# Mortality and Cancer Incidence 1952–1998 in UK Participants in the UK Atmospheric Nuclear Weapons Tests and Experimental Programmes

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## ABSTRACT

An updated analysis has been conducted of mortality and cancer incidence among men from the United Kingdom who took part in the UK atmospheric nuclear weapon tests and experimental programmes in Australia and the Pacific between 1952 and 1967. Rates of multiple myeloma, leukaemia, other cancers, and non-cancer causes of death were studied, as in previous analyses of these men. Based on a total of 21,357 test participants and 22,333 controls identified from the same Ministry of Defence (MOD) archives, information was obtained on deaths and cancer registrations up to the end of 1998. Compared with national mortality rates, rates of deaths from all causes increased to a similar extent in both test participants and controls with longer follow-up, with Standardised Mortality Ratios (SMRs) of 89 and 88 respectively over the full follow-up period and a relative risk of 1.01 (90% confidence interval (CI) 0.98-1.05). For all cancers, the corresponding SMRs were 93 for test participants and 92 for controls, with a relative risk of 1.01 (90% CI 0.96-1.08) for all cancers. Mortality from multiple myeloma was consistent with national rates both for test participants and controls, and the relative risk of myeloma incidence among test participants relative to controls was 1.14 (90% CI 0.74-1.74) over the full follow up period and 0.79 (90% CI 0.45-1.38) during the extended period of follow up (1991-98). Over the full follow-up period, leukaemia mortality among test participants was consistent with national rates, whilst rates among controls were significantly lower (SMR 68), and there was a suggestion of a raised risk among test participants relative to controls (relative risk 1.45 (0.96-2.17), one-sided p=0.07, two-sided p=0.14); the corresponding relative risk for leukaemia incidence was 1.33 (0.97-1.84), one-sided p=0.07, two-sided p=0.14. After excluding chronic lymphatic leukaemia (CLL), which is not thought to be radiation-inducible, the relative risk of leukaemia mortality increased to 1.83 (1.15-2.93, one-sided p=0.015, two-sided p=0.027), whilst that for incidence was little changed. Among other types of cancer, only for liver cancer incidence was there evidence of differences in rates between participants and controls in

This study was funded by the Ministry of Defence.


Chilton
Didcot
Oxon OX11 0RQ

Approval: January 2003
Publication: February 2003
£22.50
ISBN 0 85951 499 4

both the earlier period of follow-up and in the additional period. Mortality rates among test participants from causes other than cancer were generally similar to those among the controls.

It is concluded that that overall levels of mortality and cancer incidence in UK nuclear weapons test participants have continued to be similar to those in a matched control group, and for overall mortality to be lower than expected from national rates. There was no evidence of an increased risk of multiple myeloma among test participants in recent years. The suggestion in the first analysis of this study of a raised risk of myeloma has not been confirmed in longer periods of follow-up and is likely to have been a chance finding. Analyses of subgroups with greater potential for exposure provided little evidence of increased risks, although the numbers of men involved were smaller and the statistical power was therefore less. In common with earlier analyses, there is some evidence of a raised risk of leukaemia among test participants relative to controls, particularly when focussing on leukaemia other than CLL. This could be a chance finding, in view of low leukaemia rates among the controls and the generally small radiation doses recorded for test participants. However, the possibility that test participation caused a small absolute risk of leukaemia other than CLL among men cannot be ruled out; the evidence for any increased risk appears to have been greatest in the early years after the tests, but a small risk may have persisted in more recent years.

**The following amendments have been made to this report since its first publication (February 2003)**

**March 2004**

| | |
|---|---|
| Page v | Paragraph 1 - wording 'other diseases' amended to specify 'other fatal diseases'. |
| Page 8 | Table 2.2 amended to clarify duration of 1953 Kittens trials. |
| Page 10 | Table 2.4 - clarified wording with regard to 'attendance other than..' for Monte Bello and Maralinga. Note (c) included to cover the 1953 Kittens trials. Note (d) added to define MEP. |
| Page 93 | Table A1 corrected to reflect the final categorisation of the cases identified by the University of Dundee. |
| Pages 94-95 | Table A2 corrected to reflect the final categorisation of the cases identified by the University of Dundee. |
| Page 107 | Appendix C – description of Table C2 corrected to remove the reference to lagging by 10 years. |
| Page 124 | Appendix E table (c) – corrected figures for 'Leukemia: whole follow-up period' and 'Leukemia excluding CLL: whole follow-up period' |

# EXECUTIVE SUMMARY

Two analyses have previously been conducted of mortality and cancer incidence among men who participated in the UK atmospheric nuclear weapon tests and experimental programmes that took place in Australia and the Pacific Ocean between 1952 and 1967. Participants were identified from archives of the Ministry of Defence and a matched control group was selected from the same archives. The rates of mortality and cancer incidence, as determined from death certificates and national records of cancer registration, were compared in the two groups. The numbers of deaths observed were also compared with those that would have been expected if the men had experienced the death rates recorded for all men of the same ages over the same years in England and Wales. In the previous analysis, based on follow up to the end of 1990, it was concluded that participation in the nuclear weapon testing programme had not had a detectable effect on the participants' expectation of life nor on their risk of developing cancer or other fatal diseases. An excess of leukaemia in test participants compared with controls in the period 2-25 years after the tests was thought likely to be a chance finding, although the possibility that test participation may have caused a small risk of developing leukaemia in the early years after the tests could not be completed ruled out.

This report describes an extended follow-up of both test participants and controls, by a further eight years. The study population is essentially the same as that studied previously. It comprises 21,357 test participants and 22,333 controls, of whom 99.9% were traced to 1 January 1999.

Particular emphasis was placed on multiple myeloma in this analysis, because of prior concerns that the incidence of this disease was raised among test participants. An exercise took place in which data on multiple myeloma held by NRPB were compared with data held by researchers at the University of Dundee. This exercise detected no extra death certificates or cancer registrations for multiple myeloma during the period for which follow-up data are largely complete, among test participants previously identified from MOD archives. The few extra individuals identified as falling within the study definition were in line with earlier estimates of the coverage of test participants. Some cases reported in the intercomparison were based on information other than death certificates or cancer registrations, and – in part – reflected conditions other than myeloma itself. In order to allow data for test participants to be compared with data collected in a similar manner for controls, it was not possible to include these additional cases in the current analysis, although a wider definition of multiple myeloma was considered.

Scientists at the Leukaemia Research Fund were asked to undertake an independent validation of diagnoses of haematological neoplasms among test participants and controls, including cases of multiple myeloma, using an independent register dedicated to haematological neoplasms that covers three regions in northern England and four in southern England. No new haematological neoplasms were identified in a sample of test participants or controls residents in these areas during the period of operation of the register. There were a few small differences in the diagnoses recorded, which would have had little effect on the analyses described below.

Among both test participants and controls, the total number of deaths has approximately doubled since the last analysis, to approximately 5,000 in both groups. Compared with national mortality rates, rates of deaths from all causes among test participants were still lower than national rates and similar to those in the controls, with Standardised Mortality Ratios (SMRs) of 89 and 88 respectively over the full follow-up period and a relative risk (RR) of 1.01 (90% confidence interval (CI) 0.98-1.05). For all cancers, the corresponding SMRs were 93 for test participants and 92 for controls, with a relative risk of 1.01 (90% CI 0.96-1.08) for all cancers. As with mortality, the incidence of all cancers combined was similar among test participants and controls (RR 0.99, 90% CI 0.94-1.03). Similar results arose after excluding the first ten years following initial test participation. Mortality both from all causes and all cancers among both test participants and controls was closer to national rates during the most recent eight years of follow-up than in the period of the previous analysis, possibly reflecting a "wearing off" of the healthy worker effect at long periods from employment in the services. During these additional eight years, mortality from all causes combined was similar in test participants and controls (RR 1.03, 90% CI 0.98-1.08). For all cancers combined during the same period, the relative risk of mortality among test participants compared with controls was 1.07 (90% CI 0.98-1.17, one-sided p=0.09, two-sided p=0.18), whilst the corresponding relative risk based on cancer incidence data was 1.01 (90% CI 0.95-1.07, one-sided p=0.44, two-sided p=0.9).

Over the period to the end of 1998, there were 22 deaths with multiple myeloma as underlying cause among test participants and 18 among controls. Mortality rates in both groups were consistent with national rates (SMRs of 96 and 73 respectively), and the relative risk among test participants relative to controls was 1.43 (90% CI 0.81-2.54). During the most recent eight years of follow-up, there were 13 multiple myeloma deaths among participants and 12 among controls, corresponding to SMRs of 114 and 98 respectively and a relative risk of 1.21 (90% CI 0.58-2.53). Data on the incidence of multiple myeloma, based on cancer registrations or mention of the disease as either underlying or contributory cause on death certificates, showed 35 cases among test participants and 35 cases among controls over the full follow-up period, with a RR of 1.14 (90% CI 0.74-1.74). During the period post-1990, there were 18

myeloma cases among participants and 25 cases among controls, with a RR of 0.79 (90% CI 0.45-1.38). Whilst cancer registrations are likely to be incomplete for the last few years of follow-up, this is unlikely to have led to bias because the same follow-up procedures were used for test participants and controls. The findings from the mortality and incidence analyses were similar when the first ten years after test involvement were omitted, and when a somewhat wider definition of multiple myeloma was considered that included some related diseases.

Over the full follow-up period, rates of leukaemia mortality among test participants were consistent with national rates, whilst those among controls were significantly lower (SMRs of 98 and 68 respectively), and there was some suggestion of a raised risk among test participants relative to controls (RR 1.45, 90% CI 0.96-2.17, one-sided p=0.07, two-sided p=0.14). A similar RR arose in the corresponding data for leukaemia incidence. After excluding chronic lymphatic leukaemia (CLL), which is not thought to be radiation-inducible, the RR of mortality increased to 1.83 (90% CI 1.15-2.93, one-sided p=0.015, two-sided p=0.027), whilst the RR in the incidence data was little changed. It had previously been reported that the relative risk of leukaemia was increased during the period 2-25 years after first test participation (eg. RR of 3.38, 90% CI 1.45-8.25, based on mortality from leukaemia of all types). Over the most recent eight years of follow-up, the relative risk of mortality from leukaemia of all types appeared to be lower than in earlier periods (RR 1.12, 90% CI 0.59-2.13). However, there was less evidence from the incidence data and from analyses of leukaemia excluding CLL that the RR had decreased over recent years (eg. RR 1.81, 90% CI 0.80-4.18, for mortality from leukaemia excluding CLL during 1991-98, corresponding to SMRs of 102 in test participants and 59 in controls).

Mortality for specific cancer types other than multiple myeloma and leukaemia among both test participants and controls was usually less than expected from national rates, sometimes to a statistically significant extent. Based on analyses for over 20 different types of cancer, there were significant differences between the test participants and controls only for bladder cancer (increased among participants) based on mortality data, and for liver and prostate cancer (both increased among participants) plus kidney cancer (increased among controls) based on incidence data. Amongst these findings, only for liver cancer incidence was there evidence of differences in rates between participants and controls in both the earlier period of follow-up and in the additional period. However, the interpretation of these results is complicated, since chance findings would be expected when many different cancer types are studied. Results for a grouping of cancers related to smoking were fairly similar to those for all cancers combined, suggesting that smoking habits have not biased the comparisons of participants and controls. Among men monitored for radiation exposure or who had potential for exposure, risks of cancers other than leukaemia and multiple

myeloma were generally not raised. Mortality rates among test participants from causes other than cancer were generally similar to those among the controls.

It is concluded from this third analysis that overall levels of mortality and cancer incidence in UK nuclear weapons test participants have continued to be similar to those in a matched control group. Furthermore, overall levels of mortality in both test participants and controls continue to be lower than expected from national rates, although this difference has become smaller with longer follow-up. There was no evidence of an increased risk of multiple myeloma among test participants in recent years: rates of this disease were similar in test participants and controls, and mortality among participants was consistent with national rates. In view of the equivocal nature of the evidence linking multiple myeloma with radiation exposure, it is concluded – in line with the second analysis – that the possible risk of myeloma among test participants identified in the first analysis is likely to have been a chance finding. Analyses of subgroups with greater potential for exposure provided little evidence of increased risks, although the numbers of men involved were smaller and the statistical power was therefore less.

In common with earlier analyses, there is some evidence of a raised risk of leukaemia among test participants relative to controls, particularly when focussing on leukaemia other than CLL, although the relative difference in rates between the two groups appears to have narrowed with increasing follow-up. This difference might represent a chance finding, given that mortality in controls was low relative to national rates and that recorded radiation doses to test participants were generally small, if not zero. However, the possibility that test participation caused a small absolute risk of leukaemia other than CLL cannot be ruled out; the evidence for any increased risk appears to have been greatest in the early years after the tests, but a small risk may have persisted in more recent years.

# CONTENTS

# 1 INTRODUCTION

Between 1952 and 1958, the UK Ministry of Supply conducted a series of 21 atmospheric nuclear weapon tests in Australia and at islands in the Pacific Ocean. Experiments related to the nuclear weapon tests programme in which radioactive materials were dispersed into the environment were carried out at Maralinga in Southern Australia between 1953 and 1963; survey and clean-up operations continued until 1967, when the sites were returned to Australian control. UK personnel also participated in US nuclear weapon tests based at Christmas Island in 1962, finally vacating the island in 1964.

Media interest in the early 1980s highlighted concern among veterans' organisations that participants in the UK nuclear weapon tests and experimental programmes may have suffered ill-health because of their involvement. Knox *et al* (1983a,b) reported numbers of cancer deaths in a group of self-identified participants in the nuclear test programme. However, at that time, it was unclear how many deaths would have been expected in these men. In response to these concerns, the Ministry of Defence (MOD) commissioned the National Radiological Protection Board (NRPB) in 1983 to study the health of the participants. Two analyses of mortality and cancer incidence have been undertaken by NRPB, in conjunction with the Imperial Cancer Research Fund. These analyses were based on data for over 20,000 men who were identified from MOD archives as having participated in the test programme, and for a similar-sized control group selected from the same archives. Both the first analysis (Darby *et al*, 1988a,b), based on follow-up to the end of 1983, and the second analysis (Darby *et al*, 1993a,b), based on follow-up to the end of 1990, suggested that test participation had not had a detectable effect on life expectancy or on the total risk of cancer. The first analysis also found that for leukaemia and multiple myeloma both the mortality rate and the rate of incident cancers were higher among the test participants than among the controls (Darby *et al*, 1988a, 1988b). However, this suggestion of small hazards of leukaemia and multiple myeloma was not supported by data from the longer follow-up. It was concluded in the second analysis that the earlier excesses of these diseases appeared to have been chance findings, although the possibility that test participation may have caused a small risk of leukaemia in the early years after the tests could not be completely ruled out (Darby *et al*, 1993a, 1993b).

During the last few years, there have been reports of raised numbers of multiple myeloma among test participants, based on records for just over 2,000 British servicemen in the British Nuclear Tests Veterans Association (BNTVA) (Rabbitt Roff, 1999a,b). In order to make a comparison between myeloma rates among the test participants and the controls, and between these groups and national rates, MOD commissioned NRPB in 1999 to conduct a new analysis. An Advisory Group, set up for this study under the Chairmanship of Professor N Wald, with

members listed in Appendix F, recommended that this analysis should examine mortality and cancer incidence generally, in line with the previous two analyses, but that special attention should be given to multiple myeloma. This report describes the findings from an extended period of follow-up, and from intercomparisons of data on myelomas held by NRPB and by the University of Dundee and the Leukaemia Research Fund (LRF).

# 2 STUDY DESIGN AND DATA COLLECTION

The study design is essentially the same as that used in the second analysis, as described in detail by Darby *et al* (1993b), with the exception that the period of follow-up has been extended. The main features of the study are summarised here.

## 2.1 Test participants

Table 2.1 describes the series of 21 UK atmospheric nuclear weapon tests conducted in Australia and at islands in the Pacific Ocean between 1952 and 1958, while Table 2.2 outlines the experimental programme and clean-up operations conducted at Maralinga in Southern Australia between 1953 and 1967. UK personnel also participated in US nuclear weapon tests based at Christmas Island in 1962. No complete contemporary lists exist of men who took part in these tests. Therefore, in the course of the first analysis (Darby *et al*, 1988b), considerable effort was directed to the construction of a cohort of test participants, based on material stored in MOD archives.

There are 21,357 test participants in the present analysis (see Table 2.3). Most of the participants were in the Armed Forces, but they also included some employees of the Atomic Weapons Establishment (AWE) and a few from the Atomic Energy Research Establishment (AERE) Harwell. The total of 21,357 test participants is one less than in the last analysis because further investigation failed to confirm participation in the tests for a man in the RAF. Another man, who was previously listed as employed by AWE, is now recorded as serving in the RN, as he was found to have participated in the tests whilst he was in the RN prior to joining AWE. The main cohort does not contain 1,503 men who were judged to have no more potential for radiation exposure from the tests than the general public, eg. because they had left test locations before the first detonation. These men were included in the first analysis, but were excluded from the main part of the second analysis. In common with the second analysis, results for this group are reported separately (see Appendix C). Also excluded from the study were the small number of female participants, civilian employees of organisations other than AWE and AERE, and all non-UK nationals, with the exception of men with regular engagements in the UK Services and permanent

employees of AWE or AERE (for ease of reference, the AERE employees are included hereafter in the AWE group). NRPB had previously considered broadening the criteria for inclusion, but this has not been practicable owing a lack of adequate records for other groups of participants (eg. men in the Merchant Navy).

## 2.2 Controls

Participants in the nuclear weapons test programme would have differed in some ways from men of the same age in the general UK population. For example, test participants needed to have been fit enough to be selected for overseas service, and they would have experienced a different lifestyle during their period in a tropical or desert environment. Consequently, rather than solely comparing mortality and cancer rates among test participants with the corresponding national rates, use was made of a control group constructed from MOD archives (Table 2.3). This control group contained roughly the same number of men as the participants and, apart from not participating in the tests, the controls were chosen to have similar characteristics to the participants. For test participants in the Services, the controls were selected from Servicemen who served in tropical or sub-tropical areas other than the test locations around the time that the tests were taking place. For AWE test participants, the controls were chosen from other men working for AWE at around the same time as the weapons tests. The 22,333 men in the control group were very similar to the participants with respect to the split between Services, ranks/social class, year of birth, year of enlistment/employment and year of discharge/end of employment.

## 2.3 Follow-up

In common with the previous two analyses, follow-up data on mortality and cancer incidence have been collected. Mortality is of interest because:

a its recording is compulsory, and details are available from national registers;
b mortality rates are commonly used as indicators of the health of communities;
c it would have been impracticable to have contacted all of the participants and their controls directly, and to have obtained information from their GPs and hospital records;
d national registration schemes do not exist for most types of illness.

Furthermore, since cancer is likely to be the major effect of exposure to low dose radiation, and since there exists a national system of cancer registration, mortality data supplemented by cancer registration data should prove the best means of studying this outcome.

More details of the method of follow-up are given in section 3. In brief, the records of test participants and controls were flagged at the National Health Service Central Registers for England, Wales and Scotland, in order that the study investigators could be sent details of deaths and cancer registrations in these men. Corresponding data was also sought from offices in Northern Ireland. Deaths and cancers registered up to the end of 1998 have been included in this analysis.

## 2.4 Extent of radiation exposure in test participants

The 21,357 test participants in the present analysis were recorded as having a total of 27,505 test involvements (Table 2.4). This is four more than in the last analysis (Darby *et al*, 1993b). The small change in the number of test involvements arises from improvements in the details of test involvement for a few men. The later operations tended to involve more men than earlier ones (Table 2.4). About three-quarters of test participants were involved in a single operation, but a few men participated in as many as eight operations (Table 2.5).

Most of the information on radiation exposures to test participants comes from AWE Health Physics records of radiation dosemeters (film badges) issued to some of the participants, as described below. The film badges would have detected gamma radiation doses from fallout, but not doses from internal contamination by radioactive materials. Neutron doses were also not recorded on these dosemeters, although MOD made estimates for members of the Buffalo Indoctrinee Force (defined below) – the one group considered by MOD to have potential for neutron doses – on the basis of free-standing neutron dosemeters. MOD has reported that the general policy during the early tests in Australia was to monitor almost all of the participants for radiation exposure. However, by the time of the later Pacific tests, this policy had been reviewed and, if it was judged on the basis of the previous tests that measurable exposure was unlikely to occur, then monitoring was not carried out. Health Physics records were available for 21% of the participants, in most instances indicating a zero dose (Table 2.6). Only 8% of the total cohort had non-zero recorded radiation doses. The distribution of doses in these individuals by Service or employer is shown in Table 2.7.

For the majority of test participants, the information that was available on the duties they performed was limited. However, MOD advised that men whose test involvements fell in any of the following groups were potentially more liable to be exposed to significant doses of radiation:

i Members of the Buffalo Indoctrinee Force, a group of volunteer Army officers assembled to observe at first hand the effects of a nuclear explosion.
ii RAF aircrews involved in sampling the radioactive clouds of the explosions.
iii The RAF active handling flights, who decontaminated aircraft used in cloud sampling.
iv Members of the crew of HMS Diana, who sailed through the fallout plume in Operation Mosaic.
v The Target Response Group at Buffalo (largely Army officers and civilians from the Atomic Weapons Establishment, AWE) who re-entered the area of the explosion, in some cases shortly after the detonation, in order to recover data from experiments designed to determine the effects of the explosion on various kinds of target.

