 7.1). This range would be greater if uncertainties in the A-bomb data – including uncertainties in the modifying effects of age, gender and time – were taken into account. Although the data from the 3rd NRRW analysis provide perhaps the most precise estimates to date of the risks of cancer in humans following protracted low dose exposure, the width of the confidence intervals indicates that these data do not yield sufficient precise estimates of DDREF that could supersede existing estimates based on a combination of A-bomb data and radiobiological findings. Nevertheless, the NRRW-3 data are valuable in indicating that the risk from occupational radiation exposure of all malignant neoplasms excluding leukaemia combined is greater than zero but is unlikely to be more than about two times greater than that estimated from the A-bomb data using a linear dose-response model. If a DDREF of 2 were applied to the A-bomb estimate, as in ICRP (2007), then the risk implied by NRRW-3 is unlikely to be more than four times greater than this value. The NRRW data are also consistent with risks equal to or less than that based on a DDREF of 2, as well as with risks based on the low dose extrapolation factors reported by the BEIR VII Committee (NRC, 2006) of 1.5 - based on a joint analysis of the Japanese A-bomb solid cancer incidence data and of radiobiological data – and of 1.3 – based on the A-bomb data alone. Whilst the NRRW-3 data provide more evidence in favour of a DDREF for solid cancers that is less than 2 than of a DDREF greater than 2, this latter possibility cannot be ruled out.

Figure 7.3 shows that similar inferences can be made based on mortality for the grouping of all malignant neoplasms other than leukaemia, lung and pleural cancer. In the absence of a BEIR VII model for this disease grouping, the A-bomb estimate in this graph has been assumed to be equal to the BEIR VII estimate for all solid cancers. The 90% confidence interval for the ERR estimate from NRRW-3 ranges from just above zero to about two and a half times the central estimate from the A-bomb data in the case of mortality, and from just above zero to less than twice the central estimate from the A-bomb data in the case of incidence (see Table 7.1). If a DDREF of 2 were applied to the A-bomb estimate, then the risks implied by NRRW-3 are unlikely to be more than about five times greater than this value. The NRRW data for all malignant neoplasms other than leukaemia, lung and pleural cancer are also consistent with risks equal to or less than that based on a DDREF of 2, as well as with risks based on the low dose extrapolation factors reported by the BEIR VII Committee (NRC, 2006).

Figure 7.3 Trends with dose in relative risk (and 90%CI) for mortality from all malignant neoplasms excluding leukaemia lung and pleural cancer



The incidence analysis includes about 45% more cancers than does the mortality analysis in NRRW-3. Even though virtually all of the cases in the mortality analysis are also included in the incidence analysis, the findings from analyses of trends in relation to radiation dose based on the two sets of data are remarkably similar (see Table 7.1). Whilst non-melanoma skin cancers represent a sizeable fraction of the non-fatal cancers in the incidence analysis, omitting these cancers has little impact on the results in relation to radiation exposure. In addition, other than the analysis that excluded internally-monitored workers (discussed earlier in this sub-section) and the removal of the adjustment for industrial classification (which, as expected, led to an upward bias), the various subsidiary analyses conducted did not have a large effect on tests for trend in risk with external dose. As with the 15-country nuclear worker study (Cardis *et al*,

2007), there is little evidence for variations in the ERR per Sv with attained age, probably because of low statistical power.

7.2.3 Multiple myeloma

Although there are indications from other studies of links with agricultural work and possibly with radiation exposure, the causes of multiple myeloma are not well understood (De Roos *et al*, 2006). The analyses conducted here found a statistically significantly increasing trend in the risk of multiple myeloma incidence with external dose (one-sided p=0.008), whereas there was no evidence of such a trend from the corresponding mortality analysis (one-sided p=0.221). Previous NRRW analyses reported some evidence of a trend with dose in myeloma mortality (Kendall *et al*, 1992a,b; Muirhead *et al*, 1999a,b). The present analysis contains nearly three times the number of myeloma deaths that were considered in the 2nd analysis and another 36 incident cases. However, it can be seen from Table 6.10 that the evidence for a trend with external dose is largely dependent on fairly small numbers of cases among workers with relatively high doses. The subsidiary analyses show that, as in the 2nd NRRW analysis, the evidence for this trend disappears if workers who were monitored for internal exposure are omitted from the analysis. However, stratifying for internal monitoring gives similar results to the main analysis. With the exception of stratifying according to whether or not the duration of radiation work was at least 10 years, the other subsidiary analyses did not have a major impact on the evidence for a trend in the incidence data.

Analyses of multiple myeloma in other populations exposed to ionising radiation have given mixed results (AGIR, 2003; UNSCEAR, 2008). Among the Japanese atomic bomb survivors, mortality data have shown an association with radiation, whereas incidence data within the same cohort have not (Preston *et al*, 1994). In particular, there were indications in that study that the mortality findings might have been artefacts due to differential misclassification of myeloma on death certificates. Studies of medical and occupational exposures have also given variable results (AGIR, 2003; UNSCEAR, 2008). Some studies of radiation workers, such as the IARC-coordinated 3-country study (Cardis *et al*, 1995), have reported significantly raised risks of myeloma mortality, whilst the 15-country study (which included cohorts from the 3-country study) reported borderline evidence of an increasing trend in myeloma mortality with external dose (Cardis *et al*, 2007). AGIR (2003) noted that those studies suggesting an association between myeloma and radiation were generally studies of mortality, whereas studies of myeloma incidence have tended not to show an association.

The findings from NRRW-3 do not fit into this pattern, in that the evidence for an association with radiation in the present study comes primarily from the cancer incidence data. As mentioned previously, greater weight would normally be placed on these data than on mortality data. However, as noted earlier, the results here are dependent on a few cases at relatively high doses. Consequently, the interpretation of the myeloma results is unclear.

7.2.4 Thyroid cancer

The 1st NRRW analysis (Kendall *et al*, 1992a,b) reported a statistically significantly raised SMR for thyroid cancer, but did not find any association between thyroid cancer mortality and external dose. The 2nd NRRW analysis (Muirhead *et al*, 1999a,b) found a raised SMR for thyroid cancer – although the increase was not statistically significant - and again did not find an association with dose. The mortality findings from the 3rd analysis continue this pattern, with an non-significantly raised SMR (123, 95% CI 72-197, from the lagged analysis) and no statistically significant trend in thyroid cancer mortality with dose.

Since many cases of thyroid cancer are not fatal, the incidence data collected for this analysis should be more informative than the corresponding mortality data. Indeed, the number of thyroid cancer cases studied here is over three times the number of deaths. There is weak evidence of a trend with external dose in thyroid cancer incidence (one-sided p=0.079), with an ERR per Sv of 3.236 (90% CI -0.19, 13.9). Subsidiary analyses showed that this evidence disappeared if workers who were monitored for internal emitters are excluded, whilst stratification on the basis of internal monitoring or according to whether or not the duration of radiation work was at least 10 years provided very little evidence of a dose trend. Table 6.10 indicates that the weak evidence for a trend in incidence with dose appears to be driven by a couple of cases among workers with a cumulative dose of 400 mSv or more.

Studies of the Japanese atomic bomb survivors and of medically-exposed groups have shown that external radiation exposure in childhood increases the risk of thyroid cancer (Ron *et al*, 1995; UNSCEAR, 2008). Indeed, radiation is one of the few risk factors clearly associated with thyroid cancer, whilst the role of other possible factors such as genetic susceptibility is not well understood at present (Ron and Schneider, 2006). Based on a pooled analysis of data from medically-exposed groups and the Japanese A-bomb survivors, Ron *et al* (1995) estimated the ERR per Sv from childhood exposure to be 7.7 (95% 2.1, 28.7), which is higher than the estimated ERR for many other types of cancer (UNSCEAR, 2008). Furthermore, various studies conducted in the former Soviet Union following the Chernobyl accident have reported raised risks of thyroid cancer associated with exposure to radioiodine in childhood (UNSCEAR, 2008). In contrast, studies of adult exposures to either external radiation or to radioiodine have provided less evidence of a raised risk of thyroid cancer (UNSCEAR, 2008). The 15-country worker study did not show an association with dose (Cardis *et al*, 2007), but that analysis was based on mortality data. An analyses of radiation workers in Canada found a raised incidence of thyroid cancer relative to national rates, based on a total of 129 cases, although the authors did not analyse incidence in relation to dose because “there were few high doses” (Sont *et al*, 2001). A raised incidence relative to national rates has also been reported among US radiologic technologists (Sigurdson *et al*, 2003) and - both in this population (Zabel *et al*, 2006) and in a group of Chinese medical x-ray workers (Wang *et al*, 2002) - there were suggestions of an association between thyroid cancer incidence and year of starting employment. However, inferences based on these two studies are limited by a lack of dosimetry data. Studies of Chernobyl clean-up workers have also found raised incidence rates relative to national values, but did not show an association with recorded dose (Ivanov *et al*, 2003; Rahu *et al*, 2006). Among both the Chernobyl clean-up workers and the afore-mentioned medical workers, thyroid

cancers may have been ascertained in a more complete and accurate fashion than was the case in the general population. Consequently, standardised incidence ratios for thyroid cancer among such groups of workers should be interpreted with caution.

The findings from these studies do not rule out a raised risk of thyroid cancer from exposure to radiation in adulthood, but they do suggest strongly that any risk would be smaller than that associated with exposure in childhood. The results on thyroid cancer incidence from the 3rd NRRW analysis – which are very imprecise and dependent on a couple of cases at relatively high doses – are consistent with this conclusion.

7.2.5 Other specific cancers

Studies of populations such as the Japanese A-bomb survivors have indicated that many types of cancer can be induced by radiation exposure (UNSCEAR, 2008; Preston *et al*, 2007). However, the current analysis has less statistical power than the A-bomb study to detect raised risks for specific cancers. Consequently, it is likely that some of the raised risks found here for specific cancers are at least partly due to chance and that the failure to detect trends with dose in the risk of some other cancers is a reflection of this limited power.

This analysis found statistically significant trends in risk with dose (based on a one-sided test) for several specific cancers other than those discussed earlier in this section. These findings arose for cancers of the rectum (based on both mortality and incidence data), larynx (based solely on mortality data), all skin combined (based on incidence data), non-melanoma skin (based on incidence data) and uterus (based on mortality and - specifically for endometrial cancer - incidence data). With the exception of skin, these cancers have rarely been associated with radiation in other studies (Boice, 2006). Since cancers are likely to have been better identified using incidence rather than mortality data, then the findings for laryngeal cancer based solely on mortality data are unlikely to be robust. The dose trend findings for uterine cancers (which mainly reflect endometrial rather than cervical cancers) are based on relatively small numbers when compared with other cancers. In particular, Tables 6.9 and 6.10 indicate that the evidence for an increasing trend in risk with dose is driven largely by one case with a cumulative dose in the range 200-399 mSv. Atkinson *et al* (2004) reported a statistically significantly raised SMR of 386 (95% CI 185-711) for endometrial cancer among female radiation workers at UKAEA. However, the corresponding unlagged SMR from this analysis, which includes UKAEA workers, was not statistically significantly raised (SMR 153, 95% CI 81-261). Thus, the dose trend findings for uterine cancers may be due to chance. In contrast, the results for rectal and skin cancers are based on comparatively large numbers of incident cases.

The findings for skin cancers are driven predominantly by those for non-melanoma skin cancers; there is no statistically significant trend with dose in the incidence of melanoma of the skin, although the central estimate of trend is similar for the two skin cancer groupings. The results for non-melanoma skin cancers are noteworthy because previous NRRW analyses looked solely at mortality and hence would have been unable to detect a raised risk for this grouping of cancers, which are rarely fatal. Associations between non-melanoma skin cancer and radiation have been found in several

populations, such as the A-bomb survivors (UNSCEAR, 2008; Preston *et al*, 2007). However, the evidence from these other studies arose mainly from persons exposed to doses above about 1 Sv, ie. well above the range of doses in the NRRW. In particular, there is strong evidence that the ERR per Sv in the A-bomb study is lower below 1 Sv than it is at higher doses (Preston *et al*, 2007). Furthermore, the registration of non-melanoma skin cancers is known to be poor compared to most other cancers (Karagas *et al*, 2006) and varies widely within the UK (Goodwin *et al*, 2004). There is no particular reason to think that the ascertainment of such cancers would be better among workers in this study with higher radiation exposures. Nevertheless, some degree of differential ascertainment cannot be ruled out. A further limitation on the interpretation of these findings is the absence of information on workers' exposure to ultraviolet radiation, which is a key determinant of skin cancer risk (Karagas *et al*, 2006).

Rectal and colon cancers share some hereditary and dietary risk factors, although there is some evidence of differences in their aetiology (Giovannucci and Wu, 2006). Whilst there is a clear association between colon cancer incidence and radiation among the Japanese atomic bomb survivors, the corresponding results in this population for rectal cancer were mixed, with no association found amongst men but an increasing trend in risk with dose amongst women (Preston *et al*, 2007). Studies of patients treated with radiation for prostate cancer show raised risks of rectal cancer, but based on rectal doses of tens of sieverts (UNSCEAR, 2008). Some studies of radiation workers – for example, in Canada (Sont *et al*, 2001) and Japan (Iwasaki *et al*, 2003) – have reported increased risks of rectal cancer in relation to radiation exposure. However, the 15-country study of nuclear workers (which included data from the 2nd NRRW analysis) did not find a statistically significant trend with dose in rectal cancer mortality (Cardis *et al*, 2007). UNSCEAR (2008) concluded that it is difficult to characterise any risk of rectal cancer due to radiation doses below 1 Sv. Although the findings for rectal cancer from the current analysis are based on a relatively large number of cases when compared with some other types of cancer, the 90% confidence interval for the ERR per Sv is wide, based on either mortality data (0.19, 4.12) or incidence data (0.21, 2.85), and encompasses the estimated ERR per Sv from this analysis for all malignant neoplasms other than leukaemia combined. Taken together with the lack of clear evidence for associations with radiation from other studies and the fact that many types of cancer have been studied here, there is little evidence to suggest that rectal cancer is particularly radiosensitive.

The comparison with national mortality rates highlighted a statistically significant SMR for only one type of cancer, namely pleural cancer. The unlagged SMR from this analysis, namely 209, is comparable to that observed in the 2nd NRRW analysis, ie. 198 (Muirhead *et al*, 1999a,b). Furthermore, the results here are based on about three times as many deaths (112 compared with 42 in the 2nd analysis). As with the previous NRRW analysis, there is no evidence of a trend in pleural cancer mortality with increasing dose. Furthermore, there is also no evidence of a trend with dose in pleural cancer incidence, based on about 50% more cases than were available for the mortality analysis. These findings accord with those from other studies of populations exposed to x- and gamma radiation in not showing a clear excess (IARC, 2000). The overwhelming risk factor for pleural cancer is exposure to asbestos (Boffetta and Stayner, 2006). Whilst there is no information in the NRRW on individuals' potential for asbestos

exposure, it is highly likely that the raised SMR for pleural cancer in this study is due to asbestos rather than radiation exposure.

A limitation of the NRRW is to the absence of information on smoking habits. However, some indication of the extent to which the findings might be confounded by smoking can be gained by examining the results for smoking-related diseases. Non-cancer diseases are discussed in section 7.3; for now, consideration will be given to lung cancer, which is overwhelmingly due to smoking (Stewart and Kleihues, 2003). Inspection of Tables 6.9 and 6.10 shows that, both for mortality and incidence, the ratio of the observed number of lung cancers to the number that would be expected in the absence of any radiation effect tends to increase with increasing dose, except for the highest dose group where this ratio falls below 1 (although not to a statistically significant extent). A similar pattern was seen in lung cancer mortality in the 2nd NRRW analysis (Muirhead *et al*, 1999a,b), although based on only about half the number of lung cancers as in the current analysis. Studies of the Japanese A-bomb survivors, medically-exposed groups and populations exposed to radon have demonstrated increases in lung cancer risk following radiation exposure (UNSCEAR, 2008). However, there was no statistically significant trend with dose in lung cancer incidence or mortality in the current NRRW analysis. The apparent downturn in the dose-response in the highest dose category suggests that workers with the highest doses in this study might have tended to smoke less than workers with lower doses, perhaps because of restrictions on smoking in their workplace. It should be stressed that this conjecture cannot be proved in the absence of data of individual smoking habits. Nevertheless, the lung cancer findings suggest that – in studying the risk of cancers other than leukaemia - greater weight should be given to analyses that exclude lung cancer, so as to reduce the impact of any confounding by smoking. As was shown previously in Table 7.1, estimates of the ERR per Sv for malignant neoplasms other than leukaemia are slightly higher when lung and pleural cancers are omitted.

In addition to the cancers mentioned earlier in this section, there are several types of cancer for which the observed number of cases is considerably greater than the corresponding number of deaths. A notable example is breast cancer in women, for which the number of cases is about three times the number of deaths. However, here – as for many specific cancer types – the incidence data are still too sparse to draw firm conclusions. In particular, the low power of the breast cancer analysis is due mainly to the relatively small proportion of females in the study population.

7.3 Non-cancer mortality

Previous analyses of the NRRW have examined data on mortality from non-malignant causes in order to assess the potential for confounding in the cancer analyses. In particular, since the NRRW does not contain data on individual smoking habits, trends in mortality from non-malignant causes related to smoking have been studied in order to gauge the possible impact of smoking on tests for trend with dose in cancer risks. However, in recent years, greater attention has been paid to findings from other studies concerning radiation exposure and non-malignant disease, particularly circulatory

diseases (UNSCEAR, 2008). Both this topic and the potential for confounding will be considered here.

Mortality from all of the non-malignant causes studied here was less than expected from national rates, mostly to a statistically significant extent. For a grouping of non-malignant diseases that are strongly related to smoking, there was no evidence of a trend in risk with dose, although – as in the 2nd NRRW analysis and as also seen here for lung cancer - the observed number of deaths in the highest dose group was somewhat less than the number that would be expected in the absence of a radiation effect. The findings for the diseases that make up this grouping of non-malignant smoking-related diseases were disparate. Coronary heart disease (CHD), which is one of the largest causes of death not only in the NRRW but also in the general population, increased to a near-statistically significant extent with increasing dose (ERR per Sv 0.259, 90% CI 0.00, 0.55; one-sided p=0.053). In contrast, there was a strong decreasing trend with increasing dose in mortality from bronchitis, emphysema and chronic obstructive disease (two-sided p=0.001), whereas there was no evidence of a dose trend in mortality from aortic aneurysm. The trend with dose in mortality from circulatory diseases that are not strongly related to smoking was not statistically significant, but the estimate of the ERR per Sv (0.28, 90% CI -0.12, 0.75) was similar to that for CHD. For all circulatory diseases combined, the trend in mortality with dose was statistically significant (ERR per Sv: 0.251, 90% CI 0.03, 0.49; one-sided p=0.03). The subsidiary analyses showed that the evidence for a dose trend was reduced if the data were stratified according to whether or not the time since start of radiation work was at least 10 years, was greatly diminished if the data were stratified according to whether or not the duration of radiation work was at least 10 years, and this evidence disappeared if the cohort were restricted to that included in the 15-country study.