These men, who total 759, comprise Group A in section 6.6 of this report. MOD also advised that undocumented inhalation or ingestion of radionuclides, if any, was most likely to have occurred among test participants employed by AWE or in men directly involved with the programme of minor trials at Maralinga; these men total 1,041, and comprise Group B in section 6.6.

## 2.5 Completeness of cohort of test participants

Since it could not be assumed that all participants had been identified, information was sought from other sources, such as veterans' organisations. By examining the overlap between the men identified from these sources and the men identified from MOD archives, it was possible to estimate that the main cohort of participants studied in the second analysis was 85% complete (Darby *et al*, 1993b). Examination of information on some additional men notified by veterans' organisations since the previous analysis has not changed this estimate of the coverage of test participants (see section 4.2).

The 'independent responders' who were confirmed to have attended the tests have been studied previously as a separate group (Darby *et al*, 1988b, 1993b), and details of cases of multiple myeloma in these men are given in Appendix A. The independent responders could not be included in the study cohort of test participants, because this would have introduced a bias when comparing cancer incidence and cause-specific mortality in test participants with that in controls. In particular, there would not be the same reason for men with cancer to come forward and present themselves in the control group as in the test participant group. Findings for mortality among independent responders identified as of the time of the second analysis are presented in section 6.7.

**TABLE 2.1 UK atmospheric nuclear weapons tests in Australia and the Pacific Ocean, 1952-1958[a]**

| Operation | Round and Name | Location | Date of firing[b] | Yield | Height (m) | Explosion conditions |
|---|---|---|---|---|---|---|
| Hurricane | | Off Trimouille Island, Monte Bello Islands, Western Australia | 3 Oct 1952 | 25 kt | -3 | Ocean surface burst |
| Totem | 1 | Emu Field, South Australia | 14 Oct 1953 | 10 kt | 31 | Tower mounted |
| | 2 | Emu Field, South Australia | 26 Oct 1953 | 8 kt | 31 | Tower mounted |
| Mosaic | 1 | Trimouille Island, Monte Bello Islands, Western Australia | 16 May 1956 | 15 kt | 31 | Tower mounted |
| | 2 | Alpha Island, Monte Bello Islands, Western Australia | 19 Jun 1956 | 60 kt | 31 | Tower mounted |
| Buffalo | 1 | One Tree, Maralinga Range, South Australia | 27 Sep 1956 | 15 kt | 31 | Tower mounted |
| | 2 | Marcoo, Maralinga Range, South Australia | 4 Oct 1956 | 1.5 kt | 0 | Ground surface burst |
| | 3 | Kite, Maralinga Range, South Australia | 11 Oct 1956 | 3 kt | 150 | Air dropped - air burst over land |
| | 4 | Breakaway, Maralinga Range, South Australia | 21 Oct 1956 | 10 kt | 31 | Tower mounted |
| Grapple | 1 Short Granite | Off Malden Island, Pacific Ocean | 15 May 1957 | 0.3 Mt[c] | 2200 | Air dropped - air burst over ocean |
| | 2 Orange Herald | Off Malden Island, Pacific Ocean | 31 May 1957 | 0.72 Mt[c] | 2400 | Air dropped - air burst over ocean |
| | 3 Purple Granite | Off Malden Island, Pacific Ocean | 19 Jun 1957 | 0.2 Mt[c] | 2400 | Air dropped - air burst over ocean |
| Antler | 1 | Tadje, Maralinga Range, South Australia | 14 Sep 1957 | 1 kt | 31 | Tower mounted |
| | 2 | Biak, Maralinga Range, South Australia | 25 Sep 1957 | 6 kt | 31 | Tower mounted |
| | 3 | Taranaki, Maralinga Range, South Australia | 9 Oct 1957 | 25 kt | 300 | Balloon suspended-air burst over land |
| Grapple X | | Off Christmas Island, Pacific Ocean | 8 Nov 1957 | 1.8 Mt[c] | 2200 | Air dropped - air burst over ocean |

| Operation | Round and Name | Location | Date of firing[b] | Yield | Height (m) | Explosion conditions |
|---|---|---|---|---|---|---|
| Grapple Y | | Off Christmas Island, Pacific Ocean | 28 Apr 1958 | 3 Mt[c] | 2500 | Air dropped - air burst over ocean |
| Grapple Z | 1 Pennant | Christmas Island, Pacific Ocean[d] | 22 Aug 1958 | 24 kt[c] | 450 | Balloon suspended - air burst over land |
| | 2 Flagpole | Off Christmas Island, Pacific Ocean | 2 Sep 1958 | 1 Mt[c] | 2800 | Air dropped - air burst over ocean |
| | 3 Halliard | Off Christmas Island, Pacific Ocean | 11 Sep 1958 | 0.8 Mt[c] | 2600 | Air dropped - air burst over ocean |
| | 4 Burgee | Christmas Island, Pacific Ocean[d] | 23 Sep 1958 | 25 kt[c] | 450 | Balloon suspended - air burst over land |

*Notes for Table 2.1*

(a) A series of 25 American tests, part of Operation Dominic, and known as Operation Brigadoon, took place off Christmas island between 25 April and 11 July 1962. UK personnel known to have attended are also included in the present study.

(b) Dates according to Greenwich Mean Time.

(c) MOD's best estimates of the yields of the Christmas and Maiden Island tests made available in October 1993 together with revisions to heights of explosions.

(d) Over the southeast peninsula of the island.

**TABLE 2.2 Maralinga Experimental Programme**

| Operation | Type | Dates |
|---|---|---|
| Kittens | Initiator trials | Sep-Oct 1953[a], Apr-Jun 1955, Mar 1956, Mar-Jul 1957, Apr-May 1959, May 1961 |
| Tims | Timing experiments | Jul 1955, Mar-Jul & Sep-Nov 1957, Apr-Jul & Sep-Nov 1958, May-Nov 1959, Apr-Oct 1960, Aug-Dec 1961, Mar-Apr 1963 |
| Rats | Timing experiments using gamma ray sources | Apr-Jul & Oct-Nov 1958, Mar-Jul 1959, Sep-Nov 1960 |
| Vixen | Effects of fire or uncontrolled explosions | Jun-Aug 1959, May-Oct 1960, Mar-Jun & Sep-Nov 1961, Apr-May 1963 |
| Ayres | Clean-up operation | Feb-Mar 1960, Mar 1963 |
| Hercules | Clean-up operation | Aug-Nov 1964 |
| Brumby | Clean-up operation | Mar-Aug 1967 |

*Note* (a) The first Kittens trials took place at Emu Field.

**TABLE 2.3 Test participants and controls by Service or employer, rank or social class and, for the Services, whether or not on National Service**

| | | Test participants | | | | Controls | | | |
|---|---|---|---|---|---|---|---|---|---|
| Service or Employer | Rank | National service-men | Regular | Total no. | % | National service-men | Regular | Total no. | % |
| RN[a] | Officer | 54 | 434 | 488 | | 22 | 559 | 581 | |
| | Other ranks | 340 | 5,477 | 5,817 | | 261 | 6,502 | 6,763 | |
| | Total | 394 | 5,911 | 6,305 | 29.5 | 283 | 7,061 | 7,344 | 32.9 |
| Army | Officer | 24 | 537 | 561 | | 174 | 488 | 662 | |
| | Other ranks | 1,563 | 3,670 | 5,233 | | 1,727 | 3,093 | 4,820 | |
| | Total | 1,587 | 4,207 | 5,794 | 27.1 | 1,901 | 3,581 | 5,482 | 24.5 |
| RAF | Officer | 17 | 1,594 | 1,611 | | 43 | 1,755 | 1,798 | |
| | Other ranks | 404 | 6,428 | 6,832 | | 765 | 6,139 | 6,904 | |
| | Total | 421 | 8,022 | 8,443 | 39.5 | 808 | 7,894 | 8,702 | 39.0 |
| AWE[b] | Social class 1 | 0 | 380 | 380 | | 0 | 361 | 361 | |
| | Other social classes | 0 | 435 | 435 | | 0 | 444 | 444 | |
| | Total | 0 | 815 | 815 | 3.8 | 0 | 805 | 805 | 3.6 |
| All Services and employers | Total officers/ social class 1 | 95 | 2,945 | 3,040 | 14.2 | 239 | 3,163 | 3,402 | 15.2 |
| | Total other ranks/social classes | 2,307 | 16,010 | 18,317 | 85.8 | 2,753 | 16,178 | 18,931 | 84.8 |
| | Total | 2,402 | 18,955 | 21,357 | 100.0 | 2,992 | 19,341 | 22,333 | 100.0 |

*Notes* (a) RN includes members of the RM, RNVR and NAAFI.

(b) AWE includes a few employees of AERE Harwell.

**TABLE 2.4 Numbers of men involved at each operation by Service or employer**

| | Service or employer | | | | |
|---|---|---|---|---|---|
| Location and operation | RN | Army | RAF | AWE | Total |
| Monte Bello Islands | | | | | |
| Hurricane | 1,076 | 206 | 21 | 95 | 1,398 |
| Mosaic | 1,134 | 72 | 128 | 49 | 1,383 |
| Attendances at Monte Bello, other than at the time of an explosion | 9 | 0 | 0 | 0 | 9 |
| Total Monte Bello | 2,219 | 278 | 149 | 144 | 2,790 |
| Emu Field | | | | | |
| Totem | 1 | 11 | 9 | 85 | 106 |
| Maralinga Range | | | | | |
| Buffalo | 5 | 194 | 883 | 203 | 1,285 |
| Antler | 60 | 136 | 1,156 | 196 | 1,548 |
| MEP | 3 | 174 | 49 | 329 | 555 |
| Attendances at Maralinga, other than at the time of an explosion unless involved in the MEP | 324 | 630 | 1,554 | 47 | 2,555 |
| Total Maralinga | 392 | 1,134 | 3,642 | 775 | 5,943 |
| Christmas Island | | | | | |
| Grapple | 1,722 | 638 | 1,038 | 117 | 3,515 |
| Grapple X | 597 | 625 | 1,011 | 107 | 2,340 |
| Grapple Y | 851 | 1,331 | 1,427 | 114 | 3,723 |
| Grapple Z | 738 | 1,438 | 2,016 | 182 | 4,374 |
| Brigadoon | 63 | 228 | 395 | 43 | 729 |
| Attendances at Christmas Island, other than at the time of an explosion | 636 | 1,779 | 1,533 | 37 | 3,985 |
| Total Christmas Island | 4,607 | 6,039 | 7,420 | 600 | 18,666 |
| Total involvements | 7,219 | 7,462 | 11,220 | 1,604 | 27,505 |

*Notes*

(a) Visits to RAAF Edinburgh field in connection with Operation Buffalo or Antler and visits to RAAF Pearce in connection with Mosaic are included under the appropriate operation.

(b) Other involvements at Edinburgh Field are included under other attendances at Maralinga.

(c) The small number of individuals involved in the first Kittens trials at Emu Field in 1953 have been included under Totem.

(d) MEP is the Maralinga Experimental Programme

**TABLE 2.5 Numbers of operations attended by each man, by Service or employer**

| | Service or employer | | | | |
|---|---|---|---|---|---|
| No. of Operations | RN | Army | RAF | AWE | Total |
| 1 | 5,506 | 4,255 | 6,298 | 430 | 16,489 |
| 2 | 688 | 1,426 | 1,665 | 171 | 3,950 |
| 3 | 107 | 100 | 355 | 106 | 668 |
| 4 | 4 | 11 | 106 | 59 | 180 |
| 5 | 0 | 1 | 12 | 28 | 41 |
| 6 | 0 | 1 | 6 | 13 | 20 |
| 7 | 0 | 0 | 1 | 4 | 5 |
| 8 | 0 | 0 | 0 | 4 | 4 |
| Total number of test participants | 6,305 | 5,794 | 8,443 | 815 | 21,357 |
| Mean number of visits | 1.1 | 1.3 | 1.3 | 2.0 | 1.3 |

**TABLE 2.6 Numbers of men mentioned in Health Physics (HP) records, with and without recorded doses as a percentage of all participants at each operation**

| | Number of men | | | | |
|---|---|---|---|---|---|
| Location and operation | Number of test participants | Number mentioned in HP | Mentioned in HP with zero dose | Mentioned in HP with non-zero dose | Collective dose (man mSv) |
| Hurricane | 1,398 | 1,340 (96%) | 1,134 | 206 | 2,470 |
| Mosaic | 1,383 | 599 (43%) | 404 | 195 | 1,274 |
| Monte Bello | 9 | 0 (0%) | 0 | 0 | 0 |
| Totem | 106 | 78 (74%) | 19 | 59 | 1,209 |
| Buffalo | 1,285 | 786 (61%) | 404 | 382 | 2,156 |
| Antler | 1,548 | 737 (48%) | 418 | 319 | 1,874 |
| MEP | 555 | 510 (92%) | 314 | 196 | 775 |
| Other attendances at Maralinga | 2,555 | 253 (10%) | 228 | 25 | 111 |
| Grapple | 3,515 | 83 (2%) | 4 | 79 | 1,018 |
| Grapple X | 2,340 | 179 (8%) | 53 | 126 | 1,081 |
| Grapple Y | 3,723 | 114 (3%) | 18 | 96 | 981 |
| Grapple Z | 4,374 | 618 (14%) | 395 | 223 | 3,814 |
| Brigadoon | 729 | 379 (52%) | 29 | 350 | 231 |
| Other attendances at Christmas Island | 3,985 | 11 (0%) | 3 | 8 | 1 |
| Total | 27,505 | 5,687 (21%) | 3,423 | 2,264 | 16,995 |

**TABLE 2.7 Numbers of men and collective dose in different dose categories by Service or employer**

| | Service or employer | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | RN | | Army | | RAF | | AWE | | Total | |
| Dose category (mSv) | No | Collective Dose[a] | No | Collective Dose[a] | No | Collective Dose[a] | No | Collective Dose[a] | No | Collective Dose[a] |
| 0.01- 0.99 | 113 | 43 | 267 | 129 | 349 | 161 | 159 | 76 | 888 | 410 |
| 1.00- 4.99 | 48 | 130 | 78 | 193 | 109 | 219 | 110 | 260 | 345 | 802 |
| 5.00- 9.99 | 25 | 184 | 50 | 304 | 33 | 233 | 52 | 372 | 160 | 1,094 |
| 10.00-49.99 | 36 | 668 | 49 | 1,296 | 69 | 1,590 | 88 | 1,970 | 242 | 5,523 |
| 50.00-99.99 | 0 | 0 | 4 | 275 | 32 | 2,349 | 8 | 627 | 44 | 3,251 |
| >100.00 | 0 | 0 | 0 | 0 | 34 | 5,363 | 3 | 553 | 37 | 5,915 |
| Total | 222 | 1,026 | 448 | 2,197 | 626 | 9,915 | 420 | 3,858 | 1,716 | 16,995 |

*Note* (a) Sum of doses among men in each group, in units of man mSv.

# 3 METHOD OF FOLLOW-UP

## 3.1 Determination of deaths and emigrations

Work was undertaken to determine the vital status of all test participants and controls on 1 January 1999, 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 are flagged at the National Health Service Central Registers (NHSCRs) for England and Wales (at the Office for National Statistics, ONS, in Southport) and for Scotland (at the General Register Office for Scotland, GRO(S), in Edinburgh), and at the regional registry (Central Services Agency, CSA, Belfast) in Northern Ireland. Each of these offices routinely sends details of deaths and emigrations among study members. 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 ninth revision of the International Classification of Diseases (ICD-9).

For men who could not be traced on the NHSCRs, the available information was reviewed both at NRPB and by the Service Record Offices. Only 13 study members (8 participants and 5 controls) remained in service at the end of follow-up period compared with 305 for the last analysis. Attempts were made to find the remaining men, with the help of the Health Departments in Belfast, the Isle of Man, Jersey, or Guernsey, as appropriate. The General Register Office of Ireland was approached for death certificates for men reported to have died in

Ireland. MOD Medical Statistics provided cause of death information on men who had died while in service.

The Department of Social Security (DSS) was also used as an extra source of information for individuals when tracing or flagging at the NHSCRs appeared uncertain. In the first and second analyses, it had been possible to obtain emigration data from DSS but this service was not available for the current analysis. In the second analysis it had also been possible to have a computerised check of vital status for all men who had not died or emigrated. As this service was also not available from DSS for the current analysis, particular groups of interest were submitted to DSS for manual checking (see Section 4.2).

## 3.2 Determination of cancer incidence

Information on deaths from cancer was supplemented by other information indicating that a man had developed cancer. This supplementary information was derived from death certificates where cancer was listed as a contributory cause, or from cancer registrations. Cancer registration data are collected in regional cancer registries covering England, Wales and Scotland. Since 1971 these data have been passed on to the NHSCRs. Cancer registrations supplied to the study team were coded to ICD-9, excepting 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 Northern Ireland Cancer Registry provided cancer registration information for members who had died and were registered with cancer in Northern Ireland.

The analysis of cancer incidence was based on the earliest cancer mentioned in any of the above sources, with the following exceptions:

- leukaemia, 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.

This approach differs slightly from that used in the previous two analyses. First, it places more emphasis on myeloma, in view of the interest in this disease in the current analysis. Secondly, information from cancer registrations – where available – tends to be given more weight than death certificates. In the first

and second analyses, men whose underlying cause of death was not cancer had been included in the incidence analyses if cancer was listed as contributory cause of death. In particular, two participants were included in the myeloma incidence analysis in Darby *et al* (1993b) on this basis. However, for men with cancer listed as both underlying and contributory cause of death, the procedure adopted previously was to select the underlying cause for the incidence analyses. The only exception to this approach was taken for men with leukaemia as contributory cause of death, in which case leukaemia was selected for the incidence analyses, even if the underlying cause was another type of cancer. However, this approach was not applied to other haematopoetic neoplasms. In particular, one participant with myeloma as contributory cause of death and another cancer as underlying cause was not included in the previous analysis of myeloma incidence (Darby *et al*, 1993b). Consequently, as indicated above, cases of myeloma and lymphoma recorded as contributory cause of death have been included in the analyses of the incidence of these diseases reported here, even when the underlying cause was another type of cancer.

The second analysis included both deaths and cancers registered up to the end of 1990 that had been received by NRPB by the time of the analysis. However, as stated by Darby *et al* (1993), registrations were not complete as of that time, and NRPB has since received details of two additional myelomas registered among participants before 1991. The current analysis includes all cancers registered during the period of the mortality follow-up (ie. up to 1/1/1999) and which had been received from the NHSCRs by the time of the analysis.

# 4 VALIDATION

## 4.1 Introduction

For the first and second analyses, members of the study team carried out a large number of checks to ensure that the data on test participation supplied by MOD for use in the study were as complete and accurate as the available sources of information would allow (Darby *et al*, 1988b, 1993b). Since the cohort for the third analysis is essentially the same as that for the second analysis, no new systematic checks of this type were made for this analysis, although details for a few men have been improved (see Section 2).

## 4.2 Completeness of coverage of test participants

In the first two analyses, the completeness of coverage of test participants was estimated by comparing the list of test participants in the main study, which was compiled from MOD archival material, with lists of test participants compiled by other organisations independently of MOD material (Darby *et al*, 1993b). For

this analysis, these organisations were not approached for new lists of participants. However, some men have been added to the list of independent responders, based on data supplied by the British Nuclear Tests Veterans Association (BNTVA) and Royal British Legion, and subsequently checks at the SROs to confirm test participation. These independent respondent details were provided in response to approaches made during the second analysis but were received too late to be included in that analysis. The list of participants supplied by the University of Dundee for the multiple myeloma intercomparison exercise (see section 4.5) has also been included as a source of information independent of MOD.

As a result of these extra data, the number of men not included in the main study has increased by 30 since the last analysis, to 504. The number of independent responders included in the main study is 2,481 compared to 2,335 in the last analysis. After standardising the results for Service or employer to the proportions seen in the main study, the coverage of test participants by the main study was estimated to be 85%, the same proportion as estimated in the last analysis (Darby *et al*, 1993a,b).

## 4.3 Completeness of ascertainment of deaths and emigrations

National statistics on deaths up to and including 1998 have been published (eg. ONS, 1999), based on data collated by the NHSCRs. Whilst this information is thought to be largely complete, it is useful to check information on deaths and emigrations provided by these Registers for men in this study. Consequently, requests were made to the NHSCRs for England and Wales, and Scotland, for listings - in electronic format - of the vital and emigration status of all study members flagged on their computerised systems. These listings were cross-checked with data held by the study. CSA Belfast provided a paper listing of all men currently flagged in their system.

In order to obtain or cross-check information on vital status, groups of records were submitted to the Department of Social Security (DSS):

(a) all men reported as untraced by the NHSCRs;

(b) all men traced at the NHSCRs who were not currently registered with an NHS doctor;

(c) all men who were alive according to the NHSCRs and aged over 75 at the end of follow-up;

(d) all men who had emigrated according to the NHSCRs, DSS or MOD and who were not reported to have died;

(e) a 1% sample of all other men not covered under a) – d) for whom the NHSCRs had not reported a death.

The checks at DSS for men in categories (a) to (d) found 87 cases where death details were missing from study records – these were subsequently obtained for the study. The 1% cross-check at DSS did not suggest that death data were missing from study records in general because of the 266 men submitted for the check, 262 were returned as alive, 2 as dead but with dates of death after the end of follow-up and 2 were untraced.

Members of the study who are AWE employees are also included in studies (Beral *et al*, 1988; Muirhead *et al*, 1999) of nuclear workers. Cross-checks were made of follow-up information held by these studies with that for the current study.

Details of the status of test participants and controls at the end of the follow-up period are given in Table 4.1. Less than 0.1% of test participants and controls were lost to follow-up (i.e. untraced or not currently registered with a doctor at NHSCRs and not traced at DSS). These consisted of: (a) 5 men (3 test participants and 2 controls) untraced at the NHSCRs and DSS; (b) 19 men (10 test participants, 9 controls) not currently registered with a doctor at the NHSCRs and untraced at DSS; and (c) 3 men for whom notification of death had been received but without a date of death.

In the eight years of additional follow-up available compared with the previous analysis, the number of deaths among test participants and controls increased by about 2150 and 2250 respectively. In the analysis, the NHSCRs, DSS and MOD provided the source of information on cause of death for 4818, 63 and 21 test participants respectively, and for 5118, 72 and 27 controls respectively. Most of the men for whom MOD provided cause-of-death details had already been identified as having died, based on information from DSS or the NHSCRs. Men whose death details were obtained from DSS were mainly untraced or not currently registered with a doctor at the NHSCRs.

The number of new emigrations during the eight additional years of follow-up was 132 among test participants and 125 among controls. Whilst it was not be feasible to ascertain deaths and cancers among these men after they had emigrated, they have been included in the study up to the time of emigration (see section 5). Furthermore, the proportion of men who emigrated over the whole period of the study is similar for test participants and controls (8.8% and 7.8% respectively), so indicating that comparisons of disease rates in the two groups should not be biased.

## 4.4 Completeness of ascertainment of cancer incidence

In addition to the routinely supplied information, the NHSCRs were asked to provide electronic listings, giving details of whether a study member had been registered with cancer or not. These were cross-checked with data held by the study.

At the time of the previous analysis it was reported that, over the period for which cancer follow-up was thought to be complete (to end of 1987), cancer registrations had not been received for 144 men for whom there was a mention of cancer on the death certificate (Darby *et al*, 1993b). However, it may be noted that the national system for cancer registrations was poorly developed prior to 1971 and is still incomplete for non-melatomatous cancers of the skin. At the time that the follow-up was being conducted, cancer registration data were thought to be largely complete up to 1994 (Quinn, 2000; ONS, 2000); this period has subsequently been extended (M Quinn, ONS, personal communication, 2001). When the study databases were examined over the period up to 1995 inclusive, there were 230 new cases where men had died in England, Wales or Scotland with a mention of cancer on the death certificate but for whom no cancer registration had been received. There appeared to be particular shortfalls in cancer registration in the years 1988-1990 and 1994 and 1995. Investigations at the NHSCRs resolved all but 48 of the missing cancer registrations. Some of the cancer deaths without cancer registrations could be explained by issues relating to implementation of the computerised system (CHRIS) at ONS in April 1991. In particular, some study members who died around the time of computerisation were not flagged for this study on CHRIS and so it had not been possible to receive cancer registrations for these men. As a result of these investigations, ONS flagged a further 62 records for men who died between 1$^{st}$ July 1990 and 31$^{st}$ March 1991 and six additional cancer registrations were received as a result of this flagging exercise.

There are variations in the completeness of cancer registration data supplied by regional cancer registries to the NHSCRs (Quinn, 2000). This raises the potential for bias in the reporting of cancers between participants and controls if the cohorts are differently distributed between cancer registry regions. Consequently, the geographical distribution of participants and controls was studied by examining, for study members registered in England and Wales, the local health authority (LHA) at which study members were last registered (obtained from electronic listings supplied by the NHSCRs). LHA areas were converted to areas covered by cancer registries using data supplied by the East Anglian Cancer Registry.

The distribution of participants and controls in cancer registry regions in England and Wales, or their location in other regions of the UK, is shown in Table 4.2.

For about 20% of controls and test participants it was not possible to specify the region of the UK in which they were located. This was because they were no longer on the NHSCR computerised listing, having died prior to computerisation in 1991, or because NHSCR Southport had no information on the health authority for the men. Furthermore, men flagged at NHSCR Scotland have not been further categorised by Scottish regional cancer registry regions. However, there does appear to be a generally similar distribution of test participants and controls between cancer registry regions, suggesting that the potential for bias from variations in completeness of cancer data at cancer registries is low.

Information on the completeness and accuracy of cancer registration data, specifically for multiple myeloma and haematological neoplasms, was also available from the results of the comparisons with data held by University of Dundee and the Leukaemia Research Fund (LRF) (Sections 4.5 and 4.6). The LRF has a database of haematological registrations registered in certain regions of Great Britain. The cancer registrations on the LRF database are independently assessed for diagnosis and presented an opportunity to check a subset of the registrations held on the study database. Further details are given below.

## 4.5 Comparison of multiple myeloma data held by NRPB and the University of Dundee

Appendix A gives a detailed description of a comparison performed of data on multiple myeloma held by NRPB and the University of Dundee. There were a total of 73 cases in the intercomparison. Of these, 28 were known to both NRPB and Dundee, 15 were known to NRPB but were not on the Dundee list, and 30 were on the Dundee list but not on the NRPB list. A summary of these cases is given in the Annex to this report.

The data collected by Dundee allowed two important questions to be answered:

1. Had alternative methods of follow-up brought to light death certificates or cancer registrations for men included in the NRPB study where the methods of follow-up described in sections 3, 4.3 and 4.4 had failed?

- No. The intercomparison did not reveal additional death certificates or cancer registrations with multiple myeloma among test participants known to NRPB, during the period for which mortality and cancer data were largely complete. Whilst the completeness of myeloma registration is not known precisely, an exercise conducted for Hodgkin's disease during the 1970s and 1980s (Swerdlow *et al*, 1993) would suggest that about 90% of cases during this period are contained on the NHSCRs. The findings of the intercomparison and of related checks mentioned below are consistent with this estimate.

2. Had the Dundee research identified an unexpectedly large number of men falling within the definition of test participants but who were not in the NRPB cohort?

- No. 38 out of 47 confirmed test participants on the Dundee list were included in the NRPB cohort. This percentage (ie. 81%) is compatible with the value of 85% estimated previously based on information for independent responders (see section 4.2) (two-sided p=0.41).

  The Dundee research included some men who participated in the tests but who did not fall within the definition of the study population given by Darby *et al* (1993b) (for example, men in the Merchant Navy or employees of the Meteorological Office). It should also be noted that the definition of a study participant requires there to have been some contemporary written record of the individual's involvement.

It is not unexpected that some cases on the Dundee list would not have arisen on the NRPB list, since the lists have been constructed in different ways. However, in order to avoid bias, it is paramount that the cases included in this study should be ascertained in the same manner for test participants and controls. For example, the NRPB follow-up could not have been expected to be complete (or largely so for cancer incidence) until a couple of years have passed in the case of mortality and longer for cancer incidence (see sections 4.3 and 4.4 respectively). The Dundee research reported some deaths and cancers in the period for which the NRPB follow-up is expected to be incomplete. These cases could not be included in the analysis in the absence of corresponding information from the control group, since this would have led to bias. By contrast, cancer registrations up to the end of 1998 that had been identified by the NHSCRs have been included in the analysis, since these data – whilst possibly incomplete towards the end of the period (see section 4.4) – were obtained in the same way for both test participants and controls.

In addition, the Dundee research included some individuals within the NRPB study group for whom there was a report of multiple myeloma which was not based on a death certificate or cancer registration; for example, a War Pensions tribunal might have accepted alternative information. Such cases could not be included in the analysis because no such alternative data source was available for controls. As a check, clinical details for two men in the NRPB cohort who were awarded war pensions, were reported by Dundee as being pre-1995 cases and for whom NRPB had neither a death certificate nor a cancer registration mentioning myeloma were forwarded to a haematologist for review. The men's relatives gave their agreement to this review. The haematologist concluded that:

- one man had myelodysplastic syndrome, which is different from myeloma, and

- the other man had a very mild form of myeloma that was unrelated to his death.

As mentioned earlier, registrations may have been around 90% complete during the period of this study. It is therefore not unexpected to find a case of multiple myeloma that was not picked up by the cancer registration system, and undetected cases may have also arisen in the control group. Section 4.6 describes separate checks undertaken to ensure that death certificates and cancer registrations did not overlook a significant number of cases of multiple myeloma. Also, the analysis considered a grouping consisting of myeloma and closely-related diseases, as reported on death certificates and cancer registrations, which could be studied both for test participants and controls (see section 5).

To conclude, this investigation did not bring to light additional death certificates or cancer registrations with multiple myeloma among test participants known to NRPB, during the period for which mortality and cancer data are thought to be largely complete. Furthermore, the proportion of men identified by Dundee who were confirmed as test participants but who were not in the NRPB study cohort was similar to that estimated previously based on data for independent responders. Since corresponding data are not available for the control group, none of the multiple myeloma cases identified by Dundee, but not NRPB, could be added to the NRPB database without leading to bias.

## 4.6 Comparison of data on haematological malignancies held by NRPB and the Leukaemia Research Fund

The Leukaemia Research Fund (LRF) Data Collection Study (DCS) maintains a registry, covering parts of England, of haematological neoplasms (Cartwright *et al*, 1990). These neoplasms are mostly cases of leukaemia, lymphoma and multiple myeloma. Cancer registrations held by the LRF are collected independently of data provided to NHSCRs and are the subject of detailed review. Hence the LRF registry presented an opportunity to assess the accuracy of the diagnosis of haematological neoplasms held on the study databases. The completeness of haematological cancer registrations on the study could also be assessed by checking at LRF for registrations among study men without haematological neoplasms. A detailed account of the comparison of LRF and study data is given in Appendix B.

LRF were sent details of all persons in the test participant and control cohorts recorded as having a haematological neoplasm, as underlying or contributory cause of death, or as a cancer registration (478 men). LRF were also sent details of samples of participants and controls who did not have haematological neoplasms in the study, in order to check the completeness of study data; they included 543 men with another type of cancer, 141 men who died without

mention of cancer, and 650 men recorded as being alive without cancer (ie. a total of 1334 men). These groups were selected without reference to the area of residence of the men. Details of cancer registrations or causes of death were not supplied to LRF. Where the LRF matched a record to their registry, they were asked to supply a diagnosis and ICD coding, which were compared with the corresponding diagnosis and ICD coding that would be selected for the man for the study.

The LRF did not match any records among the sample of men without haematological neoplasms. This provides reassurance that cases of haematological cancer are not missing from the study databases. The overall success rate (15%) in matching study members with haematological neoplasms to the LRF Registry was consistent with the smaller population and time period of data held on the LRF registry compared to the NHSCRs. A greater proportion of controls (21%) was matched to the LRF registry than test participants (10%).

There was good overall agreement between the LRF and study diagnoses, with 66 out of the total of 75 matching (see Table 4.3). The most consistent difference between the diagnoses concerned four cases listed by the LRF as chronic lymphatic leukaemia (CLL) and as non-Hodgkin's lymphoma (NHL) in the study database. The discrepancies between the diagnosis of NHL and CLL probably reflect the difficulties in distinguishing between borderline cases of these diseases (Cartwright *et al*, 1990). However, CLL is not thought to be radiation inducible (UNSCEAR, 2000) and has been excluded from some of the analyses of leukaemia among test participants. Thus, changes in the numbers of CLL are unlikely to affect the conclusions of the study. For multiple myeloma, which is of special interest to the study, the LRF agreed with nearly all the diagnoses of multiple myeloma by the study. The one difference involved a man who LRF diagnosed with Waldenström's macroglobulinaemia, a type of NHL. There were two discrepancies in the diagnosis of acute myeloid leukaemia, although the differing diagnoses were not of a consistent type (NHL and chronic myeloid leukaemia, CML). In one of these cases, the study diagnosis (CML) was based on information from the death certificate and it is possible that when the cancer registration is received this may give a different diagnosis, based on the symptoms at the time of cancer registration.

Overall, the results do not suggest any notable omissions of haematological neoplasms from the study nor any important inconsistencies in study diagnoses. Given the different rates of matching at LRF among test participants and controls, replacement of study data with LRF data could only be unequally and incompletely done on the control and test participant cohorts. Consequently, the study data have been retained in the analyses described in sections 5 and 6 of the report.

**TABLE 4.1 Status of test participants and controls on 1 January 1999**

| | Test Participants | | Controls | |
|---|---|---|---|---|
| Status | Number | % | Number | % |
| Alive | 14560 | 68.2 | 15364 | 68.8 |
| Dead | 4902 | 22.9 | 5217 | 23.4 |
| Emigrated | 1882 | 8.8 | 1738 | 7.8 |
| Lost to follow-up | 13 | 0.1 | 14 | 0.1 |
| Total | 21357 | | 22333 | |

**TABLE 4.2 Distribution of test participants and controls among Cancer Registry Regions**

| | Test Participants | | Controls | | Independent Responders | |
|---|---|---|---|---|---|---|
| | Number | % of total | Number | % of total | Number | % of total |
| England/Wales Cancer Registries | | | | | | |
| East Anglia | 1156 | 5% | 1136 | 5% | 25 | 5% |
| Merseyside & Cheshire | 469 | 2% | 510 | 2% | 14 | 3% |
| North Western | 779 | 4% | 861 | 4% | 23 | 5% |
| Yorkshire | 1847 | 9% | 1884 | 8% | 58 | 12% |
| Oxford | 1023 | 5% | 1087 | 5% | 29 | 6% |
| South & West | 3848 | 18% | 4226 | 19% | 52 | 10% |
| Thames | 3293 | 15% | 3468 | 16% | 55 | 11% |
| Trent | 1237 | 6% | 1373 | 6% | 41 | 8% |
| Wales | 717 | 3% | 805 | 4% | 28 | 6% |
| West Midlands | 1037 | 5% | 1198 | 5% | 35 | 7% |
| Unspecified | 1684 | 8% | 1570 | 7% | 17 | 3% |
| Subtotal | 17090 | 80% | 18118 | 81% | 377 | 75% |
| Scotland[a] | 1325 | 6% | 1275 | 6% | 30 | 6% |
| N. Ireland, Channel Islands | 165 | 1% | 167 | 1% | 2 | 0% |
| Remainder (not on listings) | 2777 | 13% | 2773 | 12% | 95 | 19% |
| **Total** | 21357 | 100% | 22333 | 100% | 504 | 100% |

*Note* (a) Subdivision according to regional cancer registry not attempted.

**TABLE 4.3 Comparison of LRF and study diagnoses**

| | Study diagnosis | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| LRF diagnosis | ALL | AML | CLL | CMD | HD | MDS | MM | NHL | UL | Total |
| ALL | 2 | | | | | | | | | 2 |
| AML | | 7 | | 1 | | | | | | 8 |
| CLL | | | 4 | | | | | 4 | 1 | 9 |
| CMD | | | | 8 | | | | | | 8 |
| HD | | | | | 2 | | | | | 2 |
| MDS | | | | 1 | | 1 | | | | 2 |
| MM | | | | | | | 15 | | | 15 |
| NHL | | 1 | | | | | 1 | 27 | | 29 |
| Total | 2 | 8 | 4 | 10 | 2 | 1 | 16 | 31 | 1 | 75 |

*Notes:*

Diagnoses used in intercomparison

| | |
|---|---|
| ALL | acute lymphatic leukaemias |
| AML | acute myeloid leukaemias (excluding hairy cell leukaemia, ICD-9 code 202.4) |
| CLL | chronic lymphatic leukaemias (including unspecified lymphatic leukaemias), |
| CMD | chronic myeloproliferative disorders (including chronic myeloid leukaemias, polycythaemia vera and lymphatic and haematopoietic neoplasms of unknown behaviour) |
| HD | Hodgkin's disease |
| MM | multiple myeloma |
| MDS | myelodysplastic syndromes |
| NHL | non-Hodgkin's lymphoma (including hairy cell leukaemia and mycosis fungoides) |
| UL | unspecified leukaemia |

# 5 METHOD OF ANALYSIS

The methods of analysis were similar to those used in the two previous reports (Darby *et al*, 1988a,b, 1993a,b). Test participants were entered into the study on the date of their first test involvement. For controls the date of entry to the study was the first day such that, if the man had died on that day, his death would have been included in the study. For controls who had been Army Officers or who had been in the RN or RAF, this date was around the time of the overseas visit that led to their inclusion in the control group, while soldier controls were entered into the study on the date of termination of their reserve liability. Civilian (ie. AWE) controls were entered into the study on the date of the first test involvement of the test participant with whom they were matched.

For the analysis of mortality, men were regarded as being at risk until their date of death or emigration, their 85$^{th}$ birthday, or 1$^{st}$ January 1999, whichever came earliest. For the analysis of cancer incidence, they were regarded as being at

risk similarly, except that men were also removed on their date of cancer registration where appropriate. Deaths and cancer at ages of 85 years and over were excluded from the analyses, because of problems of disease ascertainment at these ages. A total of 134 test participants were excluded from the study on reaching their 85$^{th}$ birthday, among whom 45 deaths and 10 incident cancers occurred before the end of the follow-up period (including one death from acute myeloid leukaemia). The corresponding numbers for the control group were 173 excluded on reaching age 85 years, among whom there were 55 deaths and 20 incident cancers (including one cases of chronic lymphatic leukaemia). There were no cases of multiple myeloma among these deaths and cancers after age 85 years.

There were two main components to the analysis. The first involved comparisons with national mortality rates, both for the participant and the control groups. The second involved comparing the participants and controls directly, both for mortality and cancer incidence. In both instances, the analysis used numbers of person-years, ie. the length of time that each man was in the study, multiplied by the number of men. Person-years were subdivided, as appropriate, by Service or employer, rank, 5-year age group and calendar period. To compare mortality rates in each of the participant and control groups with those of the general population, expected numbers of deaths in each group were calculated by multiplying the person-years in each age and calendar year group by the corresponding specific mortality rates for men in England and Wales, and summing the resulting values. 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 mortality analyses were based on the underlying cause of death, coded according to the ninth revision of the ICD (WHO, 1977). Where the analysis considered disease groupings whose ICD codes varied between revisions, these rates were bridge-coded to take account of the changes. The statistical significance of the SMRs was calculated by assuming that the observed number of deaths from a given cause had a Poisson distribution. Two-sided tests and 95% confidence intervals were used to assess whether the SMRs differed to a statistically significant extent from 100, since both increases and decreases relative to national rates were of interest. Since cancer incidence was assessed in this study using both registration and mortality data, as described in section 3.2, these rates have not been compared with national rates based on cancer registrations.

To compare mortality rates among the test participants directly with those in the control group, the deaths and person-years were subdivided by age (in 5-year groups), calendar period (in 5-year groups), Service or employer (ie. RN, Army, RAF, AWE) and either by rank (officers or other ranks) for those in the Services or by social class (class 1 or not) for AWE employees. The relative risk (RR) of mortality in participants compared with controls was then estimated by the

method of maximum likelihood (Breslow and Day, 1987). In particular, within each of the strata created using the variables cited above, the number of deaths among the participants – given the total number among participants and controls – was assumed to have a binomial distribution. Based on this distribution, significance tests and confidence intervals were calculated using the associated score statistic (Breslow and Day, 1987). When the total number of strata in which at least one death occurred was less than 60, significance levels were calculated using 10,000 simulations. When the observed deaths arose all among the test participants or all among the controls, significance levels and confidence intervals were calculated using exact methods. The same methods were applied in the analysis of cancer incidence. When the RR was observed to be greater than 1, a one-sided significance test was performed of any increase in mortality or cancer incidence rates among test participants compared with controls, in view of the prior interest as to whether risks were raised among participants. For the same reason, 90% confidence intervals for the RRs were used. When the RR was observed to be less than 1, a one-sided significance test was performed of any decrease in rates among participants compared with controls. Two-sided significance tests were also conducted for any increase or decrease in RR.

In testing for any trend in cancer rates among participants with different levels of recorded gamma dose, the cancers and person-years were stratified on the same basis as for the comparison of the participant and control groups. Given the total number of cancers in each stratum, the number of cancers expected in each dose category was calculated in proportion to the distribution of person-years across doses, and then summed over strata. Dose categories were indexed by the median of the doses within each category, and a one-sided test for an increasing trend in the relative risk with increasing dose was performed using the associated score statistic (Breslow and Day, 1987). For each participant in this dose-response analysis, the entry date was taken to be the date of his involvement in a test at which a dose was recorded. For the few men who were recorded as having received a dose at more than one test, the entry date was taken to be the date of involvement in the latest relevant test.

The disease categories studied here are mostly the same as those considered in the previous analysis (Darby *et al*, 1993b). However, some additional categories have been included here, as follows.