Analyses of data for the Japanese atomic bomb survivors have found increasing trends with dose in mortality from circulatory diseases, as well as from respiratory and digestive disease (Preston *et al*, 2003). The A-bomb data are consistent with a linear dose-response relationship for circulatory diseases, but they are also consistent with no increase in risk below doses of about 0.5 Sv (Preston *et al*, 2003). Studies of patients who received high dose radiotherapy to the heart (eg. during treatment for breast cancer) have also shown raised rates of heart disease (UNSCEAR, 2008). However, aside from the A-bomb study, other epidemiological studies have generally not provided strong evidence of raised risks of circulatory diseases below doses of a few Sv (McGale and Darby, 2005; UNSCEAR, 2008). The 15-country worker study did not show an association between radiation and circulatory disease mortality, although – reflecting its relatively low statistical power – it could not rule out an ERR per Sv of the magnitude seen among the Japanese A-bomb survivors (Vrijheid *et al*, 2007b). An analysis of around 42,000 radiation workers at BNFL – virtually all of whom are in NRRW-3 – followed to the end of 2005 found an association between circulatory disease mortality and external radiation dose, although the form of this association varied between sub-groups of workers (McGeoghegan *et al*, 2008). Furthermore, it was not possible in this and most other analyses of radiation workers – including NRRW-3 – to adjust for known risk factors for circulatory diseases, such as smoking habits, alcohol consumption and diet.

The estimated ERR per Sv for all circulatory diseases combined from the 3rd NRRW analysis is comparable with that estimated in the A-bomb study (Preston *et al*, 2003). However, much of the evidence for a trend in the risk of circulatory diseases arises for CHD, which is particularly influenced by smoking. It is notable that, for each of CHD, aortic aneurysm and cerebrovascular disease as well as for all circulatory diseases combined, the ratio of the observed number of deaths to the number that would be expected in the absence of any radiation effect tends to increase with increasing dose, except for the highest dose group where this ratio falls below 1. A similar pattern is seen for lung cancer. In addition, the analysis by duration of radiation work suggests that some feature of long-term radiation work other than radiation exposure *per se* might influence the risk of circulatory diseases. In the absence of direct information on smoking and on other non-radiation factors – related to either lifestyle or occupation - that influence circulatory disease risk, it is difficult to interpret the findings obtained here for circulatory diseases. Nevertheless, the similar patterns with dose in the risk of circulatory disease and lung cancer indicate some degree of confounding by smoking, although the direction and magnitude of this effect cannot be quantified.

Among other non-malignant causes of death, there was evidence of an increasing trend with dose in mortality for a grouping of respiratory diseases that are not related to smoking, although the corresponding SMR was particularly low (ie. 63 in the lagged analysis). These findings are similar to those reported in the 2nd NRRW analysis (Muirhead *et al*, 1999a.b), although the evidence for a dose trend is weaker in the current analysis. Whilst a trend with dose in mortality from respiratory diseases has been reported among the Japanese atomic bomb survivors (Preston *et al*, 2003), there is little information on this disease grouping from other studies (UNSCEAR, 2008). In view of the lack of data on non-radiation causes of these diseases - which may be particularly important here, in view of the very low SMR - as well as the possibility of a chance finding associated with analysing a number of different diseases, the findings obtained here for respiratory diseases not related to smoking cannot be interpreted further.

7.4 Uncertainties in estimates of radiation risks based on the NRRW

A key aspect of this analysis was to derive more precise estimates of mortality and cancer incidence risks relating to occupational radiation exposures, when compared with previous studies. As can be seen from Table 7.1, this aim has been achieved. The 90% confidence intervals for the ERR per Sv for non-CLL leukaemia and for the grouping of cancers other than leukaemia are about 30-40% narrower than those derived from the 2nd NRRW analysis. This is line with power calculations that were undertaken in advance of the 3rd analysis. Furthermore, these confidence intervals are narrower than those from the 15-country study of radiation workers in the nuclear industry (Cardis *et al*, 2005, 2007). Whilst this study considered over twice the number of workers in NRRW-3 (including roughly half of the number of workers in NRRW-3), the there was a greater proportion of workers with higher external doses in NRRW-3 than in the 15-country study, due largely to the exclusion from the latter study of workers with potential internal exposure. In addition, the average length of follow-up was greater in

NRRW-3 and, whereas the 15-country study focussed on mortality, the current analysis was also able to use incidence data.

The confidence intervals from NRRW-3 are still wider than those based on extrapolation down to low doses of findings from the Japanese atomic bomb survivors. Nevertheless, particularly for leukaemia, the difference between NRRW-3 and the A-bomb survivors in the width of the confidence interval for the ERR per Sv at low doses is not that great. This is not to say that the NRRW data are sufficient to form the main basis of radiation risk estimates at low doses. The A-bomb data cover a smaller population, but one which has a wider range of ages – including many people exposed in childhood – and a higher proportion of females than of males (Preston *et al*, 2003, 2007). In contrast, women still form only about 10% of the NRRW population, although this proportion has tended to rise over time. In addition, the Japanese A-bomb survivors have been followed up for mortality and cancer incidence more than 50 years, whereas relatively few of the workers in NRRW-3 have been followed for this length of time. Consequently, the A-bomb data, which have been used by bodies such as the BEIR VII Committee (NRC, 2006), ICRP (2007) and UNSCEAR (2008) as the main basis for radiation risk estimates, are likely to continue to fulfil this role. However, the findings from NRRW-3 are valuable in providing direct information on cancer risks following protracted or fractionated low dose exposures that can be used to assess the validity of risk estimates based on the A-bomb data.

The findings for many specific types of cancer are clearly less precise than those for the grouping of all cancers other than leukaemia, although an advantage of the current analysis is the availability of cancer registration data that should provide more accurate diagnostic information than mortality data. Given that only about 15% of the study cohort had died by the end of the current follow-up period, continued follow-up should provide more precise results for specific cancers and for specific non-cancer causes of death. In particular, it should be clearer with continued follow-up whether or not some of the suggestions of raised risks for certain cancers and causes of death are chance findings due to small numbers, particularly at higher doses. Longer follow-up might also reveal small raised risks for some other cancers or death causes. To date, other than for leukaemia, the focus in the NRRW has been on examining large groupings of cancers because of the small numbers for specific cancers.

Aside from limitations on statistical power, particular consideration has to be given in studies such as this to the potential for confounding. Aside from the impact of age, gender and calendar period, attempts have been made to remove confounding associated with geographical and social class variations in mortality and cancer incidence rates. Furthermore, since smoking is a major cause of cancer and death in the UK and elsewhere (Doll *et al*, 2004; Stewart and Kleihuis, 2003), the extent to which the findings here for specific cancers and causes of death might be due to confounding by smoking has been considered. As data on individual smoking habits are not available in the NRRW, the focus here has been on looking at diseases or groupings of diseases strongly linked to smoking and those for which any link is likely to be relatively weak. The irregular pattern with dose in the risk for lung cancer and the main forms of circulatory disease suggest that – as in the previous NRRW analysis - they may well be some degree of confounding by smoking. Consequently, particular emphasis should be placed on the findings for the grouping of solid cancers that excludes lung cancer. Also,

whilst the NRRW does not contain information on occupational exposures to agents other than ionising radiation, the raised standardised mortality ratio for pleural cancer indicates strongly that many of the workers in the NRRW have been exposed to asbestos. Again analyses were conducted of solid cancers excluding pleural cancer, although there was no suggestion from the dose-response analysis of pleural cancer of confounding by asbestos.

As in all epidemiological studies that attempt to quantify risks in relation to radiation exposure, a potentially important component of uncertainty relates to the accuracy and precision of the radiation doses. Depending upon their form, errors in dose estimates can have differing effects on analyses of trend in risk with dose; more details are given by Schafer and Gilbert (2006). So-called "classical" measurement errors, under which the observed dose represents the sum of a "true" dose and an error which has zero mean and is independent of the true dose, represent imprecision in the measurement of dose. They can lead to an under-estimation of the magnitude of any radiation effect, although their effect on statistical tests for trends in risk with dose is usually relatively small. Gilbert (1998) has argued that such measurement errors are unlikely to have a major impact on studies of radiation workers, because the larger cumulative doses - which are most influential in dose-response analyses - are the sums of large numbers of independent dosimeter readings. In contrast to these classical measurement errors, so-called "Berkson" errors, under which the "true" dose equals the sum of the observed dose and an error which has zero mean and is independent of the observed dose, can arise – for example – if a dosemeter reading were missing and the average dose for workers at the same facility and over the same period were imputed in its place. Berkson errors do not tend to bias the estimated trend in risk with dose, but the confidence interval for the trend estimate is wider than would be the case in the absence of such errors. An additional complexity is that sometimes a common correction factor might be applied to doses for groups of workers; for example, to allow for changes over time in dosemeter sensitivity. Unless such corrections were known accurately and precisely, they would induce errors that are shared across individuals.

The 3rd NRRW analysis did not incorporate formal statistical modelling of the impact of errors in external doses. However, it has been shown here that the main findings are insensitive to the form of the adjustments that were applied to the raw doses in this study. It is also instructive to consider the findings from a study of errors in dosimetry that was conducted as part of the 15-country nuclear worker study (Thierry-Chef *et al*, 2007). This concluded that the major sources of uncertainty in estimates of higher energy photon doses were dosimetry technology, exposure conditions in the workplace and historical calibration practices. Based on a review of information from participating facilities, Thierry-Chef *et al* (2007) derived a set of period- and facility-specific estimates of bias and imprecision in recorded doses that were used to calculate the doses used in the 15-country study. These bias correction factors were not greatly different from 1 in most situations. The 15-country analysis did not take account of "shared" errors relating to the uncertainty in the correction factors (Cardis *et al*, 2007). However, methodological work undertaken based on data from a study of workers at a US nuclear facility indicates that adjusting for shared errors has relatively little impact in this instance (Stayner *et al*, 2007).

Whereas the NRRW contains good information on external radiation dose, for the most part it does not hold information on doses due to intakes of radionuclides. The doses received by workers monitored for internal exposure are likely to be lower than their external doses in most instances. Indeed, some of the monitored workers may not have received any internal dose. However, particularly for doses to lung from actinides such as plutonium, internal doses may sometimes form a substantial proportion of the total occupational dose, although the assessment of these doses is not straightforward (Riddell *et al*, 2000). In the absence of internal dose estimates, the approach taken in NRRW-3 has been to examine the impact on the findings in relation to external dose of (i) excluding workers who were monitored for internal exposure and (ii) stratifying the results on the basis of whether or not a worker had ever been internally monitored. In interpreting the results of option (i), it should be borne in mind that many of the workers who had been internally monitored had also received relatively high external doses. Consequently, estimates of the ERR per Sv were less precise after excluding this group. On the other hand, option (ii) retained information on these workers. For the most part, this stratification tended to give similar results to those from the main analysis, at least for the large disease groupings. Consequently, the absence of internal doses is unlikely for the most part to have biased the findings from NRRW-3. Nevertheless, it is likely that for a few cancer sites such as lung, information on both external doses and internal doses – as well as non-radiation factors such as smoking – would be required in order to make more definitive inferences. This topic is being considered under the European Commission's *Alpha-risk* project, in which doses following plutonium and uranium intakes are being calculated for groups of nuclear workers in the Belgium, France and the UK (including some workers who are also in the NRRW), as part of a nested case-control study of lung cancer and leukaemia: see http://www.alpha-risk.org/.

7.5 Future analyses

It is intended to continue to follow workers in the NRRW and to identify deaths and cancers beyond the end of the current follow-up for inclusion in future analyses. As mentioned earlier, only 15% of the study population was known to have died by the end of 2001. Further follow-up would therefore be valuable in:

- Increasing yet further the precision of analyses that look for any trend with dose in the risk of leukaemia and of all other cancers combined;
- Looking for any evidence that radiation-associated risks might vary by factors such as age or time;
- Studying specific cancers and causes of death in more detail.

Such follow-up would also be valuable in examining whether, for example, the suggestion of an association between radiation exposure and circulatory disease mortality persists. However, since the NRRW lacks information on potential confounding factors such as smoking, it should be recognised that – for this disease grouping – continued follow-up may not be sufficient to determine whether or not there is a causal link and that findings from other studies would need to be considered. In particular, circulatory disease mortality and morbidity is currently being studied among

workers at Mayak plant in Russia in an analysis that takes account of smoking habits and alcohol consumption; see http://www.helmholtz-muenchen.de/soul/ and Azizova *et al* (2008).

Since annual doses have continued to decrease in recent years, the inclusion of new radiation workers in the NRRW is unlikely to have a major impact on the statistical power of future analyses. Nevertheless, there is value in continuing to add these workers to the NRRW, in that it would allow patterns of mortality amongst them to be studied in a similar manner to workers who are already in the study. There are also logistical advantages in continuing to add these workers to the study, in that it is necessary to collect annual updates of personal and dose information from participating organisations and this procedure is easier to perform if it covers all eligible workers (other than those who have declined to participate) rather than specific sub-groups. There are some groups of workers whom it was not possible to include in the current analysis owing to concerns about data completeness; in particular, persons who started radiation work at British Energy Generation and Magnox Electric sites in England and Wales after 1990, as well as Approved Scheme (non-classified) workers at Royal Dockyards. We hope that, in cooperation with the relevant organisations, that these data can be improved to the extent that such groups of workers can be included in future analyses. In addition, whilst data on category B and category C workers are now available for many of the organisations in the NRRW, the feasibility of adding data on these categories of workers from some of the other employers or sites (eg. BE/ME Hunterston and GE Healthcare) will be considered. It should also be recognised that the NRRW does not include all groups of radiation workers in the UK; for example, those in the NHS. However, very careful consideration would have to be given to the feasibility of collecting complete and accurate data for relatively large numbers of workers from any new participating organisation before including any such data in the NRRW.

A more detailed analysis of the impact of uncertainties in external doses may be of value, although – as indicated previously – the effect of such uncertainties may not be particularly large compared by other sources of uncertainty. An area that is certainly worthy of consideration would be to quantify not only external photon doses but also doses from other types of radiation. The NRRW is providing an input to research on exposures to alpha emitters as part of the afore-mentioned *Alpha-risk* project and it would be helpful to build upon this in future work. In addition, the Advisory Group on Ionising Radiation (AGIR) has recommended that a comprehensive database of tritium doses be constructed for use in epidemiological studies (AGIR, 2007). Since the NRRW contains the main groups of tritium-exposed workers in the UK, it would be well-placed to act as a focus for future epidemiological research in this area.

Finally, the international dimension to studies of radiation workers needs to be recognised. Anonymised data from the 2nd NRRW analysis formed the UK contribution to the 15-country study and, subject to the agreement of the participating organisations, it is hoped that data from the 3rd NRRW analysis could be used in any follow-on to the 15-country study. In addition, AGIR has pointed out that attempts to study tritium-exposed workers would be best performed on an international basis, in view of the likely low statistical power of studies in individual countries. International collaboration on this

topic and in examining other radiation types as well as external photon doses would be valuable.

8 CONCLUSIONS

As in previous NRRW analyses, total mortality and mortality from major causes has continued to be less than expected from rates for England and Wales. This "healthy worker effect" was still present after adjustment for social class. The only cause for which mortality was statistically significantly greater than expected from national rates was pleural cancer, probably reflecting exposure to asbestos.

Mortality and incidence from both leukaemia excluding chronic lymphatic leukaemia and the grouping of all malignant neoplasms other than leukaemia increased to a statistically significant extent with increasing external radiation dose. The corresponding central estimates of the trend in risk with dose were similar to those for the survivors of the atomic bombings of Hiroshima and Nagasaki, whilst the 90% confidence intervals for the NRRW trends excluded values more than about 2-3 times greater than the A-bomb risk estimates as well as values of zero or less. Whilst there was some evidence of an increasing trend with dose in mortality from all circulatory diseases combined, the irregular pattern in risk with dose and similarities with the corresponding pattern for lung cancer suggest that this finding may, at least in part, be due to confounding by smoking. In contrast, both for mortality and incidence, the trend with dose in the risk of all malignant neoplasms other than leukaemia was maintained when lung and pleural cancer were excluded from this disease grouping, so indicating that the trend is not an artefact due to smoking. Statistically significantly increasing trends with dose were seen for several specific cancers, although some of these results might be chance findings or artefacts.

This analysis provides the most precise estimates to date of the risks of mortality and cancer incidence following occupational radiation exposure and strengthens the evidence for raised risks due to these exposures. The cancer risk estimates obtained here are consistent with values used by national and international bodies in setting radiation protection standards. Continued follow-up of these workers should be valuable to see whether radiation-associated risks vary over time or by age, and to study specific cancers and causes of death in more detail. The NRRW is also well-placed to contribute to wider national and international studies on the effects of occupational radiation exposures.

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APPENDIX A Participating Organisations and Definition of the Study Population at Each Site or Establishment

A1 GENERAL ASPECTS

General exclusions to the study population defined below are foreign nationals and vacation or other students who may have spent short periods at the relevant organisation. Contractors– including those on maintenance work - who worked at the site were also usually excluded. This was because the prime responsibility for dose record keeping usually did not lie with the site and, as a consequence, the quality of the data was not as good as that for permanent employees and the possibilities for pursuing queries were much reduced.

The categories A, B, C and D mentioned below are defined in section 2.1 of the report.

A2 PARTICIPATING ORGANISATIONS

A2.1 Atomic Weapons Establishment (AWE)

AWE was formed in 1948 as HER (High Explosive Research) at Fort Halstead, the Royal Arsenal Woolwich and elsewhere. Operations involving radioactive materials and ionising radiations began in 1948 at the Royal Arsenal. Over the next few years further sites became involved, including the site now known as AWE (Foulness). In 1952 the main research and production effort was in place at Aldermaston (named AWRE Aldermaston at the end of 1952); this site provided dosimetry services from 1952 onwards and has continued so to do up to the present day. In January 1955, the AWRE sites became part of UKAEA, and remained so until April 1973 when they were transferred to the Ministry of Defence (MOD). In September 1987 AWRE became the Atomic Weapons Establishment (AWE) and two Royal Ordnance Factories at Burghfield and Cardiff were incorporated into AWE. Ten years later, in February 1997 and as part of a rationalisation programme, AWE Cardiff, which provided component manufacturing support for the nuclear weapons programme since 1961, stopped production. Its work was transferred to Aldermaston and Burghfield and the Cardiff site was subsequently decommissioned. Also in 1997, AWE withdrew from Foulness - a 1,000 acre range site on the Essex coast, which had been involved in the research and development of nuclear and conventional weapons since 1947. AWE now retain two operating sites using ionising radiations: AWE (Aldermaston) and AWE (Burghfield). AWE is now managed and operated, on behalf of the Secretary of State for Defence, by AWE Management Ltd, an independent company whose shareholders are British Nuclear Fuels Plc (BNFL), Serco and Lockheed Martin.