(i) Since there may be diseases related to multiple myeloma that do not fall within the standard definition of myeloma, a histopathologist – Dr Andrew Wotherspoon (Royal Marsden NHS Trust, London) – was asked to provide a wider definition of multiple myeloma, based on up-to-date haematological information. His suggested definition contained the following ICD 9$^{th}$ revision categories:

203.0 – multiple myeloma

203.1 – plasma cell leukaemia
238.6 – solitary myeloma, other plasmacytoma
273.1 – monoclonal gammopathy, monoclonal paraproteinaemia.

The standard definition of myeloma used both here and in previous analyses of this cohort – namely ICD 9th revision codes 203.0, 203.8 and 238.6 – contains one code (203.8) that is not contained within the wider definition. However, there were no instances where this code was found among either participants or controls. Consequently, there are no cases in the standard grouping that are not in the wider grouping.

(ii) 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.

(iii) 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 differ between participants and controls, these cancers form a substantial 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.

(iv) Since information on smoking habits is not available in this study, results are presented here both for a grouping of cancers related to smoking, as well as for mortality for a grouping of smoking-related diseases other than cancer, in common with the approach taken in previous reports. The cancer grouping consists of cancers of the tongue, mouth, pharynx, oesophagus, pancreas, lung, bladder and kidney. It should be noted that some other cancer types might also be related to smoking, but that this grouping should cover the majority of the cancer cases associated with this habit.

# 6 RESULTS

## 6.1 Mortality and cancer incidence in test participants and controls by broad cause

Table 6.1 summarises overall levels of mortality in the test participant and control groups over the full follow-up period, to the end of 1998. Shown in this table are the observed numbers of deaths among the participants and controls, the expected numbers of deaths in these groups based on national mortality rates, the associated SMRs, and the relative risk (RR) in the participants compared with the controls, split by broad cause of death. For all causes, all cancers and all other diseases, mortality rates in both participants and controls were lower than those in men of the same ages in England and Wales, whereas mortality rates for all accidents and violence were higher. Each of these differences was statistically significant at the 5% level. Comparing participants with controls, the RRs were close to 1 for each of the groupings in Table 6.1, with 90% confidence intervals that included 1, so indicating no statistically significant difference in mortality between the two groups. In particular, the RR was 1.01 (90% CI 0.98-1.05) for all causes and 1.01 (90% CI 0.96-1.08) for all cancers. Table 6.2 shows that the RR for the incidence of all types of cancer (RR 0.99, 90% CI 0.94-1.03) was similar to that based on the corresponding mortality data, and that similar findings arose when non-melanoma skin cancer - the registration of which is known to be incomplete - was excluded from this grouping.

Tables 6.3-6.6 give results up to 1990, ie. over the period of the previous analysis, and from 1991 to 1998. Table 6.3 shows SMRs for test participants, Table 6.4 shows SMRs for controls and Table 6.5 shows the RR for mortality in the former group compared with the latter, split by cause and period of death. In addition, Table 6.6 presents details of incident cancers among test participants and controls during the period of the previous analysis (ie. up to 31 December 1990) and during the extended period of follow-up (ie. from 1 January 1991 up to 31 December 1998). Since the NHSCRs had not finished the processing of cancer registrations beyond 1987 at the time of the previous analysis (Darby *et al*, 1993b), the numbers of cases up to the end of 1990 given for both participants and controls in Table 6.6 include some registrations notified by the NHSCRs after the previous analysis. For the grouping of all cancers, mortality rates among both participants and controls were significantly lower than national rates in the period up to the end of 1990. However, in the following eight years, SMRs in both participants and controls were similar to or slightly greater than – although not significantly different from - 100 (values of 106 for participants and 100 for controls). Whilst the mortality rate among participants for all cancers combined was consistent with the corresponding rate among controls up to the end of 1990 (RR 0.96, 90% CI 0.88-1.05), there was a weak suggestion of a raised total cancer mortality rate among participants

compared with controls in the following eight-year period (RR 1.07, 90% CI 0.98-1.17, one-sided p=0.09, two-sided p=0.18); see Table 6.5. In contrast, there was no evidence of a difference in the incidence of all cancers combined between participants and controls, either in the period up to the end of 1990 (RR 0.97, 90% CI 0.91-1.03) or subsequently (RR 1.01, 90% CI 0.95-1.07); see Table 6.6. Results for specific cancer types are discussed below.

For the grouping of all diseases other than neoplasms, Tables 6.3-6.5 show that mortality rates were similar among participants and controls and were significantly lower than national rates, both in the previous analysis and in the additional period of follow-up. During the latter period, the SMR was 86 for both participants and controls. For the grouping of all accidents and violence, mortality rates among participants and controls were comparable in both periods (RR 1.13, 90% CI 0.82-1.55 in the later period, with SMRs of 116 and 102 among participants and controls respectively).

In the previous analysis, rates of mortality from all causes were similar among participants and controls (RR 1.00, 90% CI 0.96-1.05) and were significantly lower than national rates (SMR of 84 in both groups); see Tables 6.3-6.5. During the extra eight years of follow-up, mortality from all causes was again similar in the two groups (RR 1.03, 90% CI 0.98-1.08) and significantly lower than national rates, although the SMRs were higher than in the earlier period (95 for participants, 93 for controls).

Table 6.7 shows mortality among test participants according to time since first test participation, and among controls by time since entry to the study. In common with the previous analysis, mortality from all neoplasms and – more particularly - from other diseases was especially low relative to national rates in the early years, both among participants and controls. This is not surprising, in view of the selection of physically fit men into service overseas. Table 6.7 shows that there were statistically significant increasing trends in the SMRs for all neoplasms and for other diseases over the full follow-up period, both for participants and controls, although much of the evidence for these trends came from the low SMRs within the first ten years. In contrast to the results for all neoplasms, the SMRs for all accidents and violence were raised among both participants and controls in the early period following first test participation, but tended to decrease subsequently.

Many of the remaining results in this section of the report are based on the period 10 or more years after first test participation (ie. entry to the study). The aim is to reduce the impact of selection into the cohort, associated with the healthy worker effect, and to increase the opportunity to detect any long-term effect on disease rates, given that radiation is known to increase cancer risks

only after a period of several years following exposure (UNSCEAR, 2000). Appendix D includes tables based on the whole follow-up period; these results are generally similar to those based on excluding the first 10 years following the initial test participation.

Table 6.8 shows mortality by broad cause among test participants and controls, split between officers (or social class 1 for AWE employees) and other ranks. Both for participants and controls, mortality among officers from all causes and from all cancers combined was significantly lower than rates for the national population, whereas mortality among other ranks was consistent with national rates. Both for officers and for other ranks, mortality by broad cause was similar among participants and controls.

Table 6.9 presents data on mortality among test participants and controls, separately for the three Services and AWE employees. Part a of this Table shows expected numbers of deaths based on the usual national mortality rates, while part b of the Table shows expected values corrected for the split between ranks in each service (or between social classes in the case of AWE). In general, similar patterns were seen for participants and controls. For all cancers combined, mortality amongst those in the RN was raised relative to uncorrected national rates, but was similar to that expected from social class specific rates. Men in the Army, RAF and AWE had lower mortality rates for all cancers combined than the general population, both with and without correction for social class. For accidents and violence, mortality was raised relative to national levels among men in the RN, but was more consistent with national rates for the RAF and for AWE employees, both with and without social class adjustments. For all other causes of death combined, mortality was less than expected from unadjusted national rates among each of the Services and for AWE employees, but – in the case of the RN and Army – was similar to that expected from social class adjusted rates. Rates of deaths from all causes tended to be similar to national rates – both with and without adjustments for social class – for the RN, whereas all cause mortality in the other Services and in AWE employees were generally significantly lower than expected from national rates.

## 6.2 Multiple myeloma mortality and incidence in test participants and controls

Tables 6.3-6.5 present details of mortality during the period of the period of the previous analysis (ie. up to 31 December 1990) and during the extended period of follow-up (ie. during 1 January 1991 up to 31 December 1998). The numbers of deaths with multiple myeloma as underlying cause that occurred in the period up to the end of 1990 are the same as those given in the report of the previous analysis, namely 9 for participants and 6 for controls (Darby *et al*, 1993b, Appendix B). The corresponding RR was 1.90 (90% CI 0.71-5.23), which is very

similar to that calculated previously. During the extended period of follow-up, from the beginning of 1991 up to the end of 1998, there were 13 deaths among participants with myeloma as underlying cause, compared with 12 deaths among controls; the associated RR was 1.21 (90% CI 0.58-2.53). The mortality rates for myeloma for both participants and controls during the additional period were consistent with national levels (SMR 114, p=0.65 for participants; SMR 98, p=1.0 for controls). Over the full period to the end of 1998, mortality among both participants and controls was consistent with national rates (SMRs of 96 and 73 respectively) and the RR among participants relative to controls – whilst greater than 1 – was not significantly different from 1 (RR 1.43, 90% CI 0.81-2.54, one-sided p=0.17, two-sided p=0.27). The numbers of deaths observed among participants and controls based on the wider definition of myeloma were identical to those based on the original definition, and the relative risk was also unchanged. The above findings over the full follow-up period were also similar to those based on excluding the first ten years following test participation, namely SMRs of 93 and 75 in participants and controls respectively, with a relative risk of 1.32 (90% CI 0.74-2.37); see Table 6.10. Table 6.7 indicates that, relative to national mortality rates, mortality from myeloma among test participants was consistent with a constant level over the follow-up period, although there was some variability in SMRs for specific time categories. In contrast, SMRs for myeloma among the controls tended to increase over time (see Table 6.7).

Table 6.6 presents details of incident cases of myeloma among test participants and controls during the period of the previous analysis (ie. up to 31 December 1990) and during the extended period of follow-up (ie. from 1 January 1991 to 31 December 1998). As indicated earlier, the numbers of cases up to the end of 1990 given in Table 6.6 include some registrations notified by the NHSCRs after the previous analysis. In particular, one case registered in 1986 and two cases registered during 1988-1990 (all among participants) were notified after the last analysis. In addition, three deaths (one among participants, two among controls) occurred during the period of the earlier analysis with myeloma as contributory cause and another cancer as underlying cause; these deaths are included under myeloma in Table 6.4, in line with the classification described in section 3.3, whereas they were included under "other neoplasms" in the corresponding table in Darby *et al* (1993b).

Based on the above modifications, there were 17 cases of myeloma among participants and 10 cases among controls up to the end of 1990 (see Table 6.6). The corresponding RR was 2.05 (90% CI 0.99-4.30, one-sided p=0.05, two-sided p=0.08), which compares with the value of 1.92 (90% CI 0.84-4.50) reported by Darby *et al* (1993b). During the extended period of follow-up, from the beginning of 1991 up to the end of 1998, there were 18 cases of myeloma among participants and 25 cases among controls, the associated RR was 0.79 (90% CI 0.45-1.38). As noted earlier, the ascertainment of cases after 1994 is

likely to be incomplete, both for participants and controls. Over the full follow-up period, myeloma incidence was similar among participants and controls (RR 1.14, 90% CI 0.74-1.74), with 35 cases observed in both groups. These findings were little changed after adding one extra case in a test participant that fell within the wider definition of myeloma (see Table 6.6), or after excluding the first 10 years after test participation (see Table 6.11).

## 6.3 Leukaemia mortality and incidence in test participants and controls

Table 6.5 shows that, as reported previously by Darby *et al* (1993a,b), there were 29 deaths with leukaemia as underlying cause among participants up to the end of 1990, compared with 17 deaths among controls, and an RR of 1.75 (90% CI 1.01-3.06). During the following eight years, there were 16 deaths among participants with leukaemia as underlying cause, compared with 16 among controls; the associated RR was 1.12 (90% CI 0.59-2.13). Leukaemia mortality rates among both participants and controls during this later period were consistent with national rates (SMRs of 94 for participants and 87 for controls – see Tables 6.3 and 6.4). For leukaemia excluding chronic lymphatic leukaemia (CLL), the relative risk among participants compared with controls during 1991-98 was greater than the corresponding value for all leukaemias combined, although it was not significantly raised (RR 1.81, 90% CI 0.80-4.18); the corresponding SMRs were 102 for participants and 59 (p=0.13) for controls. This relative risk is similar to that for leukaemia excluding CLL during the period up to the end of 1990 (RR 1.84, 90% CI 1.02-3.33). Table 6.7 indicates that, relative to national mortality rates, leukaemia mortality among test participants was fairly constant over the follow-up period, whereas rates among controls increased over time; similar results arose for leukaemia excluding CLL, although the evidence for an increasing time trend for controls was not as strong as for all leukaemias combined.

For leukaemia incidence, Table 6.6 shows that the number of cases among test participants up to the end of 1990 was the same as reported by Darby *et al* (1993b), ie. 37, whereas the number of cases among the control population increased from 24 to 29, owing to the late reporting of some cases. The corresponding RR was 1.31 (90% CI 0.84-2.04), which compares with the value of 1.61 (90% CI 1.00-2.57) reported by Darby *et al* (1993b). During the period from the start of 1991 to the end of 1998, there were 30 leukaemia cases among participants and 24 cases among controls; the associated RR was 1.37 (90% CI 0.86-2.22). For the incidence of leukaemia excluding CLL, the relative risk among participants compared with controls was 1.46 (90% CI 0.88-2.45) during the period up to the end of 1990 and was 1.39 (90% CI 0.74-2.61) during the following eight years.

Table 6.10 shows results for leukaemia mortality both over the full period of follow-up and also for the period 2-25 years after first test participation, during which time any effect of radiation exposure is most likely to have been apparent. There was statistically significant evidence of higher rates among participants compared with controls over the period 2-25 years after first test participation, both for leukaemia (RR 3.38, 90% CI 1.45-8.25, one-sided p=0.006, two-sided p=0.007) and for leukaemia excluding CLL (RR 2.99, 90% CI 1.26-7.41, one-sided p=0.01, two-sided p=0.02). In analyses over the full period, there was stronger evidence for a raised risk when CLL was omitted from the leukaemia analysis (RR 1.83, 90% CI 1.15-2.93, one-sided p=0.015, two-sided p=0.027) than when all leukaemias were studied together (RR 1.45, 90% CI 0.96-2.17, one-sided p=0.07, two-sided p=0.14). Leukaemia mortality among participants was consistent with national rates (SMR = 98 over the full follow-up period and 123 over the 2-25 year period post-first test involvement), whereas mortality among controls was significantly lower than national rates (SMR = 68 and 32 over the full follow-up period and the 2-25 year period respectively). SMRs for leukaemia excluding CLL were similar to those for all leukaemias.

As shown in Table 6.11, there was some suggestion of a raised incidence of leukaemia over the full follow-up period among participants compared with controls (RR 1.33, 90% CI 0.97-1.84, one-sided p=0.07, two-sided p=0.15). Table 6.13 shows the results for the incidence of specific leukaemia sub-types, again over the full period of follow-up. Among the various sub-types, there was a significant excess among participants relative to controls for chronic myeloid leukaemia (CML) (RR 3.08, 90% CI 1.08-9.62), based on 12 cases among participants and 4 among controls. For all leukaemia excluding CLL, the relative risk again approached statistical significance (RR 1.41, 90% CI 0.96-2.09, one-sided p=0.07, two-sided p=0.15). Table 6.13b presents results for the incidence of leukaemia and its sub-types over the period 2-25 years after initial test participation. There were significant excesses of all leukaemias combined, of leukaemia excluding CLL and of acute myeloid leukaemia and CML during this earlier period, with estimated relative risks for these diseases that were higher than those shown in Table 6.13a based on the full follow-up period.

## 6.4 Mortality and incidence for other specific types of cancer in test participants and controls

Table 6.10 shows mortality results for specific cancer types which, with the exception of leukaemia, are presented for the period 10 or more years after first test participation, in order to allow for latency in any radiation effect. Mortality among both test participants and controls was lower than national rates for many cancer types, sometimes to a statistically significant extent. The only significant excesses relative to national rates arose for cancer of the tongue, mouth and pharynx (among controls – SMR 145), malignant melanoma (among both participants and controls – SMRs of 171 and 160 respectively) and kidney

cancer (among controls – SMR 142). The relative risk of mortality among participants compared with controls was greater than 1 for some cancer types and less than 1 for other cancer types. Statistically significant differences between participants and controls, based on significance tests at the 5% level, arose only for bladder cancer (RR 1.64, 90% CI 1.11-2.42, one-sided p=0.017, two-sided p=0.026) and for leukaemia over the period 2-25 years after first test participation (see section 6.3). Rates of bladder cancer mortality among participants were consistent with national rates (SMR = 96), whereas mortality rates among controls were significantly lower than national rates (SMR = 58).

In the previous analysis, mortality rates differed significantly between participants and controls for cancer of the tongue, mouth and pharynx, for lung cancer and for bladder cancer. Tables 6.3-6.4 show that the SMRs for these causes were generally consistent with national rates for both participants and controls in the period 1991-98; an exception was cancer of the tongue, mouth and pharynx, which was raised significantly among participants (SMR 171, p=0.02), with less evidence for a raised level among controls (SMR 138, p=0.21). Table 6.5 shows that the RRs in the additional follow-up period were all consistent with a value of 1 and in no instance did rates among participants differ significantly from those in controls.

Table 6.11 presents numbers of known incident cancers among participants and controls, based on cancer registrations and death certificates (see section 3.2). Both these numbers and the relative risks among participants compared with controls are based on the period 10 or more years after first test involvement. Corresponding results based on the full follow-up period are shown in Appendix D. For most of the individual cancer types listed in Table 6.11, there was little evidence of differences in incidence rates between the two groups. However, there was a significant raised incidence of liver cancer (RR 1.99, 90% CI 1.19-3.38, one-sided p=0.012, two-sided p=0.016) and prostate cancer (RR 1.22, 90% CI 1.04-1.43), and a significantly lower incidence of kidney cancer (RR 0.74, 90% CI 0.57-0.96) among participants compared with controls. The relative risk for primary liver cancer (RR 1.83, 90% CI 0.98-3.46) was similar to that for all liver cancer, although the evidence for a raised risk was weaker (one-sided p=0.06, two-sided p=0.09). In addition, both for all liver cancer and for primary liver cancer, the relative risk was similar in the previous and the additional follow-up periods (see Table 6.6). The evidence for a raised risk of prostate cancer incidence among participants compared with controls was stronger during 1991-98 (RR 1.27, 90% CI 1.04-1.55) than in the earlier period. In analyses which, in each case, used all mentions of the cancer type in question on the death certificate or registration details in preference to other cancer types, the results over the period more than 10 years after first test involvement were similar to those from the standard analyses; for primary liver cancer: RR 1.63, 90% CI 1.00-2.67; prostate cancer: RR 1.22, 90% CI 1.05-1.42; kidney cancer: RR 0.74, 90% CI 0.57- 0.96.

Among other cancer types, there was little evidence of a difference in thyroid cancer rates between test participants and controls (RR 1.92, 90% CI 0.51-7.97); including all mentions of this disease on the death certificate or registration details did not change the numbers of cases in the two groups. Furthermore, whereas in the previous analysis the incidence of bladder cancer was significantly higher among participants than controls and the incidence of non-melanoma skin cancer was significantly lower, the incidence of both these cancer types was similar in the two groups over the period 1991-98 (see Table 6.6).

Table 6.10 and 6.11 also present findings for a grouping of cancers related to smoking, namely, cancers of the tongue, mouth and pharynx; oesophagus; pancreas; lung; bladder; and kidney. Based on a 10-year lag, there was some suggestion of a lower incidence of these diseases among test participants compared with controls (RR 0.94, 90% CI 0.88-1.01, one-sided p=0.09, two-sided p=0.17), but there was less evidence for a difference in the corresponding mortality data (RR 0.98, 90% CI 0.90-1.06). The SMRs for this grouping of cancers were 92 for participants and 95 for controls. Tables 6.3-6.4 indicate that, both among participants and controls, SMRs were higher in the period 1991-98 than in the earlier period. Whilst there was a slight suggestion that the relative risk of mortality in participants compared with controls was higher in the later than in the earlier period, this was not the case for the corresponding incidence data (see Tables 6.5 and 6.6 respectively).

## 6.5 Mortality from specific causes other than cancer in test participants and controls

Table 6.12 shows results for specific causes of death other than neoplasms. For most of these causes, mortality among both participants and controls was significantly lower than national rates. However, mortality was significantly raised for diseases related to alcohol (SMRs of 149 for participants and 160 for controls), for air accidents (SMRs of 699 and 732 for participants and controls respectively) and for the category of 'other injury and poisoning' (only for participants: SMR 128). Mortality rates were generally similar among participants and controls for the causes listed in Table 6.12, including diseases related to smoking. However, there was borderline evidence for a raised risk of deaths from 'other injury and poisoning' among participants (RR 1.24, 90% CI 0.99-1.56, one-sided p=0.063, two-sided p=0.13). Further examination showed that this difference could not be explained solely on the basis of one or two specific causes of death; there were more deaths among participants than controls from railway accidents (6 in participants, 1 in controls), fires (16 and 7 respectively), electric currents (5 and 1 respectively) and accidents caused by cutting and piercing instruments or objects (48 and 30 respectively). In addition, there was no indication of differences in rates between participants and

controls for this grouping of deaths during the additional period of follow-up (RR 1.03, 90% CI 0.67-1.57; see Table 6.5).

## 6.6 Mortality and cancer incidence in test participants by type and degree of exposure

Table 6.14 shows mortality and incidence from leukaemia, multiple myeloma and the grouping of all other cancers among test participants known to have been monitored for exposure to radiation, according to whether or not a non-zero gamma dose had been recorded. For leukaemia, mortality was similar to national rates in both groups, although based on small numbers of deaths. Multiple myeloma mortality was, if anything, raised relative to national rates among participants with a gamma dose recorded (SMR 210, p=0.18), and decreased among monitored participants with no recorded dose (SMR 24, p=0.14). Although the rates of myeloma in these two groups were based on small numbers of deaths and were not statistically significantly different from national rates, the risk of myeloma mortality among those with a recorded dose was significantly greater than that among other monitored participants (RR 16, 90% CI 1.74-314, one-sided p=0.009, two-sided p=0.01, having excluded the first 10 years following the start of test participation). In the corresponding incidence data, the risk of myeloma among those with a recorded dose was again raised, although the degree of statistical significance was weaker (RR 4.91, 90% CI 0.94-26.8, one-sided p=0.057, two-sided p=0.086); the results based on the wider definition of multiple myeloma were identical. For the grouping of all cancers other than myeloma and leukaemia, mortality was either lower than or compatible with national rates in both groups, and both mortality and incidence were similar amongst monitored participants with recorded doses greater than zero and those with zero dose (for mortality, RR 0.86, 90% CI 0.70-1.06; for incidence, RR 0.99, 90% CI 0.85-1.16, based on a 10-year lag).

Table 6.15 shows numbers of deaths and incident cases of leukaemia (both all types and all excluding CLL), multiple myeloma and all other cancers by the level of recorded gamma dose. Also shown in this table are the numbers of cases that would be expected in each dose category, if there were no relationship between cancer risk and dose. There were no significant trends with dose in the risk of these diseases, although the associated confidence intervals were wide. However, there was weak evidence of an increasing trend in multiple myeloma mortality with increasing gamma dose (p=0.094, based on a one-sided test, p=0.13 based on a two-sided test), with slightly weaker evidence of an increasing trend in the corresponding incidence data (one-sided p=0.12, two-sided p=0.22).

Findings on cancer mortality and incidence among participants according to the type of test involvement are given in Table 6.16. Among those participants who

were present at a major operation, mortality for leukaemia and multiple myeloma was consistent with national rates and mortality from all solid cancers combined was significantly lower than national rates. Furthermore, mortality and incidence rates of these diseases were consistent with those amongst the controls, with the exception of leukaemia where there was some indication of raised risks, particularly over the period 2-25 years since first test participation. Generally similar findings arose both for the five groups of men identified by MOD as being liable to exposure to radiation (referred to in Table 6.16 as Group A; see section 2 for the definition), and for participants employed by AWE or who were directly involved in the minor trials at Maralinga (referred to in Table 6.16 as Group B), although the numbers of myelomas and leukaemias in these groups were small. However, whilst mortality from all cancers other than leukaemia and myeloma was significantly lower than national rates in both Groups A and B, rates in Group A were significantly less than those in the controls (RR 0.72, 90% CI 0.55-0.95), whereas rates in Group B were significantly greater than those among the controls (RR 1.34, 90% CI 1.04-1.71). Similar relative risks were obtained in the corresponding analysis of the incidence of all cancers other than leukaemia and myeloma (see Table 6.16 (c)). For men who were either in Group A or Group B, or who were recorded as having a radiation dose, mortality from leukaemia and myeloma was consistent with national rates and with rates in controls, although the estimated relative risks compared with controls were greater than 1; mortality from all other cancers was significantly less than national rates and similar to that among the controls (see Table 6.16 (b)). The incidence of myeloma and of all cancers other than leukaemia and myeloma among men in this category was similar to that in controls; however, there was some indication of a raised risk of leukaemia incidence over the period 2-25 years after first test participation (RR 3.83, 90% CI 0.93, 13.59). For participants not in any of the preceding groups, rates of myeloma and of all cancers other than leukaemia and myeloma were consistent with national mortality rates and with the corresponding mortality and incidence rates among controls. However, leukaemia rates in this group of 'other test participants' tended to be raised relative both to national rates and to those for controls, particularly during the period 2-25 years after first test participation using data on both mortality (SMR 221; RR 7.63, 90% CI 2.73-21.8) and incidence. Throughout Table 6.16, observed numbers of multiple myeloma and associated relative risks based on the wider definition of the disease were identical to those for the standard definition in the case of mortality, and were similar in the case of myeloma incidence.

Appendix E lists results on mortality from leukaemia, multiple myeloma and all other cancers combined among participants according to the operation in which they were involved. Whilst the numbers of deaths were often small, rates of leukaemia and myeloma were consistent with national rates for all of these operations. In addition, mortality from solid cancers was either consistent with or significantly lower than national rates in each instance.

## 6.7 Mortality in independent responders

Table 6.17 shows mortality among 474 independent responders notified to NRPB by the time of the second analysis and who were found not to be in the main study cohort of test participants. As in previous analyses, mortality rates – particularly for all causes combined and all cancer combined - were high relative to national levels in the period during which the responders were notified; in this case, up to 28 February 1993. In contrast, deaths from accidents and violence were significantly lower than national rates up to this time, indicating that deaths from these causes were under-represented among independent responders. During the period after which these men were identified, mortality rates were generally closer to national values. There was some suggestion that overall mortality was raised relative to national rates after 28 February 1993, due partly to the findings for cancer. However, out of the 16 cancer deaths during this period, seven (including both of the leukaemia deaths) occurred in men registered with the same form of cancer before 28 February 1993. Consequently, the cancer findings are still likely to have been influenced by the self-selected nature of the independent responders. There were no deaths from multiple myeloma during the later period.

**TABLE 6.1 Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) among test participants and controls and relative risks (RR) of mortality in test participants compared with controls, by broad cause of death**

| | Test participants | | | | Controls | | | | Mortality rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cause of death | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] | RR | 90%CI[d] | Prob[b] one-sided | Prob[c] two-sided |
| All neoplasms | 1546 | 1666.42 | 93 | 0.0029 | 1645 | 1789.82 | 92 | 0.0005 | 1.01 | 0.96, 1.08 | 0.35 | 0.71 |
| Other diseases | 2769 | 3453.45 | 80 | <0.001 | 2961 | 3734.21 | 79 | <0.001 | 1.01 | 0.97, 1.06 | 0.32 | 0.64 |
| Accidents and violence | 436 | 358.86 | 121 | <0.001 | 417 | 359.54 | 116 | 0.0031 | 1.07 | 0.95, 1.21 | 0.16 | 0.33 |
| Unknown | 106 | - | - | - | 139 | - | - | - | - | - | - | |
| All causes | 4857 | 5483.11[e] | 89 | <0.001 | 5162 | 5888.22[e] | 88 | <0.001 | 1.01 | 0.98, 1.05 | 0.26 | 0.52 |

*Notes*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) One-sided test that the RR is greater than unity (if RR ≥ 1.00), or less than unity (RR < 1.00).

(c) Two-sided test that the RR is different from unity.

(d) Confidence interval.

(e) In this and some later tables, the expected number for all causes differs slightly from the sum of the expected values for individual known causes, owing to deaths from unknown causes.

**TABLE 6.2 Number of incident cancers among test participants and controls and relative risks (RR) in test participants compared with controls**

| | Observed cancers | | Incidence rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|
| Type of cancer | Test participants | Controls | RR | 90%CI[c] | Prob[a] one-sided | Prob[b] two-sided |
| All neoplasms | 2695 | 2918 | 0.99 | 0.94,1.03 | 0.33 | 0.65 |
| All neoplasms excluding non-melanoma skin cancer | 2362 | 2516 | 1.00 | 0.96,1.05 | 0.44 | 0.88 |

*Notes*

(a) One-sided test that the RR is greater than unity (RR ≥ 1.00), or less than unity (RR < 1.00)

(b) Two-sided test that the RR is different from unity.

(c) Confidence interval.

**TABLE 6.3 Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) for test participants for selected causes of death, by calendar period**

| | Calendar period up to 31 Dec 1990 | | | | 1 Jan 1991-31 Dec 1998 | | | |
|---|---|---|---|---|---|---|---|---|
| Cause of death | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] |
| **(I) Causes with significant difference between test participants and controls in previous analysis, plus multiple myeloma** | | | | | | | | |
| Leukaemia | 29 | 29.03 | 100 | 1.00 | 16 | 17.08 | 94 | 0.81 |
| Leukaemia excluding CLL | 27 | 24.85 | 109 | 0.69 | 13 | 12.75 | 102 | 1.00 |
| Multiple myeloma [b] | 9 | 11.63 | 77 | 0.47 | 13 | 11.38 | 114 | 0.65 |
| Cancer of mouth, tongue, pharynx | 11 | 14.80 | 74 | 0.37 | 21 | 12.26 | 171 | 0.021 |
| Cancer of lung | 242 | 329.63 | 73 | <0.001 | 238 | 232.37 | 102 | 0.72 |
| Cancer of bladder | 29 | 27.34 | 106 | 0.77 | 23 | 27.12 | 85 | 0.45 |
| Other injury and poisoning[c] | 132 | 101.73 | 130 | 0.004 | 34 | 25.93 | 131 | 0.14 |
| **(II) Other cancers, smoking-related cancers, and broad causes of death** | | | | | | | | |
| All neoplasms not in group I) | 441 | 510.16 | 86 | 0.0018 | 474 | 443.64 | 107 | 0.15 |
| Neoplasms related to smoking | 389 | 475.65 | 82 | <0.001 | 384 | 369.80 | 104 | 0.47 |
| All neoplasms | 761 | 922.57 | 82 | <0.001 | 785 | 743.84 | 106 | 0.14 |
| All diseases other than neoplasms | 1565 | 2049.66 | 76 | <0.001 | 1204 | 1403.79 | 86 | <0.001 |
| Accidents and violence | 374 | 305.42 | 122 | <0.001 | 62 | 53.45 | 116 | 0.24 |
| Unknown causes | 68 | - | - | - | 38 | - | - | - |
| All causes | 2768 | 3277.66 | 84 | <0.001 | 2089 | 2205.45 | 95 | 0.013 |

*Notes*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) The observed numbers of deaths are unchanged for the wider definition of multiple myeloma (ICD 9th revision codes 203.0, 203.1, 238.6 and 273.1).

(c) Other injury and poisoning – i.e. other than motor vehicle traffic accidents, drowning and water transport accidents, air and space transport accidents or suicide.

**TABLE 6.4 Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) for controls for selected causes of death, by calendar period**

| | Calendar period up to 31 Dec 1990 | | | | 1 Jan 1991-31 Dec 1998 | | | |
|---|---|---|---|---|---|---|---|---|
| Cause of death | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] |
| **(I) Causes with significant difference between test participants and controls in previous analysis, plus multiple myeloma** | | | | | | | | |
| Leukaemia | 17 | 30.32 | 56 | 0.011 | 16 | 18.30 | 87 | 0.64 |
| Leukaemia excluding CLL | 15 | 25.76 | 58 | 0.030 | 8 | 13.64 | 59 | 0.14 |
| Multiple myeloma [b] | 6 | 12.54 | 48 | 0.065 | 12 | 12.19 | 98 | 1.00 |
| Cancer of mouth, tongue, pharynx | 22 | 15.83 | 139 | 0.13 | 18 | 13.01 | 138 | 0.21 |
| Cancer of lung | 303 | 358.18 | 85 | 0.0031 | 232 | 248.35 | 93 | 0.31 |
| Cancer of bladder | 11 | 29.96 | 37 | <0.001 | 23 | 29.20 | 79 | 0.27 |
| Other injury and poisoning[c] | 107 | 102.96 | 104 | 0.69 | 35 | 27.58 | 127 | 0.18 |
| **(II) Other cancers, smoking-related cancers, and broad causes of death** | | | | | | | | |
| All neoplasms not in group I) | 491 | 547.01 | 90 | 0.016 | 494 | 475.15 | 104 | 0.40 |
| Neoplasms related to smoking | 462 | 515.86 | 90 | 0.016 | 395 | 395.22 | 100 | 1.00 |
| All neoplasms | 850 | 993.83 | 86 | <0.001 | 795 | 796.20 | 100 | 0.97 |
| All diseases other than neoplasms | 1665 | 2221.91 | 75 | <0.001 | 1296 | 1512.71 | 86 | <0.001 |
| Accidents and violence | 359 | 302.94 | 119 | 0.0017 | 58 | 56.62 | 102 | 0.84 |
| Unknown causes | 85 | - | - | - | 54 | - | - | - |
| All causes | 2959 | 3518.68 | 84 | <0.001 | 2203 | 2370.19 | 93 | <0.001 |

*Notes*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) The observed numbers of deaths are unchanged for the wider definition of multiple myeloma (ICD 9th revision codes 203.0, 203.1, 238.6 and 273.1).

(c) Other injury and poisoning – i.e. other than motor vehicle traffic accidents, drowning and water transport accidents, air and space transport accidents or suicide.

**Table 6.5 Observed deaths among test participants and controls, and relative risks (RR) of mortality among test participants compared with controls for selected causes of deaths, by calendar period**

| Cause of death | Calendar period up to 31 Dec 1990 | | | | | | Calendar period 1 Jan 1991 – 31 December 1998 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Observed deaths | | Mortality rate in participants relative to controls | | | | Observed Deaths | | Mortality rate in participants relative to controls | | | |
| | Test participants | Controls | RR | 90%CI[c] | Prob[a] one-sided | Prob[b] two-sided | Test participants | Controls | RR | 90%CI[c] | Prob[a] one-sided | Prob[b] two-sided |
| **(I) Causes with significant difference between test participants and controls in previous analysis, plus multiple myeloma** | | | | | | | | | | | | |
| Leukaemia | 29 | 17 | 1.75 | 1.01, 3.06 | 0.048 | 0.07 | 16 | 16 | 1.12 | 0.59, 2.13 | 0.44 | 0.86 |
| Leukaemia excluding CLL | 27 | 15 | 1.84 | 1.02, 3.33 | 0.043 | 0.08 | 13 | 8 | 1.81 | 0.80, 4.18 | 0.13 | 0.20 |
| Multiple myeloma | 9 | 6 | 1.90 | 0.71, 5.23 | 0.17 | 0.30 | 13 | 12 | 1.21 | 0.58, 2.53 | 0.39 | 0.69 |
| Multiple myeloma (wider definition)[d] | 9 | 6 | 1.90 | 0.71, 5.23 | 0.17 | 0.30 | 13 | 12 | 1.21 | 0.58, 2.53 | 0.39 | 0.69 |
| Cancer of mouth, tongue, pharynx | 11 | 22 | 0.56 | 0.28, 1.08 | 0.077 | 0.11 | 21 | 18 | 1.26 | 0.71, 2.25 | 0.29 | 0.52 |
| Cancer of lung | 242 | 303 | 0.87 | 0.76, 1.01 | 0.067 | 0.13 | 238 | 232 | 1.10 | 0.94, 1.29 | 0.15 | 0.30 |
| Cancer of bladder | 29 | 11 | 2.85 | 1.51, 5.47 | 0.002 | 0.002 | 23 | 23 | 1.13 | 0.67, 1.91 | 0.40 | 0.77 |
| Other injury and poisoning[e] | 132 | 107 | 1.28 | 1.02, 1.61 | 0.038 | 0.07 | 34 | 35 | 1.03 | 0.67, 1.57 | 0.50 | 0.90 |
| **(II) Other cancers, smoking-related cancers, and broad causes of death** | | | | | | | | | | | | |
| All neoplasms not in group (I) | 441 | 491 | 0.96 | 0.86, 1.07 | 0.27 | 0.55 | 474 | 494 | 1.05 | 0.94, 1.17 | 0.25 | 0.5 |
| Neoplasms related to smoking | 389 | 462 | 0.91 | 0.81, 1.03 | 0.10 | 0.20 | 384 | 395 | 1.05 | 0.93, 1.19 | 0.25 | 0.5 |
| All neoplasms | 761 | 850 | 0.96 | 0.88, 1.05 | 0.22 | 0.44 | 785 | 795 | 1.07 | 0.98, 1.17 | 0.092 | 0.18 |
| All diseases other than neoplasms | 1565 | 1665 | 1.02 | 0.96, 1.08 | 0.31 | 0.63 | 1204 | 1296 | 1.01 | 0.94, 1.08 | 0.45 | 0.90 |
| Accidents and violence | 374 | 359 | 1.06 | 0.94, 1.21 | 0.22 | 0.44 | 62 | 58 | 1.13 | 0.82, 1.55 | 0.28 | 0.52 |
| Unknown causes | 68 | 85 | - | - | - | - | 38 | 54 | - | - | - | |
| All causes | 2768 | 2959 | 1.00 | 0.96, 1.05 | 0.47 | 0.93 | 2089 | 2203 | 1.03 | 0.98, 1.08 | 0.20 | 0.39 |

*Notes for Table 6.5*

(a) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).

(b) Two-sided test that the RR is different from unity.

(c) Confidence interval.

(d) ICD 9$^{th}$ revision codes 203.0, 203.1, 238.6 and 273.1.

(e) Other injury and poisoning – i.e. other than motor vehicle traffic accidents, drowning and water transport accidents, air and space transport accidents or suicide.

**TABLE 6.6 Number of incident cancers among test participants and controls, and relative risks (RR) of incident cancer in test participants compared with controls for selected types of cancer, by calendar period**

| Type of cancer | Calendar period up to 31 Dec 1990 | | | | | | Calendar period 1 Jan 1991 – 31 December 1998 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Incident cancers | | Incident rate in test participants relative to controls | | | | Incident cancers | | Incident rate in test participants relative to controls | | | |
| | Test participants | Controls | RR | 90%CI[c] | Prob[a] one-sided | Prob[b] two-sided | Test participants | Controls | RR | 90%CI[c] | Prob[a] one-sided | Prob[b] two-sided |
| **(I) Types of cancer with significant difference between test participants and controls in previous analysis, plus multiple myeloma** | | | | | | | | | | | | |
| Leukaemia | 37 | 29 | 1.31 | 0.84, 2.04 | 0.17 | 0.32 | 30 | 24 | 1.37 | 0.86, 2.22 | 0.14 | 0.28 |
| Leukaemia excluding CLL | 30 | 21 | 1.46 | 0.88, 2.45 | 0.12 | 0.19 | 19 | 15 | 1.39 | 0.74, 2.61 | 0.22 | 0.39 |
| Multiple myeloma | 17 | 10 | 2.05 | 0.99, 4.30 | 0.054 | 0.08 | 18 | 25 | 0.79 | 0.45, 1.38 | 0.28 | 0.55 |
| Myeloma (wider definition) [d] | 17 | 10 | 2.05 | 0.99, 4.30 | 0.054 | 0.08 | 19 | 25 | 0.84 | 0.48, 1.45 | 0.34 | 0.65 |
| Cancer of liver | 15 | 7 | 2.31 | 1.00, 5.48 | 0.049 | 0.08 | 18 | 11 | 1.84 | 0.92, 3.71 | 0.077 | 0.13 |
| Primary liver cancer | 9 | 5 | 1.88 | 0.67, 5.53 | 0.19 | 0.28 | 13 | 8 | 1.79 | 0.79, 4.14 | 0.14 | 0.20 |
| Other skin cancer | 137 | 187 | 0.78 | 0.64, 0.95 | 0.017 | 0.03 | 196 | 215 | 0.97 | 0.82, 1.15 | 0.39 | 0.79 |
| Cancer of bladder | 81 | 67 | 1.27 | 0.95, 1.69 | 0.086 | 0.17 | 77 | 86 | 0.97 | 0.74, 1.28 | 0.46 | 0.87 |
| **(II) Other neoplasms** | 1039 | 1156 | 0.96 | 0.89, 1.03 | 0.16 | 0.33 | 1030 | 1101 | 1.00 | 0.93, 1.08 | 0.47 | 0.94 |
| Neoplasms related to smoking | 547 | 617 | 0.95 | 0.86, 1.04 | 0.18 | 0.37 | 484 | 556 | 0.94 | 0.84, 1.04 | 0.16 | 0.32 |
| All neoplasms excluding non-melanoma skin cancer | 1189 | 1269 | 1.00 | 0.93, 1.07 | 0.49 | 0.97 | 1173 | 1247 | 1.01 | 0.95, 1.08 | 0.39 | 0.78 |
| All neoplasms | 1326 | 1456 | 0.97 | 0.91, 1.03 | 0.22 | 0.43 | 1369 | 1462 | 1.01 | 0.95, 1.07 | 0.44 | 0.90 |

*Notes*
(a) One-sided test that the RR is greater than unity (RR ≥ 1.00), or less than unity (RR < 1.00).
(b) Two-sided test that the RR is different from unity.
(c) Confidence interval.
(d) ICD 9th revision codes 203.0, 203.1, 238.6 and 273.1.