Personal radiation records of the exposures of AWE employees at Aldermaston and Foulness have been retained since work started at Aldermaston in 1948; there are a few records for pre-HER employment back to 1946. Additionally, it is known that several early employees, who transferred to HER or AWRE up to about 1955, had worked with ionising radiations previously up to as far back as about 1930; however, their exposures

are not recorded and are unknown, although in some individual cases the information available indicates that exposures may have been substantial.

AWE employees are routinely approached by their Trades Union with an explanation of the NRRW and its objectives, and they are given the opportunity to be excluded from the study. The first set of data on workers in categories A and D was transferred in 1979 and there is now an established process of data provision for current workers. Annual updates supplied by Aldermaston included data for current Burghfield and Cardiff workers from 1990 to 1997 for the Cardiff workers and from 1990 to the present for Burghfield workers. Data on category B and C workers at the Aldermaston and Foulness sites were collected by AWE and UKAEA staff, in conjunction with staff from the London School of Hygiene and Tropical Medicine (LSHTM). These data, together with those on category A and D workers who started work before 1983, have been the subject of separate analyses, both of AWE workers specifically (Beral *et al*, 1988) and as part of NICEA (Carpenter *et al*, 1994). The data on category B and C workers have been transferred to the NRRW. As for 2nd NRRW analysis, this analysis incorporates the updated dosimetry and personnel data for workers in NICEA.

Definition of the study population for AWE

All employees for whom radiation dose records were kept at any time up to 31 December 1999, excluding those who refused to participate and excluding those workers employed only at the Burghfield and Cardiff sites before 1990.

A2.2 British Energy Generation and Magnox Electric Ltd (BE/ME)

British Energy Generation and Magnox Electric Ltd manage a number of nuclear power stations in Scotland, England and Wales. In 2008, some of these sites are still generating power but many are at various stages of decommissioning. British Energy Generation, formerly Nuclear Electric Ltd, was privatised as a subsidiary of British Energy plc while Magnox Electric Ltd is the Site License Company (SLC) that manages the day-to-day operations across two regions of UK reactor sites, Magnox North and Magnox South on behalf of the Nuclear Decommissioning Authority (NDA). However, for historical reasons, the workers at the nuclear power stations and related sites are considered in combination in this report. Apart from the nuclear power stations, radiation work was also undertaken at Berkeley Centre (formerly Berkeley Nuclear Laboratories) and at a few other sites. Details are given in Table A1.

A2.2.1 Sites in England and Wales

When the NRRW was introduced, records for power stations in England and Wales were held in various places, so it was agreed that the Central Computing Bureau of the then CEGB (Central Electricity Generating Board) would collect all the information for transmission to the NRRW. The first transmission of data for classified workers in categories A and D took place during 1978. Entry was originally on the basis of positive consent from each individual, but this was changed in 1982 to a positive refusal system. Data for classified workers in categories A and D were received and processed for the

second NRRW analysis for calendar years up to 1990. CEGB also set out to establish the cohort of employees who ceased radiation work before 1 January 1976, and data for these workers were passed to the NRRW in 1989 and were included in the 2nd NRRW analysis.

Following the creation of Nuclear Electric and then the division of responsibilities to British Energy Generation and Magnox Electric Ltd, the responsibility for record keeping was centralised and undertaken by the Central Dose Records Service (CDRS). The CDRS is now operated by VT Nuclear Services (formerly BIL Solutions). Data transfers for data for years 1986 to 2004 were made by CDRS between 2003 and 2004. However, despite a great deal of work by the researchers and the assistance of both British Energy and British Nuclear Group, it has not been possible to ascertain full and complete details relating to records identified as additional to the 2nd analysis cohort. The researchers therefore reluctantly decided that, although they would like to include this group of workers in a future analysis, it was not feasible to identify the relevant information for inclusion in this analysis. The researchers regret this outcome and recognised that the companies involved would also be disappointed. The researchers do plan to work, with the relevant organisations, towards resolving this for the future and they continue to be grateful for the assistance provided by these companies.

Audits at (then) CEGB sites were conducted for the 1st NRRW analysis (see Appendix E of Kendall *et al* (1992)). These indicated that the coverage of the potential study population was substantially lower than had been believed. Investigations by CEGB staff showed that before 1982 (when the positive refusal scheme was introduced) a substantial number of individuals had left employment without either agreeing or refusing to participate in the NRRW. Consequently, CEGB participants did not enter the first analysis until the beginning of 1983. Steps were subsequently taken by the operating companies to adopt a positive refusal scheme for the whole period covered by the NRRW. The procedure allowed those who objected to participation to be omitted, but resolved the problem of those who fail to reply at all.

CEGB also set out to develop an epidemiological database of its radiation workers and data on the NRRW participants within this database were transferred to the NRRW. This database, entitled EUCLID, was maintained by Nuclear Electric but, although still in existence, is not currently being maintained. It should be noted that the study population at British Electric Generation and Magnox Electric is limited to classified workers, who comprise about 90% of all those for whom dose records are kept.

Preliminary analyses of NRRW data at the time of the 2nd analysis indicated low all-cause SMRs for Hartlepool and Heysham power stations (see Appendix G of Muirhead *et al*, 1999); furthermore, as indicated in Appendix B of Muirhead *et al* (1999), the rate of non-participation was reported to be particularly high for Heysham. Since these sites commenced operations towards the end of the period for the 2nd analysis, it was not feasible to include them from a later date which might have reduced the impact of any problems associated with early data. Hartlepool and Heysham were therefore excluded from the 2nd analysis and, as the BE/ME cohort in England and Wales has not been expanded beyond 1990 for this analysis, workers who were solely employed at Hartlepool or Heysham have not been included in the analyses presented in this report. In contrast, whilst workers at Dungeness Power Stations between 1965 and 1990 had

been excluded from the 2nd analysis as a result of problems with dose data for the period 1975-85 (see Appendix E of Muirhead *et al*, 1999), these workers have been included in the 3rd analysis as a consequence of improved dose data having been made available through EUCLID. Appendix C includes details of data audits undertaken at Dungeness during 2007.

Definition of the study population for BE/ME sites in England and Wales

All employees for whom radiation dose records were kept at any time up to 31 December 1990, excluding those who refused to participate and excluding those whose employment was only at Hartlepool or Heysham Power Stations.

A2.2.2 Sites in Scotland

British Energy Generation and Magnox Electric also operate the current and former nuclear power stations at Hunterston in Ayrshire and Torness in East Lothian. These sites were formerly owned by the South of Scotland Electricity Board (SSEB) and were subsequently managed by Scottish Nuclear Limited. In 1996, Scottish Nuclear Limited was privatised as a subsidiary of British Energy plc and in 2000, management of the Hunterston site was transferred to Magnox Electric while management of the Torness site was retained by the re-titled British Energy Generation.

The first set of data for Hunterston staff in categories A and D was transferred during 1978. Data transfer from the Hunterston ADS became routine until 2001, following which the responsibility for dosimetry services and record keeping was transferred to CDRS. The transfer of dosimetry data for current workers at Hunterston is now as for workers at sites in England and Wales.

For Torness, annual data were received from the Torness Approved Dosimetry Service (ADS) from the start of operations in 1986 up to 2006. From 2007, responsibility for dosimetry services and record keeping was transferred to the CDRS, and the transfer of dosimetry data for current workers at Torness is now as for workers at sites in England and Wales.

As reported by Muirhead *et al* (1999) (Appendix A), there are indications of possible incompleteness in the composition of the Hunterston cohort prior to 1980 (M Wright, Scottish Nuclear, personal communication). Since preliminary analyses for the 1999 report indicated that the all-cause SMR for Hunterston based on Scottish mortality rates was particularly low when based on workers from 1976 onwards but was slightly higher when the entry date was moved forward to 1980 (see Appendix G of Muirhead *et a*l, 1999), the later start date was used for the main part of the 2nd analysis. This date has also been used for the current analysis.

Definition of the study population for BE/ME sites in Scotland

All employees based at the Hunterston and Torness sites for whom radiation dose records were kept between 1 January 1980 and to 31 December 1999, excluding those who refused to participate, and also excluding workers employed by the Central Maintenance Organisation and non-power station staff at Hunterston.

A2.3 British Nuclear Fuels plc (BNFL)

A number of sites in northern England and southern Scotland were operated by British Nuclear Fuels (BNFL) for most of the period covered by this analysis report. Although BNFL has now been broken up and the sites are operated and managed by other companies, for the purposes of this report, those sites which were formerly part of the old BNFL company (namely Capenhurst in Cheshire Chapelcross in Dumfries and Galloway, Risley in Cheshire, Sellafield in Cumbria and Springfields in Lancashire) are grouped together under the BNFL heading. The date when work started at each site is given in Table A1.

BNFL Management and Trades Unions agreed to recommend participation in the NRRW to the workforce in 1976. The first data were received in 1978. Originally, only radiation workers who had given written consent were enrolled, but since the beginning of 1983 all radiation workers are enrolled except those who make a written request to be excluded. Enrolment and other information for the NRRW were originally received via the BNFL Health and Safety Directorate at Risley. More recently, data have been provided on behalf of BNFL and other employees at the above sites by Westlakes Scientific Consulting Ltd.

At about the same time as the initial data were being transferred to the NRRW, BNFL started a feasibility study on the practicality of studying category B and C workers. It was found that the records were of sufficiently high quality for this to be done and work was started to assemble the data, first at Sellafield followed by Chapelcross and the other sites.

The exercise at Sellafield was carried out in conjunction with staff at the LSHTM which has led to published studies (Smith and Douglas, 1986; Douglas *et al*, 1994; Omar *et al*, 1999). Workers at the other sites and combined analyses of BNFL workers have been the subject of separate studies conducted by researchers at Westlakes Scientific Consulting Ltd (Springfields – McGeoghegan and Binks, 2000a; Capenhurst – McGeoghegan and Binks, 2000b; Chapelcross - McGeoghegan *et al*, 2001; BNFL-wide – McGeoghegan *et al*, 2003, 2008).

Data for category B and C workers at Sellafield and Chapelcross were first transferred to the NRRW for inclusion in the 1st NRRW analysis; data for category B and C workers at Capenhurst and Springfields were transferred to the NRRW in 2002. As for the 2nd analysis, the 3rd analysis incorporates the updated dosimetry data for Sellafield ex-workers that were used in the analysis by Douglas *et al* (1994).

Definition of the study population for BNFL

All employees at Capenhurst, Chapelcross, Sellafield and Springfields for whom radiation dose records were kept at any time up to 31 December 1999, and all employees at Risley for whom radiation dose records were kept between 1 January 1976 and 31 December 1999, excluding those who refused to participate.

A2.4 GE Healthcare

Radiation work commenced at Amersham in Buckinghamshire in 1940 when Thorium Ltd started operations. This led to the formation of The Radiochemical Centre, a Government-owned body managed by Thorium Ltd. In 1946 it became part of the Ministry of Supply, and then in 1954 it became part of the UKAEA. The company changed its name to Amersham International in 1981 and was privatised in 1982. In 1997 Amersham International plc merged with Nycomed ASA of Norway to become Nycomed Amersham and, following further mergers, Amersham plc is now part of GE Healthcare. The Cardiff Laboratories (now known as The Maynard Centre) opened in 1980 and their work involves the development and manufacture of essential products and technologies for medical and pharmaceutical research. The main radioactive materials used are the low energy, beta emitting, isotopes carbon-14 and tritium.

The organisation was first contacted in 1978, and it was agreed that the classified workers then employed should be approached for participation in the NRRW. Category A and B workers were approached, and new employees are asked to join as part of the signing-on procedure. The first dosimetry data to be provided were for 1981.

Entry was originally on the basis of a positive acceptance scheme. However, it was discovered that a number of individuals had failed to respond and consequently there was a low coverage of the study population. A positive refusal scheme was introduced in 1987 and work was undertaken to enrol individuals who did not reply under the positive acceptance scheme. In addition, the transfer of data for 1976-1981 was completed and leavers from this period were approached, allowing the entry date to the study to be pushed back to 1976.

Definition of the study population for GE Healthcare

All employees for whom radiation dose records were kept at any time between 1 January 1976 and 31 December 1999, excluding those who refused to participate.

A2.5 Health Protection Agency Radiation Protection Division (HPA-RPD)

The National Radiological Protection Board (NRPB) was an independent statutory body set up by the Radiological Protection Act 1970. The organisation was merged into the Health Protection Agency (HPA), a non-Departmental Public Body, in 2005, forming the Radiation Protection Division of the HPA. It has responsibilities to undertake research and provide information and advice on radiation hazards, and it provides associated technical services. It has sites at Chilton in Oxfordshire, in Leeds and in Glasgow.

An initial approach was made to NRPB staff in 1977. A second exercise in July 1980 invited those who had become radiation workers since 1977 to participate in the study. A system is now in place whereby new employees are approached routinely. These workers are covered by the Personal Dosimetry Service run by HPA-RPD.

Definition of the study population for HPA-RPD

All employees for whom radiation dose records were kept at any time between 1 January 1977 and 31 December 1999, excluding those who refused to participate.

A2.6 Medical Research Council (MRC) Harwell

The MRC Radiobiology Unit was set up at Harwell in 1947, with the aim of investigating the toxicity of radioactive substances and developing methods of protecting workers (Anon, 1997). In 1995 it was reconstituted as the Medical Research Council Harwell and new Units were created, namely the Radiation and Genome Stability Unit, and the Mammalian Genetics Unit and UK Mouse Genome Centre. In January 1996 the UK MRC Mouse Genome Centre was also established at the site. Staff have used various radiation facilities, both in-house and elsewhere on the Harwell site; in particular, research reactors, X-ray machines, cobalt-60 sources, and a neutron generator and cyclotron.

It was originally agreed that current radiation workers would be asked to participate in the study from 1 November 1980. Personal information for those agreeing to join was first transferred to the NRRW in 1981 and continues to be transferred for new and existing employees. Monitoring data are now kept by Nuvia Ltd (and were formerly kept by UKAEA). The first transfer of exposure data covered all MRC staff in UKAEA's records between 1975 and 1987 inclusive. These data allowed the identification of radiation workers who had left prior to the original start date and have enabled the start date for MRC's radiation workers to be moved back to 1976.

Definition of the study population for MRC Harwell

All employees for whom radiation dose records were kept at any time between 1 January 1976 and 31 December 1999, excluding those who refused to participate.

A2.7 Ministry of Defence (MoD)

The Defence Science and Technology Laboratory (Dstl), an agency of the MoD (formerly DRPS, the Defence Radiological Protection Service), situated at Alverstoke in Hampshire operates the approved dosimetry service and dose record keeping service for all service personnel and the vast majority of MOD civilians with the exception of AWE (formerly MoD) personnel. For the period covered by this analysis, this includes classified persons at the privatised dockyards at Devonport, Clyde and Rosyth, and for the Rolls-Royce and Associates personnel at the Naval Reactor Test Establishment at Dounreay. Until 1982 the service had been operated from the Admiralty Radiation Records Centre that had been set up in the mid-1960s. Records are now held for all MoD (and civilian) personnel who have worn approved dosemeters and for those employed before legislation was enacted. The earlier records are not fully computerised.

The first transmission to the NRRW of data for category A and D workers took place in 1979. The first dosimetry data were for 1977 and 1978. The data holders also

undertook an exercise to compile pre-1977 dose histories for individuals with a lifetime dose above 50 mSv. These data were passed to the NRRW in 1984.

In 1999, Dstl, with support from MoD, the Department of Health and the Health and Safety Executive, undertook to collate data for earlier workers, specifically Category B and C workers, as well as category A and D workers who ceased work between 1 January and 31 December 1977. Data for these workers had been held on paper but, using a combination of digital scanning and manual data-entry techniques, these were transferred to electronic media and then to the NRRW in the period up to 2003. Additional data, provided through MoD record keeping agencies (Service Record Offices), supplemented the dosimetry data with personal data items. Following validation work, it was concluded that these records could be included in the current epidemiological analysis. This has made it possible to push back the start date for MOD workers to 1961.

A data audit, relating to the addition of the pre-1977 records, was conducted and is reported in Appendix C.

Definition of the study population for MoD

All employees for whom radiation dose records were kept by Dstl (or predecessor organisations) at any time up to 31 December 1999, excluding those who refused to participate.

A2.8 Organisations using the HPA Personal Dosimetry Service (PDS)

Approaches have been made to organisations for which HPA-RPD (formerly NRPB) provides monitoring services. In particular, systems were set up so that new workers at these organisations are approached by HPA-RPD regarding participation in the NRRW. For logistical reasons, only those organisations with sizeable number of workers (about 100 or more), high participation rates and which were still using PDS in 1990 have been included in this analysis. Five organisations met these criteria. Two of them (Rolls-Royce and Associates Manufacturing Division and Rolls-Royce Nuclear Medicine Department) form part of the Rolls-Royce Submarines cohort described in section A2.9. Therefore, for the purpose of this analysis, the PDS component is taken to refer to the following three organisations, which were also included in the 2nd NRRW analysis.

(i) *CEC-TIME Ltd. (Formerly Teeside Industrial & Materials Evaluation Ltd.)*

This company has been involved in engineering inspection, welding and non-destructive testing. The first approach to workers took place in 1979.

(ii) *Honeywell Control Systems (Formerly Measurex International Systems Ltd.)*

This company has been involved in the manufacture, supply and maintenance of industrial gauging systems containing either radioactive sources (beta/gamma) or x-ray tubes. The first approach to workers took place in 1981.

(iii) *Picker International Ltd.*

This company has been involved in the manufacture, supply and maintenance of medical x-ray equipment. The first approach to workers took place in 1986.

Definition of the study population for PDS sites

All employees at CEC-Time, Honeywell Control Systems and Picker International for whom radiation dose records were kept by PDS and who were approached and agreed to participate in the study, from the time that the respective companies were approached up to 31 December 1999.

A2.9 Rolls-Royce Submarines

Rolls-Royce and Associates (RRA) was formed in 1959. The company is involved in the design, development, manufacture and procurement of Pressurised Water Reactors and associated plant for the Royal Navy's nuclear submarines. In 1998 RRA become part of Rolls-Royce and in 2006 became known as Rolls Royce Submarines.