**TABLE 6.7 Observed deaths (O) and standardised mortality ratios (SMR) among test participants and controls by time since start of first test participation and broad cause of death, plus leukaemia and multiple myeloma**

| Cause of death | | Test participants | | | | | | Controls | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Time since start of first test participation (years) | | | | | | Time since entry to study (years) | | | | | |
| | | <10 | 10-19 | 20-29 | 30-39 | 40+ | P value for trend[a] | <10 | 10-19 | 20-29 | 30-39 | 40+ | P value for trend[a] |
| All neoplasms | O | 53 | 159 | 363 | 821 | 150 | <0.001 | 63 | 195 | 459 | 732 | 196 | <0.001 |
| | SMR | 72 | 85 | 81 | 102 | 99 | | 69 | 82 | 90 | 95 | 107 | |
| Leukaemia | O | 5 | 9 | 11 | 15 | 5 | 0.82 | 2 | 3 | 6 | 14 | 8 | 0.0053 |
| | SMR | 91 | 131 | 93 | 81 | 144 | | 33 | 37 | 47 | 80 | 190 | |
| Leukaemia excluding CLL | O | 5 | 8 | 10 | 12 | 5 | 0.92 | 2 | 3 | 5 | 8 | 5 | 0.071 |
| | SMR | 95 | 129 | 103 | 86 | 198 | | 35 | 42 | 48 | 61 | 164 | |
| Multiple myeloma | O | 1 | 4 | 3 | 8 | 6 | 1.00 | 0 | 1 | 3 | 11 | 3 | 0.053 |
| | SMR | 204 | 211 | 50 | 65 | 252 | | 0 | 38 | 43 | 95 | 105 | |
| Other diseases | O | 97 | 318 | 779 | 1330 | 245 | <0.001 | 122 | 403 | 881 | 1281 | 274 | <0.001 |
| | SMR | 54 | 70 | 79 | 86 | 82 | | 54 | 72 | 81 | 86 | 75 | |
| Accidents and violence | O | 148 | 94 | 106 | 77 | 11 | 0.27 | 161 | 87 | 94 | 65 | 10 | 0.025 |
| | SMR | 135 | 109 | 122 | 113 | 138 | | 146 | 94 | 109 | 106 | 106 | |
| Unknown | O | 5 | 21 | 32 | 44 | 4 | | 7 | 21 | 43 | 57 | 11 | |
| All causes | O | 303 | 592 | 1280 | 2272 | 410 | <0.001 | 353 | 706 | 1477 | 2135 | 491 | 0.0079 |
| | SMR | 84 | 81 | 84 | 94 | 90 | | 83 | 80 | 88 | 92 | 88 | |

*Note*

(a) Two-sided test.

**Table 6.8 Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) among test participants and controls for officers and other ranks more than 10 years after start of first test participation, together with relative risks (RR) of mortality in test participants compared with controls, by broad cause of death**

| | | Test participants | | | | Controls | | | | Mortality rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cause of death | Status | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] | RR | 90%CI[d] | Prob[b] one-sided | Prob[c] two-sided |
| All neoplasms | Officers | 304 | 431.91 | 70 | <0.001 | 324 | 478.35 | 68 | <0.001 | 1.05 | 0.92, 1.21 | 0.28 | 0.55 |
| | Other ranks | 1189 | 1161.32 | 102 | 0.42 | 1258 | 1219.97 | 103 | 0.28 | 1.00 | 0.94, 1.07 | 0.48 | 0.97 |
| Other diseases | Officers | 541 | 963.15 | 56 | <0.001 | 585 | 1075.69 | 54 | <0.001 | 1.04 | 0.94, 1.15 | 0.28 | 0.56 |
| | Other ranks | 2131 | 2313.81 | 92 | <0.001 | 2253 | 2434.14 | 92 | <0.001 | 1.00 | 0.95, 1.05 | 0.49 | 0.98 |
| Accidents and violence | Officers | 44 | 37.75 | 117 | 0.33 | 49 | 43.44 | 113 | 0.40 | 0.96 | 0.66, 1.38 | 0.46 | 0.92 |
| | Other ranks | 244 | 211.28 | 115 | 0.028 | 207 | 205.79 | 101 | 0.94 | 1.15 | 0.98, 1.36 | 0.074 | 0.15 |
| Unknown | Officers | 19 | | | | 25 | | | | | | | |
| | Other ranks | 82 | | | | 107 | | | | | | | |
| All causes | Officers | 908 | 1433.59 | 63 | <0.001 | 983 | 1598.34 | 62 | <0.001 | 1.04 | 0.96, 1.12 | 0.24 | 0.47 |
| | Other ranks | 3646 | 3687.99 | 99 | 0.49 | 3825 | 3863.67 | 99 | 0.54 | 1.00 | 0.96, 1.04 | 0.46 | 0.92 |

*Notes*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) One-sided test that the RR is greater than unity (RR ≥ 1.00), or less than unity (RR < 1.00).

(c) Two-sided test that the RR is different from unity.

(d) Confidence interval.

**TABLE 6.9a Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) among test participants and controls more than 10 years after start of first test participation by Service and broad cause of death**

| | | Test participants | | | | Controls | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cause of death | Service | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] |
| All neoplasms | RN | 534 | 487.14 | 110 | 0.037 | 620 | 550.99 | 113 | 0.004 |
| | Army | 299 | 338.05 | 88 | 0.032 | 271 | 302.10 | 90 | 0.074 |
| | RAF | 578 | 653.43 | 88 | 0.0028 | 614 | 727.84 | 84 | <0.001 |
| | AWE | 82 | 114.62 | 72 | 0.0015 | 77 | 117.39 | 66 | <0.001 |
| Other diseases | RN | 929 | 987.21 | 94 | 0.063 | 1055 | 1115.19 | 95 | 0.070 |
| | Army | 608 | 675.52 | 90 | 0.0089 | 512 | 581.67 | 88 | 0.0035 |
| | RAF | 953 | 1357.42 | 70 | <0.001 | 1114 | 1540.75 | 72 | <0.001 |
| | AWE | 182 | 254.81 | 71 | <0.001 | 157 | 272.21 | 58 | <0.001 |
| Accidents and violence | RN | 109 | 75.96 | 144 | <0.001 | 118 | 88.67 | 133 | 0.0029 |
| | Army | 80 | 65.97 | 121 | 0.096 | 42 | 46.21 | 91 | 0.56 |
| | RAF | 91 | 96.55 | 94 | 0.58 | 90 | 103.96 | 87 | 0.17 |
| | AWE | 8 | 10.56 | 76 | 0.45 | 6 | 10.39 | 58 | 0.21 |
| Unknown | RN | 27 | - | - | - | 49 | - | - | - |
| | Army | 26 | - | - | - | 22 | - | - | - |
| | RAF | 44 | - | - | - | 55 | - | - | - |
| | AWE | 4 | - | - | - | 6 | - | - | - |
| All causes | RN | 1599 | 1551.58 | 103 | 0.23 | 1842 | 1756.34 | 105 | 0.043 |
| | Army | 1013 | 1080.65 | 94 | 0.039 | 847 | 931.10 | 91 | 0.0053 |
| | RAF | 1666 | 2109.16 | 79 | <0.001 | 1873 | 2374.38 | 79 | <0.001 |
| | AWE | 276 | 380.19 | 73 | <0.001 | 246 | 400.19 | 61 | <0.001 |

*Note* (a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

**TABLE 6.9b Observed deaths (O), deaths expected from social class specific national rates ($E_s$), and standardised mortality ratios corrected for social class ($SMR_s$) more than 10 years after start of first test participation, together with relative risks (RR) of mortality in test participants compared with controls, by Service and broad cause of death**

| | | Test participants | | | Mortality rate in test participants relative to controls | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cause of death | Service | O | $E_s$ | $SMR_s$ | Prob[a] | RR | 90%CI[d] | Prob[b] one-sided | Prob[c] two-sided |
| All neoplasms | RN | 534 | 538.03 | 99 | 0.86 | 0.98 | 0.88, 1.08 | 0.35 | 0.69 |
| | Army | 299 | 354.11 | 84 | 0.0029 | 1.02 | 0.88, 1.18 | 0.43 | 0.86 |
| | RAF | 578 | 669.89 | 86 | <0.001 | 1.03 | 0.93, 1.14 | 0.32 | 0.63 |
| | AWE | 82 | 108.73 | 75 | 0.0084 | 1.15 | 0.87, 1.52 | 0.22 | 0.44 |
| Other diseases | RN | 929 | 913.55 | 102 | 0.61 | 1.00 | 0.92, 1.07 | 0.47 | 0.94 |
| | Army | 608 | 621.91 | 98 | 0.59 | 1.02 | 0.92, 1.13 | 0.36 | 0.72 |
| | RAF | 953 | 1234.02 | 77 | <0.001 | 0.96 | 0.89, 1.04 | 0.21 | 0.41 |
| | AWE | 182 | 225.90 | 81 | 0.0028 | 1.34 | 1.11, 1.62 | 0.0054 | 0.011 |
| Accidents and violence | RN | 109 | 69.38 | 157 | <0.001 | 1.07 | 0.86, 1.35 | 0.32 | 0.60 |
| | Army | 80 | 60.67 | 132 | 0.017 | 1.31 | 0.93, 1.86 | 0.10 | 0.11 |
| | RAF | 91 | 87.47 | 104 | 0.71 | 1.05 | 0.82, 1.36 | 0.39 | 0.78 |
| | AWE | 8 | 9.13 | 88 | 0.75 | 1.42 | 0.52, 3.96 | 0.36 | 0.60 |
| Unknown | RN | 27 | - | - | - | - | - | - | - |
| | Army | 26 | - | - | - | - | - | - | - |
| | RAF | 44 | - | - | - | - | - | - | - |
| | AWE | 4 | - | - | - | - | - | - | - |
| All causes | RN | 1599 | 1632.43 | 98 | 0.41 | 0.98 | 0.93, 1.04 | 0.33 | 0.65 |
| | Army | 1013 | 1070.14 | 95 | 0.082 | 1.04 | 0.96, 1.12 | 0.22 | 0.45 |
| | RAF | 1666 | 2055.38 | 81 | <0.001 | 0.99 | 0.93, 1.04 | 0.36 | 0.72 |
| | AWE | 276 | 345.01 | 80 | <0.001 | 1.26 | 1.08, 1.47 | 0.0055 | 0.011 |

*Notes*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR > 1.00).

(c) Two-sided test that the RR is different from unity.

(d) Confidence interval.

(e) $E_s$ and $SMR_s$ are based on national mortality rates among men in social class 1 for officers and for AWE employees with jobs in social class 1, and on national mortality rates among men in social class 3 (manual and non-manual combined) for other men.

**TABLE 6.10 Observed deaths (O), deaths expected from national rates (E) and standardised mortality ratios (SMR) among test participants and controls, and relative risks (RR) of mortality in test participants compared with controls, for 27 distinct types of cancer. For leukaemia the whole follow-up period and the period 2 to 25 years after start of first test participation are considered, and for other specific cancers the period more than 10 years after start of first test participation is considered**

| | Test participants | | | | Controls | | | | Mortality rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Type of cancer (ICD Codes 9th Revision) | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] | RR | 90%CI[d] | Prob[b] 1-sided | Prob[c] 2-sided |
| Cancer of the tongue, mouth and pharynx (141, 143-149) | 31 | 26.16 | 119 | 0.38 | 40 | 27.63 | 145 | 0.028 | 0.82 | 0.54, 1.26 | 0.25 | 0.47 |
| Cancer of the oesophagus (150) | 74 | 72.57 | 102 | 0.86 | 83 | 77.21 | 107 | 0.53 | 0.96 | 0.73, 1.26 | 0.43 | 0.86 |
| Cancer of stomach (151) | 90 | 111.99 | 80 | 0.034 | 91 | 120.11 | 76 | 0.0062 | 1.06 | 0.82, 1.37 | 0.37 | 0.73 |
| Cancer of large intestine and rectum (153, 154 excl. 154.3, 159.0) | 172 | 182.78 | 94 | 0.44 | 174 | 194.79 | 89 | 0.14 | 1.05 | 0.87, 1.26 | 0.36 | 0.72 |
| Cancer of liver (155) | 24 | 20.70 | 116 | 0.51 | 17 | 21.95 | 77 | 0.34 | 1.51 | 0.86, 2.68 | 0.13 | 0.21 |
| Primary liver cancer (155.0) | 12 | 11.70 | 103 | 1.00 | 13 | 12.37 | 105 | 0.89 | 0.99 | 0.47, 2.05 | 0.57 | 1.00 |
| Cancer of gallbladder (156) | 2 | 6.46 | 31 | 0.077 | 5 | 6.90 | 72 | 0.57 | 0.39 | 0.06, 1.85 | 0.22 | 0.28 |
| Cancer of pancreas (157) | 72 | 69.36 | 104 | 0.76 | 72 | 73.84 | 98 | 0.86 | 1.04 | 0.78, 1.39 | 0.44 | 0.88 |
| Cancer of larynx (161) | 19 | 15.93 | 119 | 0.45 | 24 | 16.96 | 142 | 0.11 | 0.87 | 0.50, 1.50 | 0.38 | 0.66 |
| Cancer of lung (162, 163) | 466 | 541.83 | 86 | <0.001 | 517 | 580.02 | 89 | 0.0079 | 0.97 | 0.87, 1.08 | 0.31 | 0.61 |
| Cancer of bone (170) | 2 | 3.27 | 61 | 0.60 | 1 | 3.38 | 30 | 0.28 | 2.11 | 0.19, 44.14 | 0.48 | 0.62 |
| Cancer of connective and soft tissue (171) | 5 | 6.90 | 72 | 0.57 | 3 | 7.20 | 42 | 0.13 | 1.79 | 0.45, 7.75 | 0.32 | 0.49 |
| Malignant melanoma (172) | 28 | 16.38 | 171 | 0.0087 | 27 | 16.93 | 159 | 0.028 | 1.09 | 0.68, 1.76 | 0.43 | 0.79 |
| Other skin cancer (173) | 2 | 3.73 | 54 | 0.45 | 0 | 4.00 | 0 | 0.027 | 1.09 | 0.68, 1.76 | 0.17 | 0.17 |
| Cancer of prostate (185) | 106 | 91.76 | 116 | 0.14 | 97 | 100.22 | 97 | 0.76 | 1.20 | 0.94, 1.53 | 0.11 | 0.22 |
| Cancer of testis (186) | 5 | 5.26 | 95 | 1.00 | 3 | 4.89 | 61 | 0.50 | 1.60 | 0.39, 7.13 | 0.39 | 0.71 |
| Cancer of bladder (188, 189.3-189.9) | 50 | 53.22 | 94 | 0.68 | 34 | 57.48 | 59 | 0.001 | 1.64 | 1.11, 2.42 | 0.017 | 0.026 |
| Cancer of kidney (189.0-189-2) | 43 | 39.21 | 110 | 0.58 | 59 | 41.53 | 142 | 0.010 | 0.78 | 0.55, 1.11 | 0.13 | 0.26 |
| Tumours of central nervous system (191, 192, 224, 225, 239.6) | 63 | 61.92 | 102 | 0.90 | 66 | 64.21 | 103 | 0.85 | 0.99 | 0.73, 1.35 | 0.52 | 0.97 |
| Cancer of thyroid (193) | 1 | 2.73 | 37 | 0.38 | 1 | 2.89 | 35 | 0.38 | 1.00 | 0.04, 27.44 | 0.76 | 1.00 |
| Cancer of adrenals (194.0)[e] | 2 | 1.00 | 201 | 0.26 | 2 | 1.03 | 194 | 0.28 | 1.12 | 0.14 , 8.76 | 0.65 | 1.00 |
| Hodgkin's disease (201) | 6 | 9.57 | 63 | 0.27 | 9 | 9.52 | 95 | 0.88 | 0.73 | 0.27, 1.92 | 0.36 | 0.62 |
| Non-Hodgkin's lymphoma (200, 202.0-202.3, 202.5-202.9) | 41 | 44.00 | 93 | 0.71 | 44 | 46.24 | 95 | 0.77 | 0.92 | 0.62, 1.35 | 0.39 | 0.74 |
| Multiple myeloma (203 excl 203.1, 238.6)[f] | 21 | 22.52 | 93 | 0.76 | 18 | 24.03 | 75 | 0.22 | 1.32 | 0.74, 2.37 | 0.24 | 0.43 |
| Leukaemia: whole follow up period | 45 | 46.11 | 98 | 0.88 | 33 | 48.61 | 68 | 0.022 | 1.45 | 0.96, 2.17 | 0.069 | 0.14 |
| Leukaemia: 2-25 yrs (202.4, 203.1, 204-208) | 20 | 16.30 | 123 | 0.38 | 6 | 18.74 | 32 | 0.0011 | 3.38 | 1.45, 8.25 | 0.0056 | 0.0072 |
| Leukaemia excluding CLL: whole follow up period (202.4, 203.1, 204.0, 204.2-207.7 207.9-208.9) | 40 | 37.60 | 106 | 0.68 | 23 | 39.40 | 58 | 0.0066 | 1.83 | 1.15, 2.93 | 0.015 | 0.027 |
| Leukaemia excluding CLL: 2-25 yrs | 18 | 14.66 | 123 | 0.43 | 6 | 16.55 | 36 | 0.0046 | 2.99 | 1.26, 7.41 | 0.014 | 0.019 |
| Polycythaemia vera (238.4)[g] | 1 | 1.08 | 92 | 1.00 | 2 | 1.16 | 173 | 0.64 | 0.54 | 0.03, 5.84 | 0.52 | 1.00 |

| | Test participants | | | | Controls | | | | Mortality rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Type of cancer (ICD Codes 9th Revision) | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] | RR | 90%CI[d] | Prob[b] 1-sided | Prob[c] 2-sided |
| Other specified neoplasms (140-239 excl, above, 196-199 & 239) | 27 | 32 | 84 | 0.38 | 28 | 33.74 | 83 | 0.345 | 1.08 | 0.67, 1.75 | 0.44 | 0.79 |
| Unspecified neoplasms (196-199, 239, excl. 239.6) | 100 | 110.35 | 91 | 0.34 | 134 | 117.93 | 114 | 0.1532 | 0.83 | 0.66, 1.04 | 0.086 | 0.17 |
| All neoplasms excluding non-melanoma skin cancer (140-172, 174-239) | 1491 | 1589.52 | 94 | 0.013 | 1582 | 1694.33 | 93 | 0.0060 | 1.01 | 0.95, 1.07 | 0.37 | 0.78 |
| All neoplasms (140-239) | 1493 | 1593.24 | 94 | 0.011 | 1582 | 1698.32 | 93 | 0.0045 | 1.01 | 0.95, 1.08 | 0.37 | 0.75 |

*Notes for Table 6.10*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.
(b) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).
(c) Two-sided test that the RR is different from unity.
(d) Confidence interval.
(e) Cancers of the adrenal glands are included only from 1958 in the comparison with national rates; no deaths in participants and none in controls occurred before this.
(f) The observed numbers of deaths and relative risk are unchanged for the wider definition of multiple myeloma (ICD 9th revision codes 203.0, 203.1, 238.6 and 273.1).
(g) Polycythaemia vera is included only from 1968 in the comparison with national rates; no deaths in participants and none in controls occurred before this.

**TABLE 6.11 Numbers of incident cancers (I) among test participants and controls, and relative risks (RR) of incident cancer in test participants compared with controls for 27 distinct types of cancer. For leukaemia the whole follow up period, and the period 2-25 years after start of first test participation, are considered. For all other specific cancers the period more than 10 years after start of first test participation is considered**

| | Test Participants | Controls | Incidence rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|
| Type of cancer | I | I | RR | 90% CI[c] | Prob[a] one-sided | Prob[b] two-sided |
| Tongue, mouth, pharynx | 59 | 76 | 0.83 | 0.61, 1.12 | 0.16 | 0.32 |
| Oesophagus | 73 | 82 | 0.94 | 0.71, 1.25 | 0.39 | 0.78 |
| Stomach | 117 | 122 | 1.02 | 0.82, 1.28 | 0.45 | 0.90 |
| Large intestine and rectum | 316 | 326 | 1.02 | 0.90, 1.17 | 0.40 | 0.79 |
| Liver | 33 | 18 | 1.99 | 1.19, 3.38 | 0.012 | 0.016 |
| Primary liver cancer | 22 | 13 | 1.83 | 0.98, 3.46 | 0.058 | 0.090 |
| Gallbladder | 3 | 7 | 0.45 | 0.11, 1.60 | 0.19 | 0.35 |
| Pancreas | 77 | 75 | 1.08 | 0.81, 1.42 | 0.36 | 0.72 |
| Larynx | 49 | 57 | 0.93 | 0.66, 1.30 | 0.39 | 0.78 |
| Lung | 528 | 598 | 0.94 | 0.85, 1.04 | 0.15 | 0.30 |
| Bone | 5 | 5 | 1.16 | 0.35, 3.86 | 0.53 | 1.00 |
| Connective and soft tissue | 9 | 12 | 0.74 | 0.32, 1.65 | 0.32 | 0.53 |
| Malignant melanoma | 55 | 54 | 1.09 | 0.78, 1.53 | 0.36 | 0.71 |
| Other skin cancer | 332 | 395 | 0.89 | 0.78, 1.01 | 0.059 | 0.12 |
| Prostate | 244 | 216 | 1.22 | 1.04, 1.43 | 0.018 | 0.036 |
| Testis | 19 | 21 | 0.84 | 0.47, 1.49 | 0.35 | 0.63 |
| Bladder | 156 | 152 | 1.09 | 0.89, 1.32 | 0.25 | 0.50 |
| Kidney | 71 | 102 | 0.74 | 0.57, 0.96 | 0.030 | 0.060 |
| Tumours of central nervous system | 83 | 77 | 1.13 | 0.86, 1.50 | 0.24 | 0.48 |
| Thyroid | 6 | 3 | 1.92 | 0.51, 7.97 | 0.28 | 0.50 |
| Adrenals | 3 | 2 | 1.64 | 0.28, 11.13 | 0.46 | 0.68 |
| Hodgkin's disease | 15 | 18 | 0.81 | 0.43, 1.54 | 0.34 | 0.60 |
| Non-Hodgkin's lymphoma | 81 | 80 | 1.04 | 0.79, 1.36 | 0.44 | 0.88 |
| Multiple myeloma | 34 | 35 | 1.07 | 0.70, 1.64 | 0.43 | 0.81 |
| Multiple myeloma (wider definition)[d] | 35 | 35 | 1.11 | 0.72, 1.69 | 0.38 | 0.72 |
| Leukaemia: whole follow up period | 67 | 53 | 1.33 | 0.97, 1.84 | 0.072 | 0.15 |
| Leukaemia excluding CLL: whole follow up period | 49 | 36 | 1.41 | 0.96, 2.09 | 0.073 | 0.15 |
| Leukaemia: 2-25 years | 29 | 10 | 3.17 | 1.63, 6.31 | 0.0010 | 0.0018 |
| Leukaemia excluding CLL: 2-25 years | 23 | 6 | 3.97 | 1.73, 9.61 | 0.0014 | 0.011 |
| Polycythaemia vera | 12 | 13 | 0.92 | 0.44, 1.94 | 0.50 | 1.00 |
| Other specified neoplasms | 123 | 142 | 0.92 | 0.75, 1.14 | 0.28 | 0.56 |
| Unspecified neoplasms | 76 | 103 | 0.81 | 0.63, 1.06 | 0.10 | 0.20 |
| All neoplasms excluding non-melanoma skin cancer | 2309 | 2447 | 1.00 | 0.95, 1.05 | 0.47 | 0.95 |
| All neoplasms | 2641 | 2842 | 0.99 | 0.94, 1.03 | 0.31 | 0.62 |

*Notes:*

(a) One-sided test that the RR is greater than unity (RR ≥ 1.00), or less than unity (RR <1.00).

(b) Two-sided test that the RR is different from unity.

(c) Confidence interval

(d) ICD 9th revision codes 203.0, 203.1, 238.6 and 273.1.

**TABLE 6.12 Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) among test participants and controls, and relative risks (RR) of mortality in test participants compared with controls more than 10 years after start of first participation, for causes of death other than neoplasms**

| | Test participants | | | | Controls | | | | Mortality rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cause of death (ICD Codes 9th Revision) | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] | RR | 90%CI[d] | Prob[b] 1-sided | Prob[c] 2-sided |
| **A. Diseases related to smoking** | | | | | | | | | | | | |
| Coronary heart disease (410-414) | 1401 | 1726.92 | 81 | <0.001 | 1516 | 1842.03 | 82 | <0.001 | 0.98 | 0.92, 1.04 | 0.29 | 0.59 |
| Bronchitis, emphysema and chronic obstructive lung disease (491, 492, 496, 519)[e] | 161 | 233.02 | 69 | <0.001 | 173 | 254.97 | 68 | <0.001 | 0.99 | 0.82, 1.20 | 0.49 | 0.99 |
| Aortic aneurysm (441) | 82 | 82.89 | 99 | 0.96 | 86 | 89.58 | 96 | 0.71 | 1.04 | 0.79, 1.36 | 0.44 | 0.87 |
| **B. Diseases related to alcohol** | | | | | | | | | | | | |
| Cirrhosis of liver, alcoholism and alcoholic psychosis (303, 305.0, 291, 571) | 89 | 59.65 | 149 | <0.001 | 99 | 61.98 | 160 | <0.001 | 0.99 | 0.77, 1.28 | 0.51 | 0.98 |
| **C. Other diseases** | | | | | | | | | | | | |
| Infectious and parasitic diseases (1-139) | 18 | 30.40 | 59 | 0.019 | 27 | 31.93 | 85 | 0.43 | 0.73 | 0.42, 1.26 | 0.19 | 0.37 |
| Diseases of nervous system (320-389) | 64 | 76.79 | 83 | 0.15 | 55 | 80.88 | 68 | 0.0027 | 1.27 | 0.92, 1.75 | 0.11 | 0.22 |
| *Motor neurone disease (335.2)* | *16* | *15.81* | *101* | *1.00* | *14* | *16.73* | *84* | *0.55* | *1.21* | *0.62, 2.35* | *0.37* | *0.72* |
| Other diseases of circulatory system (390-459 excl. 410-414, 441) | 504 | 585.83 | 86 | <0.001 | 497 | 632.55 | 79 | <0.001 | 1.09 | 0.98, 1.21 | 0.094 | 0.19 |
| Other diseases of respiratory system (460-519 excl. 491-2, 496, 519) | 142 | 210.69 | 67 | <0.001 | 163 | 228.74 | 71 | <0.001 | 0.95 | 0.78, 1.16 | 0.35 | 0.71 |
| Other diseases of digestive system (520-579 excl. 571) | 90 | 103.19 | 87 | 0.20 | 85 | 110.18 | 77 | 0.013 | 1.14 | 0.88, 1.48 | 0.22 | 0.43 |
| Remaining diseases other than neoplasms (001-799.8 excl. above diseases and 140-239) | 121 | 174.71 | 69 | <0.001 | 137 | 186.75 | 73 | <0.001 | 0.94 | 0.76, 1.17 | 0.34 | 0.69 |
| **D. Accidents and violence** | | | | | | | | | | | | |
| Motor traffic accidents (E810-E819) | 51 | 59.65 | 85 | 0.27 | 54 | 59.01 | 92 | 0.52 | 0.91 | 0.65, 1.29 | 0.36 | 0.73 |
| Drowning and water transport accidents (E830-E838, E910, E984) | 15 | 12.07 | 124 | 0.39 | 13 | 11.96 | 109 | 0.77 | 1.12 | 0.55, 2.27 | 0.46 | 0.84 |
| Air and space transport accidents (E840-E845) | 12 | 1.72 | 699 | <0.001 | 13 | 1.64 | 793 | <0.001 | 0.89 | 0.43, 1.85 | 0.47 | 0.84 |
| Suicide E950-E959 | 84 | 76.87 | 109 | 0.42 | 74 | 77.01 | 96 | 0.73 | 1.14 | 0.86, 1.51 | 0.24 | 0.48 |
| Other injury and poisoning (E800-E999 excl. above) | 126 | 98.69 | 128 | 0.0088 | 102 | 99.59 | 102 | 0.80 | 1.24 | 0.99, 1.56 | 0.063 | 0.13 |
| All known causes, other than neoplasms | 2960 | 3534.10 | 84 | <0.001 | 3094 | 3769.86 | 82 | <0.001 | 1.02 | 0.97, 1.06 | 0.28 | 0.56 |

*Notes for Table 6.12*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).

(c) Two-sided test that the RR is different from unity.

(d) Confidence interval.

(e) ICD code 519 (other diseases of respiratory system) is included as it is impossible to separate deaths attributed to this cause from those attributed to ICD code 496 (chronic airways obstruction, not elsewhere classified) in calculating expected deaths prior to 1979.

**TABLE 6.13(a) Numbers of incident leukaemias (I) among test participants and controls, and relative risk (RR) of incident leukaemia in test participants compared with controls classified by subtype of leukaemia, based on the whole follow-up period**

| | Test participants | Controls | Incident rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|
| Subtype of leukaemia | I | I | RR | 90% CI[c] | Prob[a] one-sided | Prob[b] two-sided |
| Acute myeloid[d] | 29 | 22 | 1.41 | 0.85, 2.35 | 0.15 | 0.26 |
| Chronic myeloid[d] | 12 | 4 | 3.08 | 1.08, 9.62 | 0.035 | 0.048 |
| Acute lymphatic | 5 | 4 | 1.10 | 0.28, 4.30 | 0.59 | 1.00 |
| Chronic lymphatic | 18 | 17 | 1.16 | 0.63, 2.13 | 0.40 | 0.72 |
| Unspecified myeloid | 2 | 0 | ∞ | 0.38, ∞ | 0.22 | 0.22 |
| Unspecified lymphatic | 0 | 1 | 0.00 | 0.00, 7.94 | 0.38 | 0.38 |
| Unspecified acute | 0 | 3 | 0.00 | 0.00, 1.91 | 0.15 | 0.25 |
| Unspecified chronic | 1 | 0 | ∞ | 0.08, ∞ | 0.50 | 1.00 |
| Unspecified | 0 | 2 | 0.00 | 0.00, 3.29 | 0.27 | 0.51 |
| All subtypes | 67 | 53 | 1.33 | 0.97, 1.84 | 0.072 | 0.15 |
| All subtypes other than chronic lymphatic | 49 | 36 | 1.41 | 0.96, 2.09 | 0.073 | 0.15 |

*Notes*

(a) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).

(b) Two-sided test that the RR is different from unity.

(c) Confidence interval.

(d) Monocytic leukaemia has been classed with myeloid.

**TABLE 6.13 (b) Numbers of incident leukaemias (I) among test participants and controls, and relative risk (RR) of incident leukaemia in test participants, based on the period 2-25 years after start of first test participation**

| | Test participants | Controls | Incident rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|
| Subtype of leukaemia | I | I | RR | 90% CI[c] | Prob[a] one-sided | Prob[b] two-sided |
| Acute myeloid[d] | 14 | 4 | 3.52 | 1.24,10.90 | 0.019 | 0.025 |
| Chronic myeloid[d] | 5 | 0 | ∞ | 0.94, ∞ | 0.049 | 0.070 |
| Acute lymphatic | 4 | 1 | 5.47 | 0.69,100.9 | 0.11 | 0.17 |
| Chronic lymphatic | 6 | 4 | 1.90 | 0.55, 6.93 | 0.25 | 0.35 |
| Unspecified acute | 0 | 1 | 0.00 | 0.00,14.47 | 0.53 | 1.00 |
| All subtypes | 29 | 10 | 3.17 | 1.63, 6.31 | 0.001 | 0.002 |
| All subtypes other than chronic lymphatic | 23 | 6 | 3.97 | 1.73, 9.61 | <0.001 | 0.002 |

*Notes*

(a) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).

(b) Two-sided test that the RR is different from unity.

(c) Confidence interval.

(d) Monocytic leukaemia has been classed with myeloid.

**TABLE 6.14 (a) Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) among test participants with and without a recorded gamma dose, for selected causes of death. For leukaemia the whole follow-up period, and the period 2-25 years after start of first test participation are considered. For other neoplasms the period more than 10 years after start of first test participation is considered**

| Cause of death | Test participants with a recorded gamma dose | | | | Monitored test participants with no recorded gamma dose | | | | Mortality rate in monitored test participants with a recorded gamma dose relative to these with no recorded dose | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] | RR | 90%CI[d] | Prob[b] one-sided | Prob[c] two-sided |
| Leukaemia: whole follow up period | 3 | 4.59 | 65 | 0.51 | 8 | 7.99 | 100 | 1.00 | 0.63 | 0.14, 2.48 | 0.39 | 0.73 |
| Leukaemia: 2-25 years | 1 | 1.53 | 65 | 0.75 | 2 | 2.51 | 80 | 0.79 | 1.23 | 0.05, 16.36 | 0.66 | 1.00 |
| Leukaemia excluding CLL: whole follow up period | 3 | 3.62 | 83 | 0.81 | 5 | 6.39 | 78 | 0.70 | 1.10 | 0.22, 5.19 | 0.61 | 1.00 |
| Leukaemia excluding CLL: 2-25 years | 1 | 1.33 | 75 | 1.00 | 1 | 2.23 | 45 | 0.53 | 1.71 | 0.06, 49.30 | 0.61 | 1.00 |
| Multiple myeloma[e]: 10+ years | 5 | 2.38 | 210 | 0.19 | 1 | 4.11 | 24 | 0.14 | 15.95 | 1.74, 313.3 | 0.009 | 0.010 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 121 | 167.35 | 72 | <0.001 | 270 | 285.65 | 95 | 0.36 | 0.86 | 0.70, 1.06 | 0.12 | 0.23 |

*Notes*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).

(c) Two-sided test that the RR is different from unity.

(d) Confidence interval.

(e) The observed numbers of deaths and relative risk are unchanged for the wider definition of multiple myeloma (ICD 9$^{th}$ revision codes 203.0, 203.1, 238.6 and 273.1).

**TABLE 6.14 (b) Number of incident cancers (I) among test participants with a recorded gamma dose to these with no recorded dose, and relative risks (RR) of incident cancers among test participants with a recorded gamma dose compared with no recorded gamma dose. For leukaemia the whole follow-up period, and the period 2-25 years after start of first test participation are considered. For other neoplasms the period more than 10 years after start of first test participation is considered**

| Cause of death | Test participants with a recorded gamma dose | Monitored test participants with no recorded gamma dose | Incidence rate in monitored test participants with a recorded gamma dose relative to these with no recorded dose | | | |
|---|---|---|---|---|---|---|
| | I | I | RR | 90% CI[c] | Probability[a] one-sided | Probability[b] two-sided |
| Leukaemia: whole follow up period | 6 | 10 | 0.83 | 0.29, 2.36 | 0.48 | 0.79 |
| Leukaemia: 2-25 years | 3 | 3 | 2.19 | 0.41, 11.87 | 0.30 | 0.40 |
| Leukaemia excluding CLL: whole follow up period | 3 | 5 | 1.09 | 0.22, 5.00 | 0.61 | 1.00 |
| Leukaemia excluding CLL: 2-25 years | 1 | 1 | 1.71 | 0.06, 49.24 | 0.64 | 1.00 |
| Multiple myeloma[d]: 10+ years | 5 | 3 | 4.91 | 0.94, 26.76 | 0.057 | 0.086 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 225 | 435 | 0.99 | 0.85, 1.16 | 0.49 | 0.98 |

*Notes*

(a) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).
(b) Two-sided test that the RR is different from unity.
(c) Confidence interval.
(d) Values for the wider definition of multiple myeloma (ie. ICD 9$^{th}$ revision codes 203.0, 203.1, 238.6 and 273.1) are identical.

**TABLE 6.15 (a) Observed deaths (O) and expected ($E_I$) for monitored test participants by dose category, for selected types of cancer. For leukaemia the whole follow-up period and the period 2-25 years after start of first test participation are considered. For other neoplasms the period more than 10 years after start of first test participation is considered**

| | | Dose category (mSv) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Type of cancer | | <0.01 | 0.01-0.99 | 1.00-4.99 | 5.00-9.99 | 10.00-49.99 | ≥50.00 | Prob[a] one-sided | Prob[b] two-sided | Direction of trend[c] |
| Leukaemia: whole follow-up period | O | 8 | 1 | 2 | 0 | 0 | 0 | 0.74 | 0.50 | Negative |
| | $E_I$[d] | 7.57 | 1.73 | 0.67 | 0.22 | 0.80 | 0.01 | | | |
| Leukaemia: 2-25 years | O | 2 | 0 | 1 | 0 | 0 | 0 | 0.18 | 0.18 | Negative |
| | $E_I$[d] | 2.19 | 0.47 | 0.20 | 0.08 | 0.05 | 0.00 | | | |
| Leukaemia excluding CLL: whole follow-up period | O | 5 | 1 | 2 | 0 | 0 | 0 | 0.40 | 0.77 | Negative |
| | $E_I$[d] | 5.56 | 1.44 | 0.57 | 0.15 | 0.27 | 0.01 | | | |
| Leukaemia excluding CLL: 2-25 years | O | 1 | 0 | 1 | 0 | 0 | 0 | 0.27 | 0.27 | Positive |
| | $E_I$[d] | 1.30 | 0.41 | 0.17 | 0.07 | 0.05 | 0.00 | | | |
| Multiple myeloma[e]: 10+ years | O | 1 | 2 | 1 | 1 | 1 | 0 | 0.094 | 0.13 | Positive |
| | $E_I$[d] | 3.91 | 0.80 | 0.57 | 0.32 | 0.36 | 0.05 | | | |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | O | 270 | 60 | 20 | 10 | 29 | 2 | 0.84 | 0.32 | Negative |
| | $E_I$[d] | 255.93 | 61.02 | 28.54 | 14.48 | 26.03 | 5.00 | | | |

*Notes for Table 6.15 (a)*

(a) One-sided test that the trend is greater, or less than, zero.

(b) Two-sided test that the trend is greater, or less than, zero.

(c) Negative: Rate tends to decrease with increasing recorded dose. Positive: Rate tends to increase with increasing recorded dose.

(d) $E_I$ is calculated internally, assuming no trend in cancer mortality with dose.

(e) Values for the wider definition of multiple myeloma (ie. ICD $9^{th}$ revision codes 203.0, 203.1, 238.6 and 273.1) are identical.

**TABLE 6.15 (b) Number of incident cancers observed (I) and expected ($E_I$) for monitored test participants by dose category, for selected types of cancer. For leukaemia the whole follow-up period and the period 2-25 years after start of first test participation are considered. For other neoplasms the period more than 10 years after start of first test participation is considered**

| | | Dose category (mSv) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Type of cancer | | <0.01 | 0.01-0.99 | 1.00-4.99 | 5.00-9.99 | 10.00-49.99 | ≥50.00 | Probability[a] one-sided | Probability[b] two-sided | Direction of trend[c] |
| Leukaemia: whole follow- up period | I | 10 | 3 | 2 | 1 | 0 | 0 | 0.92 | 0.15 | Negative |
| | $E_I$[d] | 9.33 | 3.16 | 1.23 | 0.44 | 1.70 | 0.14 | | | |
| Leukaemia: 2-25 years | I | 3 | 2 | 1 | 0 | 0 | 0 | 0.45 | 0.86 | Negative |
| | $E_I$[d] | 4.18 | 1.04 | 0.35 | 0.15 | 0.18 | 0.10 | | | |
| Leukaemia excluding CLL: whole follow-up period | I | 5 | 1 | 2 | 0 | 0 | 0 | 0.52 | 0.94 | Negative |
| | $E_I$[d] | 5.23 | 1.51 | 0.66 | 0.13 | 0.47 | 0.01 | | | |
| Leukaemia excluding CLL: 2-25 years | I | 1 | 0 | 1 | 0 | 0 | 0 | 0.27 | 0.27 | Negative |
| | $E_I$[d] | 1.30 | 0.41 | 0.17 | 0.07 | 0.05 | 0 | | | |
| Multiple myeloma[e]: 10+ years | I | 3 | 2 | 1 | 1 | 1 | 0 | 0.12 | 0.22 | Positive |
| | $E_I$[d] | 5.31 | 1.31 | 0.62 | 0.30 | 0.40 | 0.06 | | | |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | I | 443 | 113 | 41 | 20 | 44 | 8 | 0.57 | 0.85 | Negative |
| | $E_I$[d] | 438.47 | 104.48 | 51 | 25.49 | 40.34 | 9.23 | | | |

*Notes for Table 6.15(b)*

(a) One-sided test that the trend is greater, or less than, zero.

(b) Two-sided test that the trend is greater, or less than, zero.

(c) Negative: Rate tends to decrease with increasing recorded dose. Positive: Rate tends to increase with increasing recorded dose.

(d) $E_I$ is calculated internally, assuming no trend in cancer incidence with dose.

(e) Values for the wider definition of multiple myeloma (ie. ICD $9^{th}$ revision codes 203.0, 203.1, 238.6 and 273.1) are identical.

**TABLE 6.16 (a) Observed deaths (O) and standardised mortality ratios (SMR) for test participants by nature of test participation for selected types of cancer. For leukaemia the whole follow-up period and the period 2-25 years after start of the first test participation are considered. For other neoplasms the period more than 10 years after start of first test participation is considered**

| Type of cancer | Test participants at a major operation (15,634 men) | | | Test participants in groups identified by MOD as liable to exposure to radiation(759 men) (Group A) | | | Test participants employed by AWE or directly involved in the minor trials at Maralinga[a](1,041 men) (Group B) | | | Test participants in Groups A and B, plus other men with a recorded dose greater than zero (2,649 men) | | | Other test participants (5,164 men) | | | All test participants (21,357 men) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | O | SMR | Prob[b] | O | SMR | Prob[b] | O | SMR | Prob[b] | O | SMR | Prob[b] | O | SMR | Prob[b] | O | SMR | Prob[b] |
| Leukaemia: whole follow-up period | 33 | 95 | 0.80 | 1 | 47 | 0.54 | 4 | 123 | 0.78 | 6 | 83 | 0.72 | 11 | 109 | 0.75 | 45 | 98 | 0.88 |
| Leukaemia: 2-25 years | 10 | 85 | 0.67 | 1 | 142 | 1.00 | 1 | 89 | 1.00 | 2 | 81 | 1.00 | 9 | 221 | 0.041 | 20 | 123 | 0.38 |
| Leukaemia excluding CLL: whole follow-up period | 30 | 106 | 0.78 | 1 | 59 | 0.74 | 4 | 159 | 0.33 | 6 | 105 | 1.00 | 9 | 108 | 0.86 | 40 | 106 | 0.68 |
| Leukaemia excluding CLL: 2-25 years | 9 | 85 | 0.65 | 1 | 165 | 0.45 | 1 | 105 | 1.00 | 2 | 93 | 1.00 | 8 | 221 | 0.058 | 18 | 123 | 0.43 |
| Multiple myeloma[c]: 10+ years | 14 | 82 | 0.47 | 1 | 89 | 1.00 | 3 | 173 | 0.43 | 6 | 159 | 0.29 | 6 | 124 | 0.64 | 21 | 93 | 0.76 |
| All neoplasms except leukaemia and multiple myeloma: 10+ yrs | 1083 | 93 | 0.011 | 49 | 62 | <0.001 | 96 | 78 | 0.013 | 210 | 79 | <0.001 | 302 | 91 | 0.11 | 1432 | 93 | 0.0045 |

*Notes*

(a) Those in whom undocumented inhalation or ingestion of radionuclides, if any, is most likely to have occurred.