Rolls Royce Submarines operates from several sites of which its main site and its Manufacturing site are included in this analysis. Data from Rolls-Royce Power and Process (Hartlepool) are also grouped with Rolls Royce Submarines in the analysis.

Following an approach by the company, the first set of data for workers at the main site were received in 1983 and covered all radiation workers employed as of 1 January 1982. Details of all other participating workers employed at main site either before or after 1982 were transferred subsequently. Manufacturing Division employees were first approached by NRPB in 1982, and the Power and Process (Hartlepool) employees were first approached (as employees of Foster Wheeler Power Products) in 1981.

Definition of the study population for Rolls-Royce Submarines

All employees at the main site for whom radiation dose records were kept at any time up to 31 December 1999, excluding those who refused to participate. All those workers at the Rolls Royce Manufacturing Division and Rolls Royce Power and Process (Hartlepool) for whom dose records were kept by PDS and who were approached and agreed to participate in the study, from 1982 up to 31 December 1999 (for the Manufacturing Division) or from 1981 up to 31 December 1990 (for the Hartlepool Power and Process workers).

A2.10 Science and Technology Facilities Council (STFC)

The Science and Technology Facilities Council is an independent, non-departmental public body of the Department for Innovation, Universities and Skills (DIUS). This Research Council was formed in 2007 through a merger of the Council for the Central Laboratory of the Research Councils (CCLRC) and the Particle Physics and Astronomy Research Council (PPARC) and through the transfer of responsibility for nuclear physics from the Engineering and Physical Sciences Research Council (EPSRC).

The Daresbury and the Rutherford Laboratories have supported the NRRW since soon after its inception.

A2.10.1 Daresbury Laboratory

The Daresbury site in Cheshire opened in 1964 - under the auspices of the National Institute for Research in Nuclear Science - with the construction of the 5 GeV electron synchrotron, NINA, for high energy physics research. NINA operated from 1967 until 1977, when it was closed down and decommissioned. The Laboratory, by then part of the Science Research Council, was subsequently involved in the construction of a 2 GeV electron storage ring (the SRS) dedicated to the production of synchrotron radiation. The SRS became operational in 1980, running until August 2008. In 1982 the Laboratory also started operation of its 20 MV Tandem Van de Graff accelerator (the NSF), for acceleration of heavy ions. On occasions both tritium and carbon-14 ions were accelerated. This facility closed down in 1993 and was decommissioned. The Laboratory is now part of the Science and Technology Facilities Council.

The earliest records at the Laboratory date back to the early 1960s when doses were measured by the RPS. In 1999, Landauer Inc. became the ADS for Daresbury. Prior to that time, dose record information was provided to NRRW by Daresbury Laboratory.

From the outset, it was agreed that workers in categories A, B, C and D would participate in the NRRW. A system that permitted an employee to opt out was set up for category A, B and D workers, and the first set of data was sent to the NRRW in 1980. The transfer of data for category C workers was completed during 1981.

Definition of the study population for Daresbury Laboratory

All employees for whom radiation dose records were kept at any time up to 31 December 1999, excluding those who refused to participate.

A2.10.2 Rutherford Appleton Laboratory

The Rutherford Laboratory was established by the National Institute for Research in Nuclear Science in 1957. It became part of the Science Research Council (subsequently the Science and Engineering Research Council) in 1965, and was merged with the Appleton Laboratory in 1979. The Rutherford Appleton Laboratory became part of the CCLRC in 1995, merging again in 2007 to become part of the Science and Technology Facilities Council. It is based at Chilton in Oxfordshire.

The primary role of the Laboratory is to provide experimental facilities and specialist support for scientists and engineers from UK universities and collaborators overseas. Major facilities include the Nimrod particle accelerator (which operated from 1964 to 1978), the ISIS pulsed neutron source and the Central Laser Facility.

The earliest dose records held at the Laboratory date from 1964. Prior to this time dose records for workers at the Laboratory were kept by UKAEA Harwell. The Rutherford Appleton Laboratory carried out its own monitoring and record keeping up until 1988

when this function was contracted out to Harwell. Landauer subsequently became the ADS for the Laboratory in 1993.

It was agreed that workers in categories A and D would be asked to participate in the NRRW and a system that permits an employee to opt out was set up. The first set of data was transferred to the NRRW in 1981. Information on category B and C workers have also been made available to the NRRW and the transfer of these data was completed in 1992.

Definition of the study population for Rutherford Appleton Laboratory

All employees for whom radiation dose records were kept at any time up to 31 December 1999, excluding those who refused to participate.

A2.11 United Kingdom Atomic Energy Authority (UKAEA)

The United Kingdom Atomic Energy Authority (UKAEA) was formed in 1954, taking over responsibility for the sites and work on atomic energy which had been the responsibility of the Ministry of Supply since 1946. It originally included employees and site that were transferred to AWE and BNFL (and also Amersham International, which separated in 1971, at the same time as BNFL). In 1996 it was split into UKAEA, AEA Technology and Johnson Controls Ltd. Since 1996, further divisions and mergers have occurred but the core coverage of workers covered in this part of the cohort continues to be those workers employed by UKAEA and those transferred since 1996 to its successor organisations, but excluding those that were transferred to new organisations in the early 1970s. In this report, UKAEA employees are taken to be those employed by the then-organisation at its major sites at Dounreay in Caithness, Harwell and Culham in Oxfordshire, and Winfrith in Dorset, together with UKAEA employees at Risley, its sister site Culcheth and Windscale (adjacent to Sellafield). Smaller numbers of employees worked at the London Headquarters. For the purposes of this report Culham and London Headquarters have been combined with Harwell, and Culcheth has been combined with Risley. Until 1997 UKAEA employees at Windscale were included with the BNFL cohort; from 1998 they are included with the UKAEA cohort.

Data on the majority of UKAEA employees was initially provided to the NRRW directly from each of the main sites, and, for most workers at UKAEA sites, are now provided via the ADS at Winfrith. Data for UKAEA staff working at Springfields, or at Windscale before 1997, are provided by Westlakes (and are included in the BNFL cohort - see section A2.3). The first set of UKAEA data was transmitted to the NRRW in 1977. With the exception of Winfrith, which enrolled category B workers, only categories A and D were originally added to the NRRW. Initially, a system of positive consent before enrolment was used but this was soon changed to a positive refusal system.

As for AWE, data on all category B and C workers were collected by staff from Harwell in conjunction with LSHTM. These data have been the subject of separate analyses, both of UKAEA workers specifically (Beral *et al*, 1985; Fraser *et al*, 1993) and as part of NICEA (Carpenter *et al*, 1994). These analyses also included category A and D workers who started radiation work up to the end of 1979. A more recent analysis of the

UKAEA workforce, including workers employed between 1946 and 31 March 1996, was published in 2004 (Atkinson *et al*, 2004). Data on category B and C workers were transferred to the NRRW and these workers have been included in all of the reported NRRW analyses. The updated dosimetry and personnel data for workers in NICEA which were incorporated in the previous NRRW analysis are also used for this analysis.

As in the previous analysis (NRPB-R307) ex-radiation workers at the UKAEA Risley site have been included in this analysis.

Definition of the study population for UKAEA

All employees for whom radiation dose records were kept at any time up to 31 December 1999, excluding those who refused to participate.

A3 DATE OF ENTRY TO THE STUDY

Workers enter the study on the first day on which their death or cancer registration, had it occurred, would have been included in the analysis. Those who refuse to participate are clearly not included in the study. Workers at organisations that use positive acceptance schemes enter the study on the date that they agreed to participate, whilst workers at the majority of organisations that use positive refusal schemes enter the study on the last day of the period during which they could refuse to participate. An exception is that, for those workers who started radiation work before 1976 (ie. category B and C workers), their date of entry to the study is the date of starting radiation work. Table A2 summarises, by organisation, the earliest date of entry to the study for the 3rd NRRW analysis.

A4 DATE OF EXIT FROM THE STUDY

For the mortality analyses, workers are at risk until their date of death or emigration, their 85th birthday, or 1st January 2002, whichever is earliest. For the cancer incidence analyses, workers are at risk similarly, except that they are also removed from the analyses on their date of cancer registration where appropriate.

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TABLE A1 Participating organisations

Employer/site	Date of starting radiation work
AWE	1948
British Energy Generation and Magnox Electric (England and Wales)	
Berkeley Centre	1960
Berkeley power station	1961
Bradwell	1961
Dungeness (A and B)	1965
Hinkley Point (A and B)	1964
Oldbury	1967
Sizewell A	1965 [a]
Trawsfynydd	1964
Wylfa	1971
Non-power station staff	1959
British Energy Generation and Magnox Electric (Scotland)	
Hunterston (A and B)	1964
Torness	1986
BNFL	
Capenhurst	1953
Chapelcross	1958
Risley	1946
Sellafield	1947
Springfields	1948
GE Healthcare	1946
HPA-RPD	1971
MRC Harwell	1947
MoD	1961
PDS	
CEC-Time	1976 [b]
Honeywell Control Systems	1976 [b]
Picker International	1977 [b]
Rolls-Royce Submarines	1959

[a] Sizewell-B power station is not included in this analysis, since work there did not begin before the end of 1990 (see also section A2.2.1).

[b] Date from which PDS provided monitoring.

TABLE A1 Participating organisations

Employer/site	Date of starting radiation work
	(continued)
STFC	
Daresbury	1964
Rutherford Appleton	1957
UKAEA	
Culcheth	1946
Culham	1960
Dounreay	1954
Harwell	1946
London	1946
Risley	1946
Winfrith	1957

TABLE A2 Earliest date of entry[a] to the study for the 3rd NRRW analysis

	Category [b]			
Employer/site	A	B	C	D
AWE	1948	1948	1948	1976
British Energy Generation and Magnox Electric (England and Wales)				
Berkeley Centre	1960	1960	1960	1976
Berkeley power station	1961	1961	1961	1976
Bradwell	1961	1961	1961	1976
Dungeness (A and B)	1965	1965	1965	1976
Hinkley Point (A and B)	1964	1964	1964	1976
Oldbury	1967	1967	1967	1976
Sizewell A	1965	1965	1965	1976
Trawsfynydd	1964	1964	1964	1976
Wylfa	1971	1971	1971	1976
Non-power station staff	1959	1959	1959	1976
British Energy Generation and Magnox Electric (Scotland)				
Hunterston (A and B)	1980	–	–	1980
Torness	–	–	–	1986
BNFL				
Capenhurst	1953	1953	1953	1976
Chapelcross	1958	1958	1958	1976
Risley	1976	–	–	1976
Sellafield	1947	1947	1947	1976
Springfields	1948	1948	1948	1976
GE Healthcare	1976	–	–	1976
HPA-RPD	1977	–	–	1977
MRC Harwell	1976	–	–	1976
MoD	1961	1961	1961	1976
PDS				
CEC-Time	1979	–	–	1979
Honeywell Control Systems	1981	–	–	1981
Picker International	1986	–	–	1986

[a] Each individual may have a later date of entering the study, as described in section 5.1. The dates given here apply to the employer/site as a whole.

[b] Categories defined in section 2.1.

TABLE A2 Earliest date of entry[a] to the study for the 3rd NRRW analysis

	Category [b]			
Employer/site	A	B	C	D
Rolls-Royce Submarines	1959	1959	1959	1976
STFC				
Daresbury	1964	1964	1964	1976
Rutherford Appleton	1957	1957	1957	1976
UKAEA				
Culcheth	1946	1946	1946	1976
Culham	1960	1960	1960	1976
Dounreay	1954	1954	1954	1976
Harwell	1946	1946	1946	1976
London	1946	1946	1946	1976
Risley	1946	1946	1946	1976
Winfrith	1957	1957	1957	1976

APPENDIX B Summary of Data Required by the NRRW

B1 INTRODUCTION

This appendix details the information that was requested from participating organisations. It follows the format of the data specification given in the NRRW protocol (Darby, 1981).

B2 DATA ITEMS

PERSONAL

1 Name
2 Date of birth
3 Sex
4 National Insurance Number
5 National Health Service Number
6 Personnel number
7 Date employment began
8 Date employment ceased
9 (a) Date of commencement as a radiation worker during this spell of employment with this organisation
(b) Date of commencement as a radiation worker in any employment (if available)
10 Date of entry to the NRRW
11 Industrial classification
12 Update status

EXPOSURE

13 Body penetrating external radiation dose
(a) Dose history on an annual basis
(b) Dose in year
14 Notional component of dose
(a) Dose history on an annual basis
(b) Dose in year
15 Neutron dose
(a) Dose history on an annual basis
(b) Dose in year
16 Internal contamination
(a) Monitored for plutonium?
(b) Monitored for tritium?
(c) Monitored for any other nuclide?
(d) Known body content?
17 Involved in radiological accident or incident?

B3 NOTES ON DATA

PERSONAL

1 **Name** - Preferably this consists of surname and full forenames, eg. John Frederick Smith. If the full name was unavailable then surname and initials should have been given, eg. Smith, J F. If an individual had changed his or her name then previous names should have been notified.

2 **Date of birth** - The exact date should have been given, eg. 23021954 or 23 Feb 1954.

3 **Sex** - Male or female.

4 **National Insurance number** - eg. AB123456. This item is very important since it is the main index used to identify individuals in the records. If there is a letter at the end of the National Insurance number, eg. AB123456A, this last letter is not needed. The National Insurance Number commonly appears on pay records.

5 **National Health Service number** - eg PZKK234. This item was needed in order to flag the individual on the National Health Service Central Registers. For any individual this number appears on his or her medical card. For people born before the end of the second World War it is the same as their wartime identification number. If any individual was unable to supply a National Health Service number, then it may have been possible to flag him or her using alternative information. This could be either full forenames (see note 1) and last permanent address (ie. address when last registered with a doctor) or place of birth or current doctor's name and address.

6 **Organisation's personnel number** - From the point of view of the NRRW this item does not constitute an essential piece of information. However, many participating organisations have found it convenient to include the personnel number or other personnel identification whenever any data concerning that individual were transferred. It could then be used as a reference in any queries.

7 **Date of employment** - This should correspond to the date of employment with the participating organisation as a whole rather than at any particular site. The exact date should have been given as in note 2 above. If the individual had had more than one spell of employment with an organisation and been a radiation worker during any previous spells, then the employment dates (both beginning and end) for these spells should also have been notified to the NRRW.

8 **Date employment ceased** - When an individual who is listed on the NRRW leaves the employment of the participating organisation, the date that employment ceased should have been supplied, even if the individual was not a radiation worker at the time. The exact date should have been given as in note 2.

9 **Date of commencement as a radiation worker** - This should have been the date of commencement as a radiation worker during the present spell of employment

with the participating organisation as a whole. If the date of first commencement as a radiation worker in any employment was known, this also should have been notified.

10 **Date of entry to the NRRW** - For positive entry systems this should have been the date on which the consent form was signed. For positive refusal systems this should have been the date on which the list of eligible personnel was compiled. The exact date should have been given as in note 2.

11 **Industrial classification** - ie. industrial or non-industrial. The classification of employees as industrial or non-industrial is a routine measure carried out by some of the participating organisations. For those organisations which do not use this classification, individual arrangements were made based on either method of payment of the employee (eg. weekly or monthly) or occupational coding.

12 **Update status** - This item would have accompanied the annual exposure data.
N - new radiation worker, ie. an individual for whom there should not have been exposure data from that site for the preceding year.
U - update for worker continuing radiation work, ie. an individual for whom there should have been exposure data from that site for both the preceding and following years.
R,L - individuals who have either retired (R) or left (L) radiation work (while continuing in employment) during that year, ie. for whom no exposure data from that site were expected in the following year.
Where the information was available, it would have been helpful for sites to have coded 'D' instead of 'R' or 'L' for individuals who died during employment. If it was possible to have distinguished those who retired (on grounds of age or ill health) from those who moved on to another employment, then 'R' should have been coded for the former and 'S' for the latter. If an individual commenced and ceased radiation work within a single calendar year, then R or L, etc. (as appropriate) should have been indicated rather than N.

EXPOSURE

13, 14, 15 **Dose data** - The dose data could be supplied using any units of dose equivalent, provided they are clearly stated; for a discussion of dose units, see Appendix D. Dose histories should have been given going as far back in time as the records permitted. It also should have been stated whether notional and neutron components were included in the body penetrating totals. Preferably they should have been included under note 13 and given separately under notes 14 and 15, if relevant. The threshold dose, the procedure regarding recording of doses below threshold and whether or not allowance for background radiation had been made should have been clearly indicated for every year for which dose data were supplied. For notional doses it also should have been stated whether the estimate of dose is realistic or whether the appropriate fraction of the dose limit for the period had been assigned. In some cases it may not have been possible to supply detailed neutron dose histories on an annual basis, and special arrangements would have been needed.

16 **Internal contamination** - Yes or No.

The answers to these questions should have shown the entire lifetime experience of the individual. For example, the answer to 16a should have been 'yes' if monitoring for plutonium was known to have been carried out at any time in the past. It also should have been stated whether an estimate of dose due to internal contamination was included in the whole body total dose. If it was included, details should have been given. If a person was likely to have a significant radiation dose from internal contamination as a result of being involved in a radiological accident or incident, individual arrangements as to further data collection would have been made as necessary. The numbers of people involved would generally have been very small. However, if the group had been large enough to merit further analysis, sufficient details would have been sought on the nuclides involved and their distribution within the body to permit all calculations to be carried out as far as possible on the same basis.

17 **Involvement in radiological accident or incident** - Yes or No.
Had the individual been involved in an incident which led to an effective dose equivalent or effective dose equivalent commitment of more than 50 mSv?

B4 REFERENCE

Darby SC (Editor). Protocol for the National Registry for Radiation Workers. Chilton, NRPB-R116 (1981) (London, HMSO).

APPENDIX C Results of Data Audits

C1 INTRODUCTION

Checks on the accuracy and completeness of data held by the NRRW were undertaken at the various participating sites for both the first and second NRRW analyses. The results of these audits are described in Appendix E of the reports by Kendall *et al* (1992) and Muirhead *et al* (1999).

Reflecting the results of the earlier audits and taking account of more recent data transfer techniques, for this analysis it was agreed that data audit work would be undertaken only for those areas where significant amounts of data had been transferred from new or significantly revised data sources and where it was considered that there was potential for error. The audits were undertaken in order to provide confidence in the study results, both for the researchers and for those parties with an interest in the findings.

Audits were therefore undertaken for three groups of workers who had not been included in the previous NRRW analysis: those with records relating to MOD workers from before 1977; those AWE workers commencing employment between 1991 and 1999; and those workers employed at either Dungeness A or Dungeness B Power Station. The details are described below.

A further group of workers added for this analysis, category B and C workers at BNFL Capenhurst or BNFL Springfields, were not subject to an audit by the NRRW researchers as the data provided to the NRRW had been collated for the purposes of epidemiological analyses (McGeoghegan and Binks, 2000a,b) and were thus believed to be complete.

C2 ATOMIC WEAPONS ESTABLISHMENT (AWE)

The development of a new dosimetry record keeping system at AWE in the mid 1990s and subsequent issues noted by AWE and by NRRW staff were followed by additional data transfers which were expected to resolve known issues.

At the completion of that work, it was agreed that it would be appropriate to conduct a data audit, in advance of the 3rd NRRW analysis, to quantify the accuracy and completeness of those areas of the dataset which were affected by the system changes.

A 1% sample of records for AWE staff monitored between 1986 and 1999 was selected from the NRRW dataset and were checked against AWE records to assess the accuracy and completeness of the dose and personal data held on the NRRW. Overall, the agreement between the AWE dose record values and NRRW dose data was good. A small number of anomalies were noted regarding the recording of the date of ceasing radiation work, in particular in cases where a worker had ceased classified work but continued being monitored as a radiation worker. These were not significant errors.

For the check of completeness of coverage, the records were stored in such a way as to make it easier to check a 1% sample of all AWE dose records, rather than to limit the check to those workers monitored between 1986 and 1991. Thus 1% of records at the site were selected randomly from both the currently active radiation worker records and the records of those workers who had ceased radiation work. Both sets of records confirmed that the NRRW coverage was good.

The audit work confirmed that the quality of the data added to the NRRW since the 2nd NRRW analysis was good and the extended AWE cohort was included in the 3rd NRRW analysis.

C3 BE/ME DUNGENESS POWER STATION

Appendix E of the report of the 2nd NRRW analysis (Muirhead *et al*, 1999) describes that a significant number of errors had been identified in EUCLID data for workers at both the Dungeness A and Dungeness B sites for the period 1975-985. Although Nuclear Electric were able to update the EUCLID data by working through Dungeness site records, they had not been able to complete this work on a timescale that enabled the data to be used in that NRRW analysis. Consequently, workers at Dungeness were excluded from the 2nd NRRW analysis.,

In advance of the 3rd NRRW analysis, site visits to Dungeness were conducted to assess whether the revised data quality and completeness were acceptable. At the time of the audits, the Dungeness A site was operated by Magnox and the Dungeness B site was operated by British Energy.

At both sites a 1% sample of site dosimetry records was checked to quantify the completeness of the NRRW study. An additional check, using a 1% sample of Dungeness workers known to the NRRW, was completed to assess the completeness and accuracy of the data held on the NRRW.

As a result, it was concluded that the work undertaken to update the EUCLID database had significantly improved the available data and both cohort coverage and data quality were judged to have improved to a level that made it possible to include the Dungeness workforces in the 3rd NRRW analysis on the same basis as those other BE/ME sites that had been included in the 2nd analysis.

C4 MINISTRY OF DEFENCE (MOD)

Section A2.7 of Appendix A describes the addition of historic MoD worker data for around 20,000 MoD staff working with radiation before 1977. Data capture involved data from the dosimetry records as well as, subsequently, personal data identifiers from other MoD personnel data sources.

In order to assess the success of this very complex data capture and transfer exercise, a data audit was undertaken by comparing resultant records on the NRRW with the original data held by the MoD dosimetry record keepers for a 1% sample of records. Dstl

staff were able to conduct checks to ensure that the upload of records to the new electronic dataset and subsequently to the NRRW was complete.

Several issues were noted but in all cases the data provided were sufficiently understood that the overall content was acceptable. Examples include those cases where the annual breakdown of doses was incomplete (in a small percentage of cases) but where the cumulative life dose for that period was available. The radiation monitoring dates for such workers were of good quality. A number of small transcription errors made record linkage more complex, but these issues did not have a significant impact on the expanded dataset.

In summary, a number of data issues were noted but the overall quality and completeness was found to be of a sufficiently high standard that the MoD component of the 3rd NRRW analysis study cohort could be extended to include those radiation workers who had ceased to be monitored prior to 1977.

C5 REFERENCES

Kendall GM, Muirhead CR, MacGibbon BH, O'Hagan JA, Conquest AJ, Goodill AA, Butland BK, Fell TP, Jackson DA, Webb MA, Haylock RGE, Thomas JM and Silk TJ. First analysis of the National Registry for Radiation Workers: occupational exposure to ionising radiation and mortality. Chilton, NRPB-R251 (London, HMSO) (1992).

McGeoghegan D and Binks K. The mortality and cancer morbidity experience of workers at the Springfields uranium production facility, 1946-95. *J Radiol Prot*, **20**, 111-37 (2000a).

McGeoghegan D and Binks K. The mortality and cancer morbidity experience of workers at the Capenhurst uranium enrichment facility 1946-95. *J Radiol Prot*, **20**, 381-401 (2000b).

Muirhead CR, Goodill AA, Haylock RGE, Vokes J, Little MP, Jackson DA, O'Hagan JA, Thomas JM, Kendall GM, Silk TJ, Bingham D and Berridge GLC. Second analysis of the National Registry for Radiation Workers: Occupational Exposure to Ionising radiation and Mortality. Chilton, NRPB-R307 (1999).

APPENDIX D Results of Subsidiary Analyses

D1 INTRODUCTION

Various subsidiary analyses were conducted in order to examine the sensitivity of the main findings to decisions that were made concerning the groups of workers to be studied, the form of the data to be analysed and the methods of analysis.

D2 DOSE CORRECTIONS

As indicated in the main text, some adjustments were made to the recorded doses, prior to using them in the internal analysis. Subsidiary analyses were conducted to examine the effect of removing some or all of these corrections.

D2.1 Doses without threshold adjustment

The whole body doses used in the main analysis included an adjustment for the threshold of detection of the workers' dosemeters. Details of these thresholds are given in Appendix D of NRPB-R251 (Muirhead *et al*, 1999b). Tables D1-D11 show that when these threshold adjustments are excluded, the results from the internal analysis – in terms of the estimated ERR per Sv, its associated 90% CI and the one- and two-sided p-values – are similar to those in the main analysis.

D2.2 Doses without NICEA adjustments

The main analysis includes adjustments to historical doses for UKAEA and AWE workers that were made as part of the Nuclear Industry Combined Epidemiological Analysis (NICEA) (Carpenter *et al*, 1994). These adjustments were included in the NRRW for the first time in the 2nd analysis (Muirhead *et al*, 1999a,b). Tables D1-D11 show that omitting the NICEA dose adjustments has generally little effect on the results of the internal analysis.

D2.3 Doses without any adjustments

For this subsidiary analysis, no adjustments were made to the doses used when looking for any trends in risks of mortality or cancer incidence. Again the findings are similar to those in the main analysis (see Tables D1-D11).

D3 INFLUENCE OF THOSE MONITORED FOR INTERNAL EMITTERS

The focus of this report is on doses from external radiation. However, it is important to consider whether the tests for any trends in mortality or cancer incidence with external dose might have been influenced by exposures from internal radiation. Since doses from internal exposures are not generally available for the NRRW cohort, two types of

subsidiary analysis were considered. The first of these involved excluding workers who had been monitored for internal radiation exposure. This mirrors the approach taken in the 15-country study of radiation workers in the nuclear industry (Cardis *et al*, 2005, 2007), where workers with potential for substantial doses (>10% of their whole body dose) from exposures other than from higher energy photon radiation were excluded from the main analysis. The second subsidiary analysis conducted here did not involve excluding workers who were monitored for internal exposure, but rather consisted of an adjustment for internal exposure by stratifying on the basis or whether or not a worker was ever monitored for internal exposure when analysing mortality and cancer incidence in relation to external dose.

Excluding workers monitored for internal exposure results in an increase in the central estimate of the ERR per Sv for all malignant neoplasms other than leukaemia, by a factor of about 2.8 based on mortality data (Table D1) and by a factor of about 1.9 based on incidence data (Table D7). However, the confidence intervals for the ERR per Sv are wider and encompass a large proportion of the range of the corresponding CIs based on the full data. Also, whilst the p-values from the test for trend in mortality with external dose are lower after excluding workers monitored for internal exposure (Table D1), the corresponding p-values for the incidence data are similar to those in the main analysis (Table D7). In contrast to the impact of excluding workers monitored for internal exposure, stratifying the data on the basis of whether or not a worker was internally monitored has little impact on the central estimates of the ERR per Sv, the associated confidence intervals or the p-values. Fairly similar results are obtained from analyses of mortality and incidence from all malignant neoplasms other than lung, pleura and leukaemia (Tables D3, D9).

For mortality from leukaemia excluding CLL, the central estimate of the ERR per Sv is decreased after excluding workers monitored for internal exposure and the test for trend in risk with external dose is no longer statistically significant, reflecting a large increase in the width of the 90% CI (Table D2). In contrast, stratifying on the basis of internal exposure leads to an increase in the central estimate of the ERR estimate and the one-sided p-value from the test for trend is 0.02, compared with 0.042 from the main analysis. For the incidence of leukaemia excluding CLL (Table D8), the central estimate of the ERR per Sv is increased after either excluding workers monitored for internal exposure or stratifying on the basis of internal exposure. In particular, the ERR per Sv and the associated 90% CI change from 1.782 (0.17, 4.36) based on the main analysis to 3.147 (0.84, 6.85) after stratifying for internal exposure monitoring, whilst the associated one-sided p-value decreases from 0.03 to 0.005.

For multiple myeloma (Tables D4 and D10) and thyroid cancer (Tables D5 and D11), excluding workers monitored for internal exposure leads to a large change in the central estimate of the ERR per Sv and increases the width of the associated 90% CI considerably, both for incidence and mortality. In particular, in none of these instances is there evidence of a trend in risk with external dose after excluding this group of workers. Stratification on the basis of internal exposure leads to a change in the central estimate of the ERR per Sv for both myeloma and thyroid cancer mortality relative to the corresponding values in the main analysis, but the trend in risk with external dose is still not statistically significant. In contrast, for myeloma incidence, both the ERR estimate and the p-value are similar to those in the main analysis following this stratification. For

thyroid cancer incidence, the estimated ERR per Sv and the associated 90% CI change from 3.236 (-0.19, 13.9) in the main analysis to 1.88 (-0.68, 11.04) after stratifying for internal exposure monitoring, while the associated p-value increases from 0.079 to 0.176.

For mortality from all circulatory diseases combined, the central estimate of the ERR per Sv is higher and the corresponding 90% CI is wider after omitting those workers who were monitored for internal exposure (see Table D6). In addition, the one-sided p-value increases from 0.03 to 0.081, reflecting the lower precision of this subsidiary analysis. In contrast, the results based on stratifying for internal exposure monitoring are similar to those from the main analysis.

D4 RESTRICTION OF COHORT TO THAT USED IN EARLIER ANALYSES

The 3rd NRRW analysis includes about 50,000 more workers than did the 2nd analysis. In order to examine the influence of the cohort expansion on the main findings for mortality, as opposed to the longer period of follow-up, a subsidiary analysis was conducted in which the cohort was restricted to those workers who were also included in the 2nd analysis, but with follow-up to the end of 2001 rather than the end of 1992, as in the previous analysis. This subsidiary analysis also excludes a few workers who, as mentioned earlier in this report**,** were included in the 2nd analysis but not in the 3rd analysis. However, the cohort in this subsidiary analysis is essentially the same as that in the 2nd analysis. Tables D1-D11 show that the findings from analyses of mortality and cancer incidence in relation to external dose based on the 2nd analysis cohort are similar to those based on the full 3rd analysis cohort.

Not all of the workers in the 2nd NRRW analysis were included in the 15-country study of nuclear workers (Cardis *et al*, 2005, 2007; Vrijheid *et al*, 2007a,b). As well as excluding those persons who undertook radiation work for less than one year and those employed at organisations outside of the nuclear industry, the 15-country study excluded workers with potential for substantial exposure (>10% of their whole body dose) from internal radiation sources or from neutrons. Since information on internal exposures within the NRRW is restricted to flags of whether or not a worker was ever monitored, a large proportion of the 2nd NRRW analysis cohort was excluded from the 15-country analysis. In particular, the 3rd NRRW analysis cohort contains about twice the number of UK radiation workers that were considered in the 15-country study.

Tables D1-D11 show results restricted to the cohort of UK workers included in the 15-country study, based on follow-up to the end of 2001 rather than to the end of 1992 as in that study. In view of changes to personal and dose records for a small proportion of workers that have arisen since the time that the UK data for the 15-country study were prepared, there is not an exact correspondence between the data used in that study and those considered in this subsidiary analysis, but the differences are small. It can be seen from Tables D1-D11 that the numbers of deaths and cancer cases in the restricted cohort are about half of the corresponding numbers in the main analysis and, consequently, the findings are less precise. Whilst the central estimate of the ERR per Sv is usually decreased and sometimes increased, the wider 90% CI means that

generally there is no evidence of dose trends in cancer risk in the restricted cohort, with the exception of weak evidence of a trend in non-CLL leukaemia incidence (Table D8) . The same pattern is seen for mortality from all circulatory diseases combined (Table D6), where the estimated ERR per Sv and the associated 90% CI change from 0.251 (0.03, 0.49) in the main analysis to -0.02 (-0.38, 0.4) in this subsidiary analysis.

D5 CLASSIFICATION OF CAUSE OF DEATH

As stated in section 5.3 of this report, any one of leukaemia, non-Hodgkin lymphoma or multiple myeloma was selected for the internal analysis of mortality if it appeared anywhere on the death certificate. Similarly, cancers mentioned on death certificates were selected in preference to non-malignant causes of death. Furthermore, in the absence of a cancer registration, any mention of cancer on a death certificate was used in the cancer incidence analysis. Subsidiary analyses were undertaken in which, rather than using this approach, the mortality data were analysed based on underlying cause of death and the cancer incidence analysis was based on cancer registration data or – in the absence of cancer registrations – on underlying cause of death.

Tables D1 and D3 show that for mortality from all malignancies other than leukaemia (either including lung and pleural cancer or excluding them), focussing on underlying cause of death reduces the central ERR estimate slightly and increases the one-sided p-value to just under 0.1. The findings for mortality from leukaemia other than CLL and for thyroid cancer are similar or identical to those in the main analysis (Tables D2 and D5 respectively), whilst the central ERR estimate for myeloma mortality is decreased (Table D4). In contrast, the central ERR estimate for mortality from all circulatory diseases is increased slightly and the associated p-value is decreased relative to the values in the main analysis (Table D6). Omitting cancers listed as contributory cause of death has little impact on the cancer incidence analyses (Tables D7-D11).

D6 USE OF CANCER REGISTRATION DATA ONLY

As mentioned above, the main analyses of cancer incidence incorporated not only cancer registrations but – in instances where a worker was recorded as having died from cancer but where no cancer registration details were available – cancers identified from mortality data. A subsidiary analysis was conducted in which cancer incidence was analysed using cancer registration data only.

Tables D7 and D9 show that restricting the incidence analysis for all malignancies other than leukaemia (either including or excluding lung and pleural cancer) reduces the number of cases by around 15% and leads to an increase in the central ERR estimate and a decrease in the one-sided p-value. The same is true for multiple myeloma (Table D10) and thyroid cancer (Table 11). In particular, the one-sided p-value in the test for trend in thyroid cancer incidence with dose decreases from 0.079 in the main analysis to 0.049 based on registration data only. In contrast, although the number of cases of leukaemia excluding CLL falls by around 20% after omitting mortality data, the findings from the analysis in relation to external dose are virtually unchanged (Table D8).

D7 CLASSIFICATION OF EMPLOYER

As explained previously, workers were classified in the main analysis on the basis of their first NRRW employer, although doses received in any later employments covered by the NRRW were also taken in account. Subsidiary analyses were conducted in which workers were classified according either to their longest or to their last NRRW employer, rather than to their first. It can be seen that from Tables D1-D11 that using these alternative classifications generally has little impact on the results.

D8 USE OF MEAN RATHER THAN MEDIAN DOSES

When testing for any trend in risk with external dose and estimating the ERR per Sv, the approach taken in the main analysis involved using the median dose within each dose category (see section 5.3). However, in some other studies of radiation workers (eg. Cardis *et al*, 1995, 2007), the mean dose for each category has been used instead. The sensitivity of this choice was examined in a subsidiary analysis.

Within each dose category, the mean dose is slightly higher than the median dose. Consequently, as can be seen in Tables D1-D11, the central estimate of the ERR per Sv is slightly closer to zero when based on mean rather than median doses, and the associated CIs are slightly narrower. However, as would be expected, there is very little change in the p-value for the test in trend in risk with dose.

D9 STRATIFICATION BY TIME SINCE START OF RADIATION WORK

As stated in section 6.1, the SMR for all malignant neoplasms combined varies by time since start of radiation work. In the main analysis of tests for trend with dose in mortality or cancer incidence, allowance was made for possible effects of time since start of radiation work by excluding data for the first 10 years (or two years in the case of leukaemia). In order to examine whether further adjustment might be required in the internal analysis, a sensitivity analysis was conducted in which time since start of radiation work was stratified as <20, 20-29 and 30 or more years. As in the main analysis, data for the first 10 years after the start of radiation work (or 2 years for leukaemia) were excluded.

For mortality and incidence for all malignant neoplasms excluding leukaemia (Tables D1 and D7) and for the corresponding disease category that also excludes lung and pleural cancer (Tables D3 and D9), the central estimate of the ERR per Sv and the p-value from the trend test do not vary greatly when this stratification is used. For the other disease groupings considered, the central ERR estimate tends to be reduced somewhat and the p-values tend to be increased, although inferences are generally similar to before. A possible exception concerns leukaemia mortality, where the estimated ERR per Sv and the associated 90% CI change from 1.712 (0.06, 4.29) in the main analysis to 1.509 (-0.13, 4.15), whilst the one-sided p-value changes from 0.042 to 0.07, although the corresponding changes are smaller for leukaemia incidence (see Table D8). For mortality from all circulatory diseases combined, the differences are more profound: the

estimated ERR per Sv and the associated 90% CI change from 0.251 (0.03, 0.49) in the main analysis to 0.167 (-0.05, 0.41) after stratification, whilst the one-sided p-value increases from 0.03 to 0.109.

D10 STRATIFICATION BY DURATION OF RADIATION WORK

Some analyses of radiation workers have included an adjustment for duration of employment or duration of radiation work. In particular, in the main analysis of the 15-country study of radiation workers in the nuclear industry (Cardis *et al*, 2005, 2007), the data were stratified according to whether or not the duration of employment or of radiation monitoring was 10 years or more, in order to allow for a possible "healthy worker survivor effect" (HWSE), ie. the idea that persons who continue in employment for many years may be healthier than those who leave after a few years.