(b) Probability from two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(c) The observed numbers of deaths are unchanged for the wider definition of multiple myeloma (ICD 9th revision codes 203.0, 203.1, 238.6 and 273.1).

**TABLE 6.16 (b) Observed deaths (O) among test participants and controls, and relative risks (RR) of mortality among test participants compared with controls. For leukaemia the whole follow-up period and the period 2-25 years after start of the first test participation are considered. For other neoplasms the period more than 10 years after start of first test participation is considered**

| Type of cancer | Test participants at a major operation (15,634 men) | | | Test participants in groups identified by MOD as liable to exposure to radiation (759 men) (Group A) | | | Test participants employed by AWE or directly involved in the minor trials at Maralinga[a] (1,041 men) (Group B) | | | Test participants in Groups A and B, plus other men with a recorded dose greater than zero (2,649 men) | | | Other test participants (5,164 men) | | | All test participants (21,357 men) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | O | RR (90% CI) | Prob[b] one/ two | O | RR (90% CI) | Prob[b] one/ two | O | RR (90% CI) | Prob[b] one/ two | O | RR (90% CI) | Prob[b] one/ two | O | RR (90% CI) | Prob[b] one/ two | O | RR (90% CI) | Prob[b] one/ two |
| Leukaemia: Whole follow-up period | 33 | 1.35 (0.87, 2.10) | 0.14, 0.25 | 1 | 0.72 (0.04, 4.81) | 0.62, 1.00 | 4 | 2.38 (0.43, 16.54) | 0.28, 0.40 | 6 | 1.21 (0.45, 3.11) | 0.44, 0.78 | 11 | 1.72 (0.89, 3.25) | 0.096, 0.14 | 45 | 1.45 (0.96, 2.17) | 0.069, 0.14 |
| Leukaemia: 2-25 years | 10 | 2.03 (0.77, 5.50) | 0.13, 0.20 | 1 | 6.02 (0.35, 42.11) | 0.18, 0.18 | 1 | 3.62 (0.04, 264.3) | 0.68, 1.00 | 2 | 2.71 (0.29, 15.68) | 0.29, 0.48 | 9 | 7.63 (2.73, 21.83) | <0.001 <0.001 | 20 | 3.38 (1.45, 8.25) | 0.006, 0.0075 |
| Leukaemia excluding CLL: Whole follow-up period | 30 | 1.72 (1.04, 2.84) | 0.036 , 0.061 | 1 | 0.82 (0.05, 5.79) | 0.67, 1.00 | 4 | 2.69 (0.44, 24.50) | 0.26, 0.40 | 6 | 1.47 (0.51, 4.00) | 0.34, 0.55 | 9 | 2.12 (1.00, 4.39) | 0.061, 0.077 | 40 | 1.83 (1.15, 2.93) | 0.014, 0.029 |
| Leukaemia excluding CLL: 2-25 years | 9 | 1.81 (0.67, 5.02) | 0.20, 0.29 | 1 | 6.02 (0.35, 42.11) | 0.18, 0.18 | 1 | 3.62 (0.04, 264.3) | 0.68, 1.00 | 2 | 2.71 (0.29, 15.68) | 0.29, 0.50 | 8 | 7.01 (2.43, 20.59) | <0.001 <0.001 | 18 | 2.99 (1.26, 7.41) | 0.014, 0.018 |
| Multiple myeloma[c]: 10+ years | 14 | 1.10 (0.57, 2.09) | 0.47, 0.85 | 1 | 1.01 (0.05, 7.63) | 0.68, 1.00 | 3 | 2.07 (0.34, 14.75) | 0.36, 0.64 | 6 | 2.15 (0.74, 5.91) | 0.13, 0.20 | 6 | 1.57 (0.62, 3.83) | 0.24, 0.41 | 21 | 1.32 (0.74, 2.37) | 0.23, 0.42 |
| All neoplasms except leukaemia and multiple myeloma: 10+ yrs | 1083 | 0.99 (0.92, 1.06) | 0.40, 0.79 | 49 | 0.72 (0.55, 0.95) | 0.022 0.044 | 96 | 1.34 (1.04, 1.71) | 0.026 0.052 | 210 | 1.01 (0.88, 1.16) | 0.45, 0.89 | 302 | 0.99 (0.89, 1.10) | 0.45, 0.90 | 1432 | 1.00 (0.94, 1.06) | 0.50, 1.00 |

*Notes for Table 6.16(b)*

(a) Those in whom undocumented inhalation or ingestion of radionuclides, if any, is most likely to have occurred.

(b) Probability from one-sided test that the RR is greater than unity ($RR \geq 1.00$), or less than unity ($RR < 1.00$), followed by the probability from the two-sided test that the RR is different from unity.

(c) Values for the wider definition of multiple myeloma (ie. ICD $9^{th}$ revision codes 203.0, 203.1, 238.6 and 273.1) are identical.

**TABLE 6.16 (c) Numbers of incident cancers (I) among test participants and controls, and relative risks (RR) of incident cancer in test participants compared with controls. For leukaemia the whole follow-up period and the period 2-25 years after start of the first test participation are considered. For other neoplasms the period more than 10 years after start of first test participation is considered**

| Type of cancer | Test participants at a major operation (15,634 men) | | | Test participants in groups identified by MOD as liable to exposure to radiation (759 men) (Group A) | | | Test participants employed by AWE or directly involved in the minor trials at Maralinga[a] (1,041 men) (Group B) | | | Test participants in Groups A and B, plus other men with a recorded dose greater than zero (2,649 men) | | | Other test participants (5,164 men) | | | All test participants (21,357 men) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | I | RR (90% CI) | Prob[b] one/ two | I | RR (90% CI) | Prob[b] one/ two | I | RR (90% CI) | Prob[b] one/ two | I | RR (90% CI) | Prob[b] one/ two | I | RR (90% CI) | Prob[b] one/ two | I | RR (90% CI) | Prob[b] one/ two |
| Leukaemia: Whole follow-up period | 51 | 1.32 (0.93, 1.86) | 0.099, 0.20 | 2 | 0.98 (0.19, 3.78) | 0.67, 1.00 | 7 | 1.21 (0.42, 3.57) | 0.49, 0.78 | 10 | 1.00 (0.48, 2.07) | 0.57, 1.00 | 15 | 1.59 (0.92, 2.71) | 0.087, 0.17 | 67 | 1.33 (0.97, 1.84) | 0.072, 0.14 |
| Leukaemia: 2-25 years | 18 | 2.89 (1.38, 6.15) | 0.0059 0.0074 | 2 | 10.37 (1.84, 44.86) | 0.023 0.023 | 2 | 7.55 (0.25, 2.81) | 0.30, 0.48 | 4 | 3.83 (0.93, 13.59) | 0.064, 0.064 | 10 | 4.50 (1.91, 10.64) | 0.0014, 0.0016 | 29 | 3.17 (1.63, 6.31) | 0.001, 0.0018 |
| Leukaemia excluding CLL: Whole follow-up period | 37 | 1.36 (0.90, 2.07) | 0.12, 0.22 | 1 | 0.57 (0.03, 3.58) | 0.50, 1.00 | 4 | 0.88 (0.23, 3.37) | 0.56, 1.00 | 6 | 0.80 (0.30, 2.01) | 0.43, 0.81 | 11 | 1.79 (0.93, 3.39) | 0.086, 0.15 | 49 | 1.41 (0.96, 2.09) | 0.073, 0.15 |
| Leukaemia excluding CLL: 2-25 years | 13 | 3.00 (1.19, 7.86) | 0.018, 0.033 | 1 | 5.66 (0.33, 38.91) | 0.19, 0.19 | 1 | 4.97 (0.04, 342.2) | 0.67, 1.00 | 2 | 2.79 (0.29, 16.12) | 0.28, 0.49 | 9 | 7.89 (2.85, 22.43) | <0.001, <0.001 | 23 | 3.97 (1.73, 9.61) | 0.0013, 0.0017 |
| Multiple Myeloma: 10+ years | 24 | 0.99 (0.62, 1.59) | 0.54, 1.00 | 2 | 1.10 (0.19, 4.77) | 0.59, 1.00 | 3 | 1.17 (0.23, 6.15) | 0.58, 1.00 | 7 | 1.32 (0.54, 3.14) | 0.35, 0.61 | 9 | 1.19 (0.58, 2.38) | 0.38, 0.68 | 34 | 1.07 (0.70, 1.64) | 0.43, 0.81 |
| Multiple Myeloma (wider definition)[c]: 10+ years | 25 | 1.04 (0.65, 1.65) | 0.50, 0.90 | 2 | 1.10 (0.19, 4.77) | 0.59, 1.00 | 3 | 1.17 (0.23, 6.15) | 0.58, 1.00 | 7 | 1.32 (0.54, 3.14) | 0.35, 0.61 | 9 | 1.19 (0.58, 2.38) | 0.38, 0.68 | 35 | 1.11 (0.72, 1.69) | 0.38, 0.71 |
| All neoplasms except Leukaemia and Multiple Myeloma: 10+ yrs | 1928 | 0.98 (0.93, 1.03) | 0.23, 0.45 | 100 | 0.83 (0.69, 1.00) | 0.052 0.10 | 171 | 1.21 (1.01, 1.46) | 0.041 0.081 | 381 | 1.01 (0.91, 1.11) | 0.47, 0.94 | 537 | 0.95 (0.88, 1.03) | 0.15, 0.30 | 2545 | 0.98 (0.94, 1.03) | 0.23, 0.46 |

*Notes for Table 6.16(c)*

(a) Those in whom undocumented inhalation or ingestion of radionuclides, if any, is most likely to have occurred.

(b) Probability from one-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00), followed by the probability from the two-sided test that the RR is different from unity.

(c) ICD 9$^{th}$ revision codes 203.0, 203.1, 238.6 and 273.1.

**Table 6.17 Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) among independent responders known at the time of the previous analysis, for selected causes of death, by calendar period**

| Cause of death | Calendar period up to 28 February 1993 | | | | Calendar period 1 March 1993 to 31 December 1998 | | | |
|---|---|---|---|---|---|---|---|---|
| | O | E | SMR | Probability[a] | O | E | SMR | Probability[a] |
| All neoplasms | 64 | 20.14 | 318 | <0.001 | 16 | 10.58 | 151 | 0.12 |
| Leukaemia | 2 | 0.66 | 302 | 0.14 | 2 | 0.24 | 832 | 0.025 |
| Leukaemia excluding CLL | 2 | 0.57 | 349 | 0.11 | 1 | 0.18 | 557 | 0.16 |
| Multiple myeloma[b] | 2 | 0.26 | 763 | 0.029 | 0 | 0.16 | 0 | 1.00 |
| Other neoplasms | 60 | 19.26 | 311 | <0.001 | 14 | 10.37 | 135 | 0.27 |
| Other diseases | 48 | 43.01 | 112 | 0.45 | 23 | 18.88 | 122 | 0.35 |
| Accidents and violence | 1 | 7.20 | 14 | 0.0093 | 2 | 0.77 | 259 | 0.18 |
| Unknown | 2 | - | - | - | 1 | - | - | - |
| All causes | 115 | 70.40 | 163 | <0.001 | 42 | 30.28 | 139 | 0.045 |

*Notes*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) The observed numbers of deaths are unchanged for the wider definition of multiple myeloma.

# 7 DISCUSSION

## 7.1 General considerations

In the previous analysis of mortality and cancer incidence among UK nuclear weapons test participants, based on follow-up to the end of 1990, it was concluded that participation in the nuclear weapon testing programme had not had a detectable effect on the participants' expectation of life, or on their risk of developing cancer or other fatal diseases (Darby *et al*, 1993a,b). Furthermore, the suggestion from the first analysis (Darby *et al*, 1988a,b) that participants may have experienced small hazards of leukaemia and multiple myeloma was considered not to have been supported by the extra seven years of follow-up included in the second analysis, and that the excesses of these diseases observed in the first analysis appeared to have been chance findings. However, Darby *et al* (1993a,b) could not completely rule out the possibility that test participation may have caused a small risk of leukaemia in the early years after the tests. In a 1995 report, the US Advisory Committee on Human Radiation Experiments (ACHRE, 1995) suggested that the findings of the first analysis for leukaemia and multiple myeloma might represent an unexpectedly large "healthy soldier effect" or, possibly methodological bias. However, a member of ACHRE explained later that when the ACHRE report was written, the committee was not aware of the second analysis and that their "brief commentary on this study was based on incomplete information" and "it was not certainly not our intention to discredit this very well designed study" (Thomas, 1998).

The following discussion will consider the extent to which the longer follow-up, to the end of 1998, and the totality of the evidence might modify the previous conclusions.

While the nature of the nuclear weapons tests has prompted suggestions that radiation exposure might have affected the health of test participants (eg. Rabbitt Roff, 1999a), the study design aims to detect effects of test participation on mortality and cancer, whatever the cause. Nevertheless, the fact that radiation is a known carcinogen has prompted several analyses that investigate whether radiation might be a possible cause of putative health effects. It must be acknowledged that if the radiation doses recorded for test participants at the time of their involvement are a fair reflection of the broad levels of exposure, then it would not be expected that effects associated with such small doses could be observed. The investigators have encountered no evidence that the recorded doses are substantial under-estimates. Nevertheless, they have conducted analyses that should have been able to detect raised risks if, in fact, doses to the groups most likely to have been exposed had been much larger than recorded.

In spite of the above points, the possibility must be considered of an effect on health of test participation that is caused by an agent other than radiation. In this context, the findings from studies of non-UK participants in nuclear weapons tests may be informative, and are considered below. The identity of any hazardous factor other than radiation that is associated with test participation is likely to depend on the disease in question. However, in the case of multiple myeloma and leukaemia, there is limited information on other risk factors (Herrinton *et al*, 1996).

## 7.2 Multiple myeloma

The current analysis was initiated because of concerns raised about a possible raised level of multiple myeloma among test participants, based on records for just over 2,000 British servicemen in the British Nuclear Tests Veterans Association (BNTVA) (Rabbitt Roff, 1999a,b). In order better to understand any differences between the data on this disease held by NRPB and researchers at the University of Dundee, an intercomparison of these data was conducted. It should be emphasised that the analysis presented in the current report would not have been expected to have included all cases of multiple myeloma among men thought to have participated in the UK nuclear weapons test programme. This is because,

- the study cohort, whilst free of bias, contains most but not all eligible test participants;
- in order to be able to compare cancer rates among test participants and controls and to make comparisons with national mortality rates, it is essential to have well-defined cohorts for whom information on mortality and cancer incidence is obtained in a standard manner; and:
- adding extra men or adding follow-up data to the test participant cohort using a different approach from that used for the control cohort or on the basis of whether or not someone has developed a disease would lead to bias.

Among men confirmed as having participated in the tests and who were known to NRPB, the intercomparison between NRPB and the University of Dundee did not identify any extra myeloma registrations up to the end of 1994, nor extra deaths up to the end of 1998 with myeloma listed on the death certificate. Furthermore, a few additional test participants were identified in the intercomparison, to a level consistent with the estimated coverage of participants in the NRPB cohort (ie. 85%). These men were added to the list of independent responders, but not to the NRPB cohort, which is restricted to men identified from searches of archival material without knowledge of disease status. In addition, analysis of independent responders notified by the time of the last analysis did not show any additional myeloma deaths in the period between that time and the end of 1998. The approach taken here means it should be possible

to make valid comparisons of rates in the cohort of test participants with rates in the controls and with national mortality rates.

On the advice of the Advisory Group, it was decided to include all cancer registrations up to the end of 1998 amongst men in the test participant and control cohorts, on the basis that – whilst this information is not complete – it was collected in the same way for the two groups. Furthermore, the geographical distribution of participants and controls among health authorities appears to be similar, so indicating that any geographical variations in the registration of more recent cancers are unlikely to have biased the findings of this analysis. It was also decided to consider a wider grouping for multiple myeloma, so as to encompass diseases that do not fall within the standard definition of the disease. However, this had little influence on the analysis; the wider grouping included one extra case (in a test participant) and no additional deaths. An additional modification in the myeloma analyses presented here was to include deaths with myeloma recorded as secondary cause and another cancer listed as primary cause of death. It should be emphasised that any cases among participants identified from, for example, War Pensions tribunals could not be put into the analysis, because of the lack of comparable data for the controls. However, the checks conducted, including a comparison of data with an independent registry of haematological diseases, indicated that myeloma cases are not generally being under-recorded.

The current analysis has shown that, over the full period of follow-up, there was little evidence of a raised risk of multiple myeloma among test participants, relative either to national mortality rates (SMR 96), or to rates of myeloma mortality or incidence among the controls. Comparing participants with controls, the precision of the relative risk for mortality was somewhat limited (RR 1.32, 90% CI 0.74-2.37), but was greater in the corresponding incidence analysis, owing to the larger numbers of cases (RR 1.14, 90% CI 0.74-1.74). Omitting the first ten years following initial test involvement provided similar results. Whilst the first analysis of UK test participants showed a significantly raised risk of myeloma relative to controls, based on follow-up to the end of 1983 (Darby *et al*, 1988a,b), this finding was not repeated in the following seven year follow-up reported by Darby *et al* (1993a,b). The findings for myeloma mortality up to the end of 1990 reported in the second analysis are essentially the same as those described in the current report. There are some differences between the results for myeloma incidence over this period given here and those in the previous report (Darby *et al*, 1993b), reflecting the late registration of some cases and re-classification of a few others where myeloma was a secondary but not a primary cause of death. The relative risk for myeloma incidence up to the end of 1990, whilst similar to that in the previous report, just attained statistical significance in the current analysis (RR 2.05, 90% CI 0.99-4.30, one-sided p=0.05, two-sided p=0.08). In contrast, there was little or no indication of raised levels of myeloma from 1991 onwards among test participants compared to controls, with

RRs of 1.21 (90% CI 0.58-2.53) for mortality and 0.79 (90% CI 0.45-1.38) for incidence. Furthermore, myeloma mortality among test participants during the period 1991-98 was similar to that expected from national rates (SMR 114). There was some indication that SMRs for myeloma in test participants varied between different time periods after first test involvement, but there was no trend in SMRs over the full follow-up period.

Myeloma rates were also studied in several sub-groups of test participants. In groups identified by MOD as liable to exposure to radiation and in men in whom undocumented inhalation or ingestion of radionuclides, if any, is most likely to have occurred, rates of myeloma were consistent with national rates and those among controls, although the numbers of cases were small. The risk of myeloma mortality among men with a recorded dose was significantly greater than that among other participants monitored for radiation exposure (RR 16, 90% CI 1.74-314, one-sided p=0.009, two-sided p=0.01, based on five deaths in the former group and one death in the latter group), although the evidence for a difference between these two groups was weaker in the corresponding incidence data (RR 4.91, 90% CI 0.94-26.8, one-sided p=0.057, two-sided p=0.086, based on five cases among men with a recorded dose and three cases among other monitored men). Further analysis of monitored participants showed weak evidence of an increasing trend in myeloma mortality with gamma dose (one-sided p=0.094, two-sided p=0.13), which was weaker still in the corresponding incidence data (one-sided p=0.12, two-sided p=0.22). The interpretation of the results for monitored participants is complicated by the small numbers of myelomas in the analyses and by indications that mortality among monitored participants with no recorded gamma dose might be lower than national rates (SMR 24, based on one death in this group).

Results from other studies are relevant to the interpretation of the above findings. In the report of the first analysis (Darby *et al*, 1988a,b), particular weight was given to the findings for myeloma, largely because of the indications at that time from the Japanese atomic bomb survivors and some other studies of an association between radiation and multiple myeloma. However, by the time of the second analysis (Darby *et al*, 1993a,b), the evidence for a link from these studies had become weaker. In particular, after a review of diagnoses, the trend with dose in the risk of myeloma incidence among the Japanese atomic bomb survivors was not statistically significant (Preston *et al*, 1994), in contrast to analyses of mortality in the same group (Pierce *et al*, 1996). Results for groups with medical or occupational radiation exposures have been inconsistent (UNSCEAR, 2000), although there was some indication of an increasing trend in risk with dose in the recent NRPB analysis of UK radiation workers (Muirhead *et al*, 1999). Overall, the present evidence for an association