The NRRW does not hold complete data on duration of employment. Consequently, in order to explore the possible influence of any HWSE on the main findings here, a stratification along the lines of that used in the 15-country study was considered; namely, stratification of duration of radiation work according to whether or not this was at least 10 years. For mortality and incidence for all malignant neoplasms excluding leukaemia (Tables D1 and D7), the corresponding disease category that also excludes lung and pleural cancer (Tables D3 and D9) and non-CLL leukaemia (Tables D2 and D8), the central estimate of the ERR per Sv does not vary greatly following this stratification, whilst the 90% CIs are wider and the p-values are either similar to or somewhat higher than those in the main analysis. For example, the one-sided p-value for the incidence of all malignant neoplasms excluding leukaemia, lung and pleural cancer increases from 0.022 to 0.115. The largest changes in the central ERR estimate arise for multiple myeloma, thyroid cancer and circulatory disease. For example, the estimated ERR per Sv and the associated 90% CI for myeloma incidence change from 3.597 (0.77, 8.94) in the main analysis to 2.121 (-0.21, 7.71), whilst the one-sided p-value changes from 0.008 to 0.077. For mortality from all circulatory diseases combined, the estimated ERR per Sv and the associated 90% CI change from 0.251 (0.03, 0.49) in the main analysis to 0.142 (-0.11, 0.43), whilst the one-sided p-value increases from 0.03 to 0.186 (Table D6).

In view of the indications from Table 6.5 of lower SMRs for all causes and for all malignant neoplasms combined among those who conducted radiation work for 30 or more years, another subsidiary analysis was conducted in which duration of radiation work was stratified according to whether or not this was at least 30 years. Tables D1-D11 show that inferences based on this stratification are generally similar to those from the main analysis. In particular, the impact on ERR estimates and on significance tests is less than that associated with the stratification <10 and 10 or more years (see above).

The stratification for duration of radiation work of <10 and 10 or more years was also applied to the cohort of UK workers included in the 15-country study (see section D4 above), since that study employed this stratification (Cardis *et al*, 2005, 2007; Vrijheid *et al*, 2007). It can be seen from Tables D1-D11 that the findings from this subsidiary analysis tend to be similar to those based on the cohort restricted to those workers in the 15-country study but without stratification by duration of radiation work.

D11 OMITTING ADJUSTMENT FOR INDUSTRIAL CLASSIFICATION

Adjustment for industrial classification was made in the main analysis, because this variable is correlated both with radiation dose (in that industrial workers tend to have higher doses than non-industrial workers – see Table 2.9) and with overall levels of mortality (with higher rates among industrial than non-industrial workers – see Table 6.1). Thus industrial classification is a confounder which – if it were not taken into account – would lead to over-estimation of the magnitude of any radiation risk and could produce spurious findings. To confirm this, a subsidiary analysis was undertaken in which industrial classification was omitted from the stratification.

For mortality from all causes combined, the ERR per Sv increases from 0.145 (90% CI 0.00, 0.3) in the main analysis to 0.23 (90% CI 0.08, 0.39) without adjustment for industrial classification. The corresponding one-sided p-value falls from 0.049 to 0.004. Based on Tables D1-D11, it can be seen that omitting this adjustment also has a sizeable impact on major disease groupings. For example, the ERR per Sv for mortality from all malignant neoplasms other than leukaemia increases from 0.275 (90% CI 0.02, 0.56) in the main analysis to 0.369 (0.10, 0.66) in the subsidiary analysis, whilst the corresponding one-sided p-value decreases from 0.04 to 0.01. For mortality from all circulatory diseases combined, the ERR per Sv increases from 0.251 (0.03, 0.49) in the main analysis to 0.354 (0.13, 0.6) in the subsidiary analysis, whilst the corresponding one-sided p-value decreases from 0.03 to 0.004. For the grouping of all malignant neoplasms other than leukaemia, lung and pleural cancer, the change in the ERR per Sv is not as marked, so indicating that industrial classification is correlated with smoking habits and that failure to adjust for industrial classification leads to a particularly strong bias when considering smoking-related diseases. For specific diseases such as leukaemia which show little or no correlation with social class, omitting the adjustment for industrial classification has – as expected – relatively little impact on the estimated ERR per Sv. Similar patterns were seen in a subsidiary analysis of data from the 15-country nuclear workers study (Cardis *et al*, 2007).

D12 ADJUSTMENT BY COUNTRY RATHER THAN BY EMPLOYER/SITE

The main analysis includes an adjustment for employer/site, in account to account for geographical variations in mortality and cancer rates and variations in occupation radiation exposure between different employers/sites. If it were the case that most of the variation in occupational doses was due to differences between employers/sites, then such an approach could reduce substantially the statistical power to look for any association between cancer or mortality and dose. To test whether this might be true, a subsidiary analysis was conducted in which, rather than stratifying on the basis of the 14 categories for first employer or site listed in section 5.3, the data were stratified according to whether the first employer/site was situated in (i) England and Wales, or (ii) Scotland. This division was chosen because of the difference in mortality rates between England/Wales and Scotland shown in section 6.1.

It can be seen from Tables D12 and D13 that the central estimate of the ERR per Sv tends to increase when stratifying by country rather than by employer/site. This increase is particularly noteworthy for mortality from causes with a strong relation to SES, whereas – for example – the findings for leukaemia are little affected. This is not surprising, since Tables 2.8 and 6.6 of the draft report show that, even within England, there are variations between sites in average doses and in mortality rates. In particular, some of the plants with the highest average doses are in northern England. Since rates of mortality and cancer in that part of England tend to be higher than the corresponding rates in southern England, not adjusting for employer/site would lead to an upward bias in the trend estimate, as seen here for diseases with a strong SES component. It is important to note that the width of the 90% confidence interval for the ERR per Sv does not vary greatly according to whether adjustment is made for employer/site or solely by country. Thus indicates that much of the variation in doses arises between workers at the same employer/site, rather than between workers at different employers/sites within either England/Wales or Scotland. Consequently there is very little loss of statistical power due to adjusting for employer/site rather than country. In contrast, adjusting solely by country would bias estimates of radiation risks.

D13 CHOICE OF LAG PERIOD

For the main analysis, doses were lagged by 10 years and the data for the first 10 years after start of radiation work were excluded when looking for trends in risk with dose, so as allow for the latency of any radiation effect (for leukaemia, a 2 year lag was used). The sensitivity of the findings to the choice of lag period was examined in a subsidiary analysis.

It can be seen from Tables D12 and D13 that the central estimate of the ERR per Sv tends to increase with increasing lag period for each of the three cancer groupings shown, both for mortality and incidence. The width of the associated CI also increases in a similar fashion. In contrast, the p-values from the test for trend in risk with dose tend to be more stable.

D14 INCLUSION OF DEATHS AND CANCERS AFTER AGE 85

As explained in section 5.1, deaths and cancers at ages 85 years or more were excluded from the analysis, because of concerns about the quality of mortality and cancer incidence ascertainment at these ages. A subsidiary analysis was undertaken in which these deaths were incorporated in the analyses of mortality in relation to dose. It can be seen from Tables D1-D11 that, whilst including deaths at age 85 or older increasing the number of deaths or cancer cases available for analysis by up to several hundred, inferences are very similar to those from the main analysis.

Table E4 in Appendix E shows SMRs by age including deaths at ages 85 years or more. As in the main analysis, there is little evidence of a trend with age in SMRs after adjusting for social class.

D15 VARIATION IN RISK BY ATTAINED AGE

The 15-country study of radiation workers in the nuclear industry indicated that, if anything, the ERR per Sv might be greater at attained ages of 70 years or more when compared with young attained ages, although there were not statistically significant differences (Cardis *et al*, 2007). To examine this issue further, a subsidiary analysis was conducted in which cancer risk estimates were calculated separately for the same attained age categories as those used by Cardis *et al* (2007); namely, less than 60 years, 60-69 years and 70 years or more.

Tables D14 and D15 show that for non-CLL leukaemia, the central ERR estimate is greatest for the oldest age group and – for mortality but not for incidence – the variation in the ERR per Sv by attained age is statistically significant. However, for the grouping of all malignant neoplasms excluding leukaemia and for the corresponding grouping that also excludes lung and pleural cancer, there is no clear pattern in the ERRs and the data are consistent with the ERR per Sv being constant across age groups.

D16 ALLOWING FOR POSSIBLE VARIATION IN RADIATION RISK BY TIME SINCE EXPOSURE, AGE AT EXPOSURE AND/OR ATTAINED AGE

D16.1 Leukaemia excluding CLL

As described in section 5.4, there is evidence from studies such as that of the Japanese atomic bomb survivors that the ERR per Sv for leukaemia excluding CLL varies with time since exposure. To determine whether there is evidence of a similar effect in the NRRW, a nested case-control analysis was carried out (Breslow *et al*, 1983). Rather than analysing the entire cohort and sub-dividing the person-years on the basis of cumulative dose, data on leukaemia cases and samples of matched controls were selected from the cohort. For each worker with a registration or a mention on the death certificate of leukaemia (other than CLL), up to a specified maximum number of 100 control workers were sampled from the cohort, matched to the leukaemia case by gender, date of birth (within two years), site of first employment and industrial classification. The controls were required to have been alive and not to have been recorded as having been diagnosed with non-CLL leukaemia at the time of the case's date of diagnosis or death from the disease. In line with the main analysis, both cases and controls were required to have started radiation work at least two years prior to the case's death. The radiation dose histories for the cases and controls were analysed by conditional logistic regression, using the computer program PECAN (Preston *et al*, 1999). In particular, the following model for the excess relative risk (ERR) was fitted to the data:

$$\mathrm{ERR} = \cdot\beta_S \sum_i \left[(D_i + \theta \cdot D_i^2)\exp\{\gamma.E_i^* + \delta.\log(T_i/25) + \varphi.E_i^*.\log(T_i/25)\}\right]$$

Here D_i represents the dose received (by a case or matched control) in a given year (indexed by i), E_i represents the person's age (in years) at the time of this exposure, E_i^* is equal to (E-30)/10 if E is less than 30 years and is equal to 0 if 30 years or more, and

T_i represents the length of time (in years) between this exposure and the case's diagnosis or death from the disease. The summation in this equation runs over each year in the period up to 2 years prior to the case's diagnosis or death from the disease. This model corresponds to that proposed for non-CLL leukaemia by the US BEIR VII Committee (NRC, 2006), based on analysis of data for the Japanese A-bomb survivors. The parameters θ, γ, δ and φ were constrained to equal the values estimated by BEIR VII, namely 0.87 per Sv, -0.40 per decade, -0.48 and 0.42 respectively, since (as shown below) the NRRW data are not sufficiently strong to estimate these parameters precisely. Under this model, the ERR decreases with increasing time since exposure and – up to age 30 – with increasing age at exposure. The parameter β_S, which represents the ERR per Sv at low doses that would arise 25 years following an exposure at age 30 or more, was estimated separately for males and females, as in the BEIR VII model, as well as based on data for both genders combined.

Table D16 shows the estimate of β_S based on fits to the NRRW mortality and incidence data, together with the corresponding BEIR VII estimates. It can be seen that, for males, the NRRW and BEIR VII estimates of β_S are very close to each other. The central estimate of β_S for mortality in females is higher based on the NRRW than on the BEIR VII model. However, the confidence interval based on the NRRW data is very wide and encompasses the BEIR VII estimate. Conversely, the estimate of β_S for incidence in females is statistically significantly less than zero. It should be stressed, however, that these findings are based on small numbers of cases among females. Since much of the information on radiation and leukaemia from the NRRW relates to males, the overall estimates of β_S from the NRRW are similar to those for males alone.

Values of the deviance (McCullagh and Nelder, 1989) – a measure of goodness-of-fit – associated with the fitting the BEIR VII model to the NRRW mortality data and incidence data are 1568.046 and 1890.859 respectively. These are close to the corresponding values associated with fitting a simple linear dose-response model with no age and time dependence to the same nested case-control data; namely, 1567.668 for mortality and 1890.927 for incidence. This shows that the NRRW data are not sufficiently powerful to identify age or time variations in the ERR per Sv, nor non-linearity in the dose-response, of the magnitude estimated by the BEIR VII Committee based on the Japanese A-bomb data.

D16.2 Cancers other than leukaemia

BEIR VII-type models were also fitted to case-control data on cancers other than leukaemia, in view of indications from the Japanese A-bomb survivors that the ERR per Sv varies with attained age (NRC, 2006). Under these models, the ERR was assumed to be of the following form:

$$\mathrm{ERR} = \cdot\beta_S \sum_i \left[D_i . \exp(\gamma . E_i^*)(A/60)^\eta\right]$$

Here D_i represents the dose received (by a case or matched control) in a given year (indexed by i), E_i represents the person's age (in years) at the time of this exposure, E_i^* is equal to $(E_i - 30)/10$ if E_i is less than 30 years and is equal to 0 if 30 years or more,

and *A* represents the attained age of the case or control at the time of the case's diagnosis or death. The summation in this equation runs over each year in the period up to 10 years prior to the case's diagnosis or death from the disease. This corresponds to the model proposed by the US BEIR VII Committee (NRC, 2006) for the grouping of all solid cancers (excluding incident cases of thyroid and non-melanoma skin cancers), based on analysis of incidence and mortality data for the Japanese A-bomb survivors, but omitting the impact of age at exposure since this mainly relates to the impact of exposure in childhood and early adulthood. The parameters γ and η were constrained to equal the values estimated by BEIR VII, namely -0.30 per decade and -1.4 respectively for incidence and -0.56 per decade and -0.67 for mortality, since (as shown below) the NRRW data are not sufficiently strong to estimate these parameters precisely. Under this model, the ERR decreases with increasing attained age and – up to age 30 – with increasing age at exposure. The parameter β_S, which represents the ERR per Sv at age 60 following exposure at age 30 years or more, was estimated separately for males and females, as in the BEIR VII model, as well as based on data for both genders combined.

As with the leukaemia case-control analysis described above, for each worker with a registration or a mention on the death certificate of a malignant neoplasm other than leukaemia (and in some instances also excluding lung and pleural cancers), up to a specified maximum number of 100 control workers were sampled from the cohort, matched to the case by gender, date of birth (within two years), site of first employment and industrial classification. The controls were required to have been alive and not to have been recorded as having been diagnosed with any of the cancers under considered at the time of the case's date of diagnosis or death from the disease. In line with the main analysis, both cases and controls were required to have started radiation work at least 10 years prior to the case's death. The radiation dose histories for the cases and controls were again analysed by conditional logistic regression, using the computer program PECAN (Preston ***et al***, 1999).

Table D16 shows the estimate of β_S based on fits to the NRRW mortality and incidence data for the grouping of all malignant neoplasms other than leukaemia and all malignant neoplasms other than leukaemia, lung and pleural cancer, together with the corresponding BEIR VII estimates for cancers other than leukaemia (considering the risk at age 60 following exposure at age 30 years or more). It can be seen that, for males, the NRRW estimates of β_S are slightly smaller than the corresponding BEIR VII values, although the confidence intervals overlap. The central estimates of β_S for females are higher based on the NRRW than on the BEIR VII model. However, the confidence intervals based on the NRRW data are very wide and encompass the BEIR VII estimates. Since much of the information on radiation and cancer risk from the NRRW relates to males, the overall estimates of $\boldsymbol{\beta_S}$ from the NRRW are similar to those for males alone.

Values of the deviance associated with the fitting the BEIR VII model to the NRRW mortality data and incidence data for all malignant neoplasm other than leukaemia are 59026.436 and 89477.31 respectively. These are close to the corresponding values associated with fitting a simple linear dose-response model with no age and time dependence to the same nested case-control data; namely, 59025.847 for mortality and 89476.024 for incidence. Very similar findings arise from the analysis of data for all

malignant neoplasms other than leukaemia, lung and pleural cancer. This shows that the NRRW data are not sufficiently powerful to identify age or time variations in the ERR per Sv of the magnitude estimated by the BEIR VII Committee based on the Japanese A-bomb data.

Table D1 Excess relative risk (ERR) estimates for mortality from all malignant neoplasms excluding leukaemia in the main analysis and in subsidiary analyses

			p-value	
Analysis	Deaths	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	7455	0.275 (0.02, 0.56)	0.04	0.08
Doses without threshold adjustment	7459	0.274 (0.01, 0.56)	0.041	0.082
Doses without NICEA adjustments	7437	0.292 (0.03, 0.58)	0.033	0.066
Doses without any adjustments	7452	0.299 (0.03, 0.59)	0.03	0.061
Excluding workers monitored for internal exposure	4940	0.758 (0.22, 1.38)	0.008	0.017
With stratification for internal exposure monitoring	7431	0.285 (0.01, 0.6)	0.046	0.093
Restriction to second analysis cohort	5663	0.271 (0.01, 0.57)	0.046	0.091
Restriction to cohort included in the IARC 15-country study	3601	0.198 (-0.25, 0.73)	0.245	0.49
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	3528	0.365 (-0.19, 1.04)	0.147	0.295
With stratification by duration of radiation work (<30,30+ years)	7453	0.347 (0.07, 0.66)	0.019	0.037
Using underlying cause of death	6927	0.217 (-0.05, 0.52)	0.093	0.187
Based on longest employer	7457	0.258 (0.00, 0.54)	0.05	0.1
Based on last employer	7459	0.26 (0.00, 0.55)	0.048	0.097
With stratification by country of first employer but without stratification by first employer	7487	0.436 (0.20, 0.7)	0.001	0.002
Using mean rather than median doses	7455	0.247 (0.01, 0.51)	0.043	0.087
With stratification by time since start of radiation work	7402	0.274 (0.01, 0.57)	0.047	0.093
With stratification by duration of radiation work (<10,10+ years)	7441	0.275 (-0.04, 0.63)	0.074	0.149
Without stratification by industrial classification	7476	0.369 (0.10, 0.66)	0.01	0.02
Including deaths and person years between 85 and 100 years	7728	0.305 (0.05, 0.59)	0.025	0.049

Table D2 Excess relative risk (ERR) estimates for mortality from leukaemia (excluding CLL) in the main analysis and in subsidiary analyses

			p-value	
Analysis	Deaths	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	198	1.712 (0.06, 4.29)	0.042	0.084
Doses without threshold adjustment	198	1.538 (-0.02, 3.99)	0.052	0.105
Doses without NICEA adjustments	197	1.389 (-0.11, 3.76)	0.068	0.135
Doses without any adjustments	197	1.468 (-0.04, 3.86)	0.057	0.113
Excluding workers monitored for internal exposure	141	1.231 (<-1.97, 6.62)	0.303	0.605
With stratification for internal exposure monitoring	197	2.47 (0.37, 5.81)	0.02	0.041
Restriction to second analysis cohort	145	2.278 (0.28, 5.62)	0.024	0.049
Restriction to cohort included in the IARC 15-country study	89	0.878 (-1.15, 5.57)	0.287	0.575
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	85	2.608 (-0.84, 10.39)	0.137	0.274
With stratification by duration of radiation work (<30,30+ years)	198	1.767 (-0.02, 4.59)	0.052	0.104
Using underlying cause of death	174	1.589 (-0.01, 4.18)	0.052	0.104
Based on longest employer	197	2.025 (0.25, 4.77)	0.025	0.049
Based on last employer	197	2.11 (0.30, 4.92)	0.022	0.044
With stratification by country of first employer but without stratification by first employer	198	1.507 (0.09, 3.66)	0.038	0.076
Using mean rather than median doses	198	1.62 (0.07, 4.09)	0.041	0.082
With stratification by time since start of radiation work	195	1.509 (-0.13, 4.15)	0.07	0.14
With stratification by duration of radiation work (<10,10+ years)	195	2.278 (-0.01, 6.29)	0.051	0.102
Without stratification by industrial classification	199	1.953 (0.22, 4.63)	0.026	0.053
Including deaths and person years between 85 and 100 years	205	1.893 (0.17, 4.54)	0.031	0.062

Table D3 Excess relative risk (ERR) estimates for mortality from all malignant neoplasms excluding pleura, lung and leukaemia in the main analysis and in subsidiary analyses

			p-value	
Analysis	Deaths	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	5118	0.323 (0.02, 0.67)	0.04	0.081
Doses without threshold adjustment	5120	0.34 (0.03, 0.69)	0.033	0.066
Doses without NICEA adjustments	5105	0.381 (0.07, 0.74)	0.021	0.042
Doses without any adjustments	5114	0.377 (0.07, 0.73)	0.022	0.043
Excluding workers monitored for internal exposure	3442	0.828 (0.21, 1.57)	0.011	0.023
With stratification for internal exposure monitoring	5101	0.39 (0.05, 0.77)	0.026	0.053
Restriction to second analysis cohort	3956	0.313 (0.00, 0.67)	0.049	0.098
Restriction to cohort included in the IARC 15-country study	2546	0.321 (-0.21, 0.96)	0.169	0.338
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	2496	0.42 (-0.20, 1.19)	0.141	0.283
With stratification by duration of radiation work (<30,30+ years)	5116	0.415 (0.09, 0.79)	0.017	0.034
Using underlying cause of death	4705	0.269 (-0.05, 0.63)	0.085	0.17
Based on longest employer	5119	0.317 (0.01, 0.66)	0.043	0.086
Based on last employer	5119	0.315 (0.01, 0.66)	0.044	0.088
With stratification by country of first employer but without stratification by first employer	5140	0.531 (0.24, 0.85)	0.001	0.002
Using mean rather than median doses	5118	0.298 (0.02, 0.62)	0.04	0.08
With stratification by time since start of radiation work	5076	0.345 (0.03, 0.71)	0.036	0.073
With stratification by duration of radiation work (<10,10+ years)	5108	0.312 (-0.04,0.73)	0.077	0.154
Without stratification by industrial classification	5131	0.369 (0.06, 0.72)	0.023	0.046
Including deaths and person years between 85 and 100 years	5341	0.348 (0.05, 0.69)	0.028	0.056

Table D4 Excess relative risk (ERR) estimates for mortality from multiple myeloma in the main analysis and in subsidiary analyses

			p-value	
Analysis	Deaths	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	113	1.195 (-0.88, 5.96)	0.221	0.442
Doses without threshold adjustment	113	0.973 (-0.94, 5.34)	0.245	0.49
Doses without NICEA adjustments	113	1.756 (-0.72, 7.33)	0.168	0.336
Doses without any adjustments	114	1.168 (-0.88, 5.79)	0.223	0.446
Excluding workers monitored for internal exposure	72	<-1.961 (<-1.96, 6.22)	0.766	0.468
With stratification for internal exposure monitoring	112	0.615 (-1.11, 5.06)	0.313	0.627
Restriction to second analysis cohort	88	0.861 (-0.99, 5.38)	0.27	0.54
Restriction to cohort included in the IARC 15-country study	52	<-1.991 (<-1.99, 2.9)	0.882	0.235
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	50	<-1.991 (<-1.99, 3.01)	0.909	0.182
With stratification by duration of radiation work (<30,30+ years)	113	1.078 (-0.96, 5.95)	0.246	0.492
Using underlying cause of death	97	0.307 (-1.16, 4.42)	0.398	0.797
Based on longest employer	113	0.926 (-0.96, 5.25)	0.257	0.515
Based on last employer	113	1.197 (-0.86, 5.84)	0.22	0.441
With stratification by country of first employer but without stratification by first employer	114	-0.431 (-1.39, 1.73)	0.646	0.707
Using mean rather than median doses	113	1.103 (-0.80, 5.62)	0.22	0.44
With stratification by time since start of radiation work	111	0.589 (-1.21, 5.36)	0.339	0.677
With stratification by duration of radiation work (<10,10+ years)	113	2.044 (-0.94, 11)	0.19	0.38
Without stratification by industrial classification	113	1.005 (-0.94, 5.48)	0.254	0.508
Including deaths and person years between 85 and 100 years	116	1.252 (-0.87, 6.06)	0.21	0.42

Table D5 Excess relative risk (ERR) estimates for mortality from thyroid cancer in the main analysis and in subsidiary analyses

			p-value	
Analysis	Deaths	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	17	3.124 (-0.88, 44.89)	0.177	0.352
Doses without threshold adjustment	17	2.974 (-0.88, 42.77)	0.188	0.376
Doses without NICEA adjustments	17	3.45 (-0.83, 46.33)	0.171	0.342
Doses without any adjustments	17	3.395 (-0.84, 50.65)	0.169	0.338
Excluding workers monitored for internal exposure	9	9.42 (<-1.96, 238.22)	0.296	0.493
With stratification for internal exposure monitoring	16	1.645 (-1.25, 83.34)	0.283	0.566
Restriction to second analysis cohort	15	4.398 (-0.81, 101.37)	0.157	0.314
Restriction to cohort included in the IARC 15-country study	9	50.176 (<-1.99, n/c [a])	0.329	0.650
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	9	<-1.991 (<-1.99, 596.96)	0.553	0.872
With stratification by duration of radiation work (<30,30+ years)	17	3.542 (-0.84, 49.67)	0.173	0.339
Using underlying cause of death	17	3.124 (-0.88, 44.89)	0.179	0.357
Based on longest employer	17	5.801 (-0.47, 52.78)	0.111	0.222
Based on last employer	17	5.773 (-0.46, 51.51)	0.111	0.222
With stratification by country of first employer but without stratification by first employer	17	2.593 (-0.78, 17.93)	0.168	0.336
Using mean rather than median doses	17	2.998 (-0.74, 44.27)	0.175	0.348
With stratification by time since start of radiation work	16	2.02 (-1.18, 45.92)	0.258	0.515
With stratification by duration of radiation work (<10,10+ years)	17	0.895 (-1.32, 28.3)	0.338	0.675
Without stratification by industrial classification	17	1.575 (-1.16, 34.25)	0.272	0.543
Including deaths and person years between 85 and 100 years	18	2.47 (-0.92, 28.39)	0.2	0.4

a This value could not be calculated.

Table D6 Excess relative risk (ERR) estimates for mortality from all circulatory diseases in the main analysis and in subsidiary analyses

			p-value	
Analysis	Deaths	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	10509	0.251 (0.03, 0.49)	0.03	0.059
Doses without threshold adjustment	10519	0.247 (0.03, 0.49)	0.032	0.064
Doses without NICEA adjustments	10487	0.246 (0.02, 0.49)	0.033	0.067
Doses without any adjustments	10507	0.238 (0.02, 0.48)	0.038	0.075
Excluding workers monitored for internal exposure	6783	0.383 (-0.06, 0.89)	0.081	0.162
With stratification for internal exposure monitoring	10487	0.275 (0.03, 0.54)	0.031	0.061
Restriction to second analysis cohort	7943	0.224 (0.00, 0.46)	0.048	0.096
Restriction to cohort included in the IARC 15-country study	4980	-0.02 (-0.38, 0.4)	0.534	0.931
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	4881	0.023 (-0.40, 0.52)	0.466	0.933
With stratification by duration of radiation work (<30,30+ years)	10505	0.301 (0.07, 0.55)	0.015	0.031
Using underlying cause of death	10905	0.298 (0.08, 0.54)	0.011	0.023
Based on longest employer	10519	0.262 (0.04, 0.5)	0.025	0.05
Based on last employer	10519	0.249 (0.03, 0.49)	0.031	0.062
With stratification by country of first employer but without stratification by first employer	10554	0.718 (0.50, 0.96)	0	0
Using mean rather than median doses	10509	0.215 (0.01, 0.44)	0.039	0.078
With stratification by time since start of radiation work	10452	0.167 (-0.05, 0.41)	0.109	0.219
With stratification by duration of radiation work (<10,10+ years)	10475	0.142 (-0.11, 0.43)	0.186	0.371
Without stratification by industrial classification	10539	0.354 (0.13, 0.6)	0.004	0.009
Including deaths and person years between 85 and 100 years	11093	0.255 (0.04, 0.49)	0.025	0.051

Table D7 Excess relative risk (ERR) estimates for the incidence of all malignant neoplasms excluding leukaemia in the main analysis and in subsidiary analyses

			p-value	
Analysis	Cases	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	10855	0.266 (0.04, 0.51)	0.025	0.05
Doses without threshold adjustment	10867	0.268 (0.04, 0.52)	0.025	0.051
Doses without NICEA adjustments	10830	0.259 (0.03, 0.51)	0.029	0.058
Doses without any adjustments	10863	0.267 (0.04, 0.52)	0.026	0.053
Excluding workers monitored for internal exposure	7377	0.468 (0.03, 0.97)	0.039	0.078
With stratification for internal exposure monitoring	10824	0.257 (0.02, 0.52)	0.038	0.077
Restriction to second analysis cohort	8362	0.271 (0.04, 0.52)	0.025	0.051
Restriction to cohort included in the IARC 15-country study	5356	0.23 (-0.16, 0.68)	0.175	0.351
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	5268	0.262 (-0.19, 0.8)	0.18	0.359
With stratification by duration of radiation work (<30,30+ years)	10853	0.349 (0.11, 0.61)	0.007	0.014
Using underlying cause of death	10788	0.258 (0.03, 0.5)	0.029	0.058
Based on longest employer	10860	0.269 (0.04, 0.51)	0.024	0.047
Based on last employer	10865	0.278 (0.05, 0.53)	0.02	0.04
With stratification by country of first employer but without stratification by first employer	10908	0.302 (0.10, 0.52)	0.006	0.011
Using mean rather than median doses	10855	0.242 (0.04, 0.47)	0.026	0.052
With stratification by time since start of radiation work	10787	0.318 (0.08, 0.58)	0.013	0.025
With stratification by duration of radiation work (<10,10+ years)	10824	0.232 (-0.03, 0.53)	0.074	0.148
Including cancers and person years between 85 and 100 years	11095	0.263 (0.04, 0.51)	0.025	0.05
Without stratification by industrial classification	10896	0.305 (0.08, 0.55)	0.012	0.025
Using only cancer registration data	10077	0.326 (0.09, 0.59)	0.011	0.022

Table D8 Excess relative risk (ERR) estimates for the incidence of leukaemia (excluding CLL) in the main analysis and in subsidiary analyses

			p-value	
Analysis	Cases	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	234	1.782 (0.17, 4.36)	0.03	0.06
Doses without threshold adjustment	234	1.535 (0.06, 3.9)	0.042	0.084
Doses without NICEA adjustments	233	1.766 (0.15, 4.37)	0.032	0.065
Doses without any adjustments	233	1.576 (0.08, 3.98)	0.039	0.078
Excluding workers monitored for internal exposure	172	2.47 (<-1.97, 8.77)	0.171	0.343
With stratification for internal exposure monitoring	234	3.147 (0.84, 6.85)	0.005	0.011
Restriction to second analysis cohort	172	2 (0.23, 4.98)	0.026	0.051
Restriction to cohort included in the IARC 15-country study	114	2.353 (-0.24, 7.89)	0.078	0.155
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	112	3.566 (0.28, 10.71)	0.03	0.06
With stratification by duration of radiation work (<30,30+ years)	234	1.719 (0.02, 4.5)	0.048	0.095
Using underlying cause of death	230	1.67 (0.11, 4.15)	0.035	0.071
Based on longest employer	233	1.984 (0.29, 4.68)	0.021	0.042
Based on last employer	233	2.081 (0.34, 4.84)	0.018	0.036
With stratification by country of first employer but without stratification by first employer	233	1.417 (0.08, 3.45)	0.038	0.077
Using mean rather than median doses	234	1.694 (0.18, 4.16)	0.028	0.056
With stratification by time since start of radiation work	231	1.674 (-0.01, 4.48)	0.051	0.102
With stratification by duration of radiation work (<10,10+ years)	231	2.043 (0.07, 5.53)	0.042	0.083
Including cancers and person years between 85 and 100 years	238	1.964 (0.28, 4.61)	0.022	0.043
Without stratification by industrial classification	235	1.834 (0.21, 4.42)	0.027	0.054
Using only cancer registration data	197	1.715 (0.12, 4.38)	0.035	0.07

Table D9 Excess relative risk (ERR) estimates for the incidence of all malignant neoplasms excluding pleura, lung and leukaemia in the main analysis and in subsidiary analyses

			p-value	
Analysis	Cases	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	8443	0.305 (0.05, 0.58)	0.022	0.045
Doses without threshold adjustment	8453	0.306 (0.05, 0.59)	0.023	0.045
Doses without NICEA adjustments	8424	0.323 (0.07, 0.61)	0.018	0.035
Doses without any adjustments	8449	0.309 (0.05, 0.59)	0.022	0.045
Excluding workers monitored for internal exposure	5813	0.395 (-0.08, 0.94)	0.087	0.173
With stratification for internal exposure monitoring	8420	0.329 (0.06, 0.63)	0.022	0.043
Restriction to second analysis cohort	6595	0.298 (0.04, 0.58)	0.027	0.054
Restriction to cohort included in the IARC 15-country study	4249	0.192 (-0.24, 0.7)	0.242	0.483
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	4180	0.08 (-0.38, 0.64)	0.396	0.792
With stratification by duration of radiation work (<30,30+ years)	8441	0.383 (0.12, 0.68)	0.008	0.016
Using underlying cause of death	8387	0.291 (0.04, 0.57)	0.028	0.055
Based on longest employer	8447	0.322 (0.07, 0.6)	0.017	0.034
Based on last employer	8450	0.328 (0.07, 0.61)	0.016	0.031
With stratification by country of first employer but without stratification by first employer	8489	0.343 (0.12, 0.59)	0.005	0.01
Using mean rather than median doses	8443	0.283 (0.05, 0.54)	0.021	0.042
With stratification by time since start of radiation work	8385	0.376 (0.11, 0.67)	0.009	0.018
With stratification by duration of radiation work (<10,10+ years)	8416	0.21 (-0.07, 0.53)	0.115	0.229
Including cancers and person years between 85 and 100 years	8636	0.293 (0.04, 0.57)	0.025	0.05
Without stratification by industrial classification	8476	0.312 (0.06, 0.59)	0.019	0.039
Using only cancer registration data	7886	0.325 (0.06, 0.62)	0.02	0.04

Table D10 Excess relative risk (ERR) estimates for the incidence of multiple myeloma in the main analysis and in subsidiary analyses

			p-value	
Analysis	Cases	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	149	3.597 (0.77, 8.94)	0.008	0.015
Doses without threshold adjustment	149	3.374 (0.51, 8.79)	0.017	0.033
Doses without NICEA adjustments	150	3.668 (0.83, 9.09)	0.007	0.013
Doses without any adjustments	151	3.221 (0.44, 8.65)	0.019	0.038
Excluding workers monitored for internal exposure	98	0.691 (-1.32, 9.61)	0.345	0.691
With stratification for internal exposure monitoring	148	2.962 (0.43, 8.15)	0.017	0.035
Restriction to second analysis cohort	115	3.216 (0.56, 8.53)	0.018	0.036
Restriction to cohort included in the IARC 15-country study	69	1.706 (-0.61, 9.82)	0.162	0.324
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	67	0.802 (-1.02, 9.4)	0.303	0.605
With stratification by duration of radiation work (<30,30+ years)	149	2.52 (0.07, 7.63)	0.043	0.086
Using underlying cause of death	147	3.589 (0.77, 8.91)	0.008	0.015
Based on longest employer	149	3.576 (0.77, 8.87)	0.008	0.015
Based on last employer	150	3.567 (0.77, 8.84)	0.008	0.015
With stratification by country of first employer but without stratification by first employer	151	0.609 (-0.60, 2.81)	0.239	0.478
Using mean rather than median doses	149	3.366 (0.74, 8.44)	0.007	0.014
With stratification by time since start of radiation work	147	2.872 (0.24, 8.29)	0.03	0.06
With stratification by duration of radiation work (<10,10+ years)	149	2.121 (-0.21, 7.71)	0.077	0.155
Including cancers and person years between 85 and 100 years	151	3.597 (0.77, 8.95)	0.008	0.015
Without stratification by industrial classification	150	3.744 (0.87, 9.14)	0.006	0.012
Using only cancer registration data	137	4.706 (1.23, 11.33)	0.003	0.006

Table D11 Excess relative risk (ERR) estimates for the incidence of thyroid cancer in the main analysis and in subsidiary analyses

			p-value	
Analysis	Cases	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Main	54	3.236 (-0.19, 13.9)	0.079	0.157
Doses without threshold adjustment	54	3.025 (-0.23, 13.12)	0.088	0.175
Doses without NICEA adjustments	54	3.615 (-0.09, 15)	0.07	0.14
Doses without any adjustments	54	3.543 (-0.12, 15.14)	0.072	0.144
Excluding workers monitored for internal exposure	35	0.681 (<-1.96, 21.97)	0.38	0.759
With stratification for internal exposure monitoring	53	1.88 (-0.68, 11.04)	0.176	0.352
Restriction to second analysis cohort	46	3.648 (-0.13, 16.05)	0.077	0.154
Restriction to cohort included in the IARC 15-country study	29	5.493 (<-1.99, 55.17)	0.301	0.6
Restriction to cohort included in the IARC 15-country study and stratification by duration of radiation work (<10,10+ years)	28	0.364 (<-1.99, 81.23)	0.438	0.876
With stratification by duration of radiation work (<30,30+ years)	54	2.781 (-0.40, 13.48)	0.107	0.214
Using underlying cause of death	54	3.236 (-0.19, 13.9)	0.082	0.163
Based on longest employer	54	3.554 (-0.06, 14.16)	0.073	0.147
Based on last employer	54	3.449 (-0.08, 13.73)	0.072	0.143
With stratification by country of first employer but without stratification by first employer	55	2.404 (-0.29, 9.49)	0.099	0.198
Using mean rather than median doses	54	3.126 (-0.10, 13.41)	0.076	0.151
With stratification by time since start of radiation work	53	3.836 (-0.22, 17.65)	0.087	0.173
With stratification by duration of radiation work (<10,10+ years)	53	1.862 (-0.78, 13.03)	0.182	0.364
Including cancers and person years between 85 and 100 years	54	3.235 (-0.19, 13.89)	0.079	0.158
Without stratification by industrial classification	54	2.138 (-0.53, 11.07)	0.141	0.283
Using only cancer registration data	50	5.041 (0.22, 19.92)	0.049	0.098

Table D12 Excess relative risk (ERR) cancer mortality estimates for various lag periods

			p-value	
Lag (years)	Deaths	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Leukaemia excluding CLL				
2	198	1.712 (0.06, 4.29)	0.042	0.084
5	188	1.554 (-0.14, 4.28)	0.07	0.141
10	164	1.541 (-0.28, 4.61)	0.094	0.188
15	132	2.553 (0.25, 6.55)	0.029	0.057
20	108	3.313 (0.21, 8.85)	0.042	0.083
All malignant neoplasms excluding leukaemia				
2	8316	0.138 (-0.09, 0.39)	0.164	0.327
5	8101	0.146 (-0.09, 0.41)	0.158	0.315
10	7455	0.275 (0.02, 0.56)	0.04	0.08
15	6602	0.275 (-0.01, 0.6)	0.058	0.116
20	5477	0.338 (0.00, 0.73)	0.052	0.105
All malignant neoplasms excluding pleura, lung and leukaemia				
2	5693	0.193 (-0.08, 0.49)	0.123	0.246
5	5530	0.222 (-0.06, 0.54)	0.097	0.195
10	5118	0.323 (0.02, 0.67)	0.04	0.081
15	4545	0.374 (0.03, 0.76)	0.034	0.069
20	3802	0.389 (-0.02, 0.86)	0.058	0.115

Table D13 Excess relative risk (ERR) cancer incidence estimates for various lag periods

			p-value	
Lag (years)	Cases	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Leukaemia excluding CLL				
2	234	1.782 (0.17, 4.36)	0.03	0.06
5	218	1.492 (-0.07, 4.03)	0.06	0.12
10	191	1.609 (-0.11, 4.53)	0.066	0.132
15	156	2.072 (0.16, 5.42)	0.033	0.065
20	121	3.252 (0.26, 8.43)	0.032	0.064
All malignant neoplasms excluding leukaemia				
2	12199	0.222 (0.02, 0.45)	0.037	0.074
5	11842	0.177 (-0.03, 0.4)	0.081	0.162
10	10855	0.266 (0.04, 0.51)	0.025	0.05
15	9550	0.234 (-0.02, 0.51)	0.063	0.127
20	7824	0.328 (0.02, 0.67)	0.039	0.079
All malignant neoplasms excluding pleura, lung and leukaemia				
2	9471	0.265 (0.03, 0.52)	0.029	0.058
5	9174	0.218 (-0.02, 0.47)	0.063	0.126
10	8443	0.305 (0.05, 0.58)	0.022	0.045
15	7436	0.298 (0.02, 0.61)	0.04	0.08
20	6119	0.408 (0.06, 0.8)	0.025	0.049

Table D14 Excess relative risk (ERR) cancer mortality estimates split by attained age

Attained age (years)	Deaths	ERR Sv^{-1} (90%CI)		p-value 1-Sided	p-value 2-Sided
Leukaemia excluding CLL					
<60	91	0.143 (<-1.99, 6.59)		0.457	0.914
60 – 70	56	-0.204 (-1.48, 3.46)		0.529	0.941
>70	51	4.617 (1.26, 11.24)		0.005	0.01
χ^2 for heterogeneity in ERR across attained age groups			4.53		
All malignant neoplasms excluding leukaemia					
<60	1748	0.055 (-0.66, 0.98)		0.456	0.911
60 – 70	2538	0.273 (-0.15, 0.78)		0.153	0.307
>70	3169	0.317 (-0.02, 0.7)		0.059	0.119
χ^2 for heterogeneity in ERR across attained age groups			1.26		
All malignant neoplasms excluding pleura, lung and leukaemia					
<60	1276	0.461 (-0.40, 1.6)		0.207	0.415
60 – 70	1647	0.575 (0.03, 1.24)		0.04	0.079
>70	2195	0.143 (-0.22, 0.57)		0.267	0.535
χ^2 for heterogeneity in ERR across attained age groups			0.42		

Table D15 Excess relative risk (ERR) cancer incidence estimates split by attained age

			p-value	
Attained age (years)	Cases	ERR Sv^{-1} (90%CI)	1-Sided	2-Sided
Leukaemia excluding CLL				
<60	122	1.714 (<-1.99, 9.13)	0.299	0.598
60 – 70	61	0.044 (-1.10, 3.17)	0.452	0.904
>70	51	3.866 (0.93, 9.66)	0.012	0.024
χ^2 for heterogeneity in ERR across attained age groups		3.09		
All malignant neoplasms excluding leukaemia				
<60	3207	0.259 (-0.31, 0.95)	0.241	0.482
60 – 70	3792	0.191 (-0.15, 0.59)	0.189	0.378
>70	3856	0.315 (0.01, 0.67)	0.047	0.094
χ^2 for heterogeneity in ERR across attained age groups		0.63		
All malignant neoplasms excluding pleura, lung and leukaemia				
<60	2641	0.25 (-0.35, 0.99)	0.26	0.521
60 – 70	2868	0.409 (-0.01, 0.9)	0.053	0.107
>70	2934	0.229 (-0.10, 0.62)	0.133	0.266
χ^2 for heterogeneity in ERR across attained age groups		0.92		

Table D16 Estimates of β_S (and 90%CI) based on fits of BEIR VII-type models to nested case-control data [a]

	Fits to NRRW data			*BEIR VII values, based on Japanese A-bomb survivors*	
Disease Group	Both sexes together	Males	Females	*Males*	*Females*
Mortality					
Leukaemia excluding CLL [b]	1.66	1.60	15.80	*1.1*	*1.2*
	(-0.19, 4.66)	(-0.22, 4.57)	(n/a, 157.5)	*(0.1, 2.6)*	*(0.1, 2.9)*
All malignant neoplasms	0.17	0.15	4.68	*0.23*	*0.47*
excluding leukaemia [c]	(-0.07, 0.44)	(-0.09, 0.42)	(-0.02, 12.1)	*(0.15, 0.36)*	*(0.34, 0.65)*
All malignant neoplasms	0.20	0.18	3.92		
excluding leukaemia, lung and pleura cancer [d]	(-0.08, 0.52)	(-0.10, 0.50)	(-0.59, 11.72)		
Incidence					
Leukaemia excluding CLL [b]	1.29	1.38	-3.25	*1.1*	*1.2*
	(-0.34, 3.93)	(-0.28, 4.10)	(n/a, -1.508)	*(0.1, 2.6)*	*(0.1, 2.9)*
All malignant neoplasms	0.21	0.19	2.96	*0.33*	*0.57*
excluding leukaemia [d]	(-0.02, 0.46)	(-0.04, 0.44)	(-0.28, 7.54)	*(0.24, 0.47)*	*(0.44, 0.74)*
All malignant neoplasms	0.22	0.21	2.33		
excluding leukaemia, lung and pleura cancer [d]	(-0.04, 0.51)	(-0.05, 0.49)	(-0.74, 6.83)		

a β_S is defined in the equations in section D16.

b The estimate cited applies to males exposed at ages of 30 years or more, at 15 years following exposure.

c The estimate cited applies to males exposed at ages of 30 years or more, at an attained age of 60 years.

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APPENDIX E Supplemental Tables

TABLE E1 Standardised mortality ratios (SMRs) for all causes by first employer with social class specific rates

Employer/Site	Number of deaths		SMR	95% CI [b]
	Observed	Expected [a]		
AWE	2746	3295.23	83***	80-87
BNFL	9216	10275.69	90***	88-92
Capenhurst	655	784.74	83***	77-90
Chapelcross	534	569.62	94	86-102
Risley	52	71.33	73	54-96
Sellafield	3904	4022.75	97	94-100
Springfields	4071	4827.25	84***	82-87
STFC	373	472.23	79***	71-87
Daresbury	103	136.34	76**	62-92
Rutherford Appleton	270	335.89	80***	71-91
MoD	4790	5862.09	82***	79-84
Navy	1552	1805.12	86***	82-90
Army	252	309.04	82***	72-92
RAF	987	1376.8	72***	67-76
Civilian	1999	2371.13	84***	81-88
MRC Harwell	19	24.77	77	46-120
HPA-RPD	5	9.28	54	17-126
British Energy and Magnox Generation (England & Wales)	2281	3172.33	72***	69-75
Berkeley Centre	167	204.78	82**	70-95
Berkeley power station	281	364.65	77***	68-87
Bradwell	257	388.51	66***	58-75
Dungeness	276	427.51	65***	57-73
Hinkley Point	349	474.76	74***	66-82
Oldbury	184	286.42	64***	55-74
Sizewell	209	333.58	63***	54-72
Trawsfyndd	231	292.67	79***	69-90
Wylfa	165	216.29	76***	65-89
Non-power station staff	162	183.17	88	75-103
GE Healthcare	204	273.71	75***	65-85
PDS	24	43.5	55**	35-82
CEC-Time	5	7.41	67	22-157
Honeywell Control Systems	1	4.82	21	1-116
Picker International	18	31.27	58	34-91
Rolls-Royce Submarines	220	267.85	82**	72-94
British Energy and Magnox Generation (Scotland)	277	323.66	86**	76-96

TABLE E1 Standardised mortality ratios (SMRs) for all causes by first employer with social class specific rates

Employer/Site	Number of deaths		SMR	95% CI [b]
	Observed	Expected [a]		
Hunterston	246	292.99	84**	74-95
Torness	31	30.67	101	69-143
UKAEA	6575	7838.49	84***	82-86
Dounreay	1494	1379.07	108**	103-114
Harwell-Culham etc	3774	4850.09	78***	75-80
Risley	643	750.74	86***	79-93
Winfrith	664	858.6	77***	72-83

Notes

(a) England and Wales rates used.

(b) Confidence interval.

*** p<0.001, ** p<0.05, + 0.05<p<0.1

TABLE E2 Standardised mortality ratios (SMRs) for all malignancies by first employer

Employer/Site	Number of deaths		SMR	95% CI [b]
	Observed	Expected [a]		
AWE	884	1028.51	86***	80-92
BNFL	2651	2945.6	90***	87-93
Capenhurst	212	216.19	98	85-112
Chapelcross	144	168.64	85	72-101
Risley	18	32.74	55**	33-87
Sellafield	1130	1200.82	94	89-100
Springfields	1147	1327.21	86***	81-92
STFC	118	151.45	78**	64-93
Daresbury	34	42.65	80	55-111
Rutherford Appleton	84	108.8	77	62-96
MoD	1547	1829.45	85***	80-89
Navy	485	537.77	90	82-99
Army	75	98.17	76	60-96
RAF	314	419.36	75***	67-84
Civilian	673	774.15	87***	80-94
MRC Harwell	8	9.82	82	35-161
HPA-RPD	3	4.43	68	14-198
British Energy and Magnox Generation (England & Wales)	747	919.21	81***	76-87
Berkeley Centre	55	69.94	79	59-102
Berkeley power station	84	102.04	82	66-102
Bradwell	77	105.2	73**	58-91
Dungeness	104	119.18	87	71-106
Hinkley Point	129	135.95	95	79-113
Oldbury	61	78.75	77	59-99
Sizewell	67	92.7	72**	56-92
Trawsfyndd	68	81.63	83	65-106
Wylfa	50	61.88	81	60-107
Non-power station staff	52	71.95	72	54-95
GE Healthcare	65	103.63	63***	48-80
PDS	11	11.66	94	47-169
CEC-Time	1	1.93	52	1-288
Honeywell Control Systems	1	1.38	72	2-404
Picker International	9	8.35	108	49-205
Rolls-Royce Submarines	79	94.61	84	66-104
British Energy and Magnox Generation (Scotland)	92	98.32	94	75-115
Hunterston	82	83.26	98	78-122
Torness	10	15.06	66	32-122
UKAEA	1901	2469.65	77***	74-81
Dounreay	404	419.23	96	87-106

TABLE E2 Standardised mortality ratios (SMRs) for all malignancies by first employer

Employer/Site	Number of deaths		SMR	95% CI [b]
	Observed	Expected [a]		
Harwell-Culham etc	1108	1519.25	73***	69-77
Risley	184	266.52	69***	59-80
Winfrith	205	264.65	77***	67-89

Notes

(a) England and Wales rates used.

(b) Confidence interval.

*** p<0.001, ** p<0.05, + 0.05<p<0.1

TABLE E3 Standardised mortality ratios (SMRs) for all malignancies by first employer with social class specific rates

Employer/Site	Number of deaths		SMR	95% CI [b]
	Observed	Expected [a]		
AWE	884	1005.54	88***	82-94
BNFL	2651	3105.63	85***	82-89
Capenhurst	212	238.49	89	77-102
Chapelcross	144	178.2	81**	68-95
Risley	18	25.24	71	42-113
Sellafield	1130	1232.64	92**	86-97
Springfields	1147	1431.06	80***	76-85
STFC	118	150	79**	65-94
Daresbury	34	43.15	79	55-110
Rutherford Appleton	84	106.85	79	63-97
MoD	1547	1877.09	82***	78-87
Navy	485	554.56	87**	80-96
Army	75	99.26	76	59-95
RAF	314	446.72	70***	63-79
Civilian	673	776.55	87***	80-94
MRC Harwell	8	8.54	94	40-185
HPA-RPD	3	3.41	88	18-257
British Energy and Magnox Generation (England & Wales)	747	1002.67	75***	69-80
Berkeley Centre	55	66.18	83	63-108
Berkeley power station	84	114.43	73**	59-91
Bradwell	77	118.41	65***	51-81
Dungeness	104	134.95	77**	63-93
Hinkley Point	129	153.46	84	70-100
Oldbury	61	89.95	68**	52-87
Sizewell	67	105.44	64***	49-81
Trawsfyndd	68	91.74	74	58-94
Wylfa	50	69.26	72	54-95
Non-power station staff	52	58.85	88	66-116
GE Healthcare	65	96.49	67***	52-86
PDS	11	14.48	76	38-136
CEC-Time	1	2.33	43	1-239
Honeywell Control Systems	1	1.56	64	2-358
Picker International	9	10.6	85	39-161
Rolls-Royce Submarines	79	91.07	87	69-108
Scottish Nuclear	92	108.01	85	69-104
Hunterston	82	96.45	85	68-106
Torness	10	11.57	86	41-159
UKAEA	1901	2377.42	80***	76-84
Dounreay	404	426.75	95	86-104
Harwell-Culham etc	1108	1452.05	76***	72-81
Risley	184	234.53	78***	68-91

TABLE E3 Standardised mortality ratios (SMRs) for all malignancies by first employer with social class specific rates

	Number of deaths			
Employer/Site	Observed	Expected [a]	SMR	95% CI [b]
Winfrith	205	264.1	78***	67-89

Notes

(a) England and Wales rates used.

(b) Confidence interval.

*** p<0.001, ** p<0.05, + 0.05<p<0.1

TABLE E4 Standardised mortality ratios (SMRs)[a] by broad cause and age at death, including deaths at ages 85 years or more

		Unadjusted		Social class adjusted	
Age group (years)	Observed deaths	SMR	95% CI [b]	SMR	95% CI
All Causes					
<25	189	84	73-97	112	96-129
25-34	583	69	64-75	93	86-101
35-39	460	64	58-70	76	69-84
40-44	762	69	64-74	83	77-89
45-49	1244	72	68-76	81	76-86
50-54	1956	75	72-78	84	77-81
55-64	6401	77	75-79	79	77-81
65-74	9017	84	83-86	85	84-87
75-84	6119	91	88-93	88	86-90
85-100	1402	82	77-86	74	70-78
χ^2 for Trend		*139.78****		*0.01*	
All malignant neoplasms					
<25	11	49	24-87	52	26-92
25-34	102	77	63-94	80	65-97
35-39	122	82	68-98	86	71-103
40-44	202	76	66-87	79	69-91
45-49	373	78	70-86	83	74-91
50-54	657	80	74-86	84	78-91
55-64	2200	79	75-82	78	75-81
65-74	2883	86	83-89	83	80-87
75-84	1557	94	89-99	87	83-92
85-100	250	94	83-106	81	71-92
χ^2 for Trend		*28.73****		*2.97+*	

Notes

(a) Based on the general population of England and Wales.

(b) Confidence interval.

*** p<0.001, ** p<0.001, * p<0.05, + 0.05<p<0.1

APPENDIX F Abbreviations and Acronyms Used

AGIR	HPA's Advisory Group on Ionising Radiation
AWE	Atomic Weapons Establishment
BE	British Energy Generation
BEIR	(US Committee on the) Biological Effects of Ionizing Radiation
BNFL	British Nuclear Fuels plc
CHD	Coronary Heart Disease
CI	Confidence Interval
CLL	Chronic Lymphatic Leukaemia
CSA	Common Services Agency, Northern Ireland
DDREF	Dose and Dose Rate Effectiveness Factor
DRPS	The former Defence Radiological Protection Service
Dstl	Defence Science and Technology Laboratory
DWP	Department of Work and Pensions
ERR	Excess Relative Risk
GRO	General Register Office for England and Wales
GRO(NI)	General Register Office for Northern Ireland
GRO(S)	General Register Office for Scotland
HPA	Health Protection Agency
HPA-RPD	HPA's Radiation Protection Division
HSE	Health and Safety Executive
HWE	Healthy Worker Effect
HWSE	Healthy Worker Survivor Effect

IARC	International Agency for Research on Cancer
ICRP	International Commission on Radiological Protection
ISD	Information and Statistics Division (NHS Scotland)
LSS	Life Span Study (of the atomic bombings of Hiroshima and Nagasaki)
ME	Magnox Electric
MoD	Ministry of Defence
MRC	Medical Research Council
NHS	National Health Service
NHS-IC	NHS Information Centre for Health and Social Care
NHS-MRIS	NHS Medical Research Information Service
NHSCR	National Health Service Central Register
NICEA	Nuclear Industry Combined Epidemiological Analysis
NIN	National Insurance Number
NRPB	National Radiological Protection Board (now HPA-RPD)
NRRW	National Registry for Radiation Workers
ONS	Office for National Statistics
PDS	HPA's Personal Dosimetry Service
SMR	Standardised Mortality Ratio
STFC	Science and Technology Facilities Council
UKAEA	United Kingdom Atomic Energy Authority
UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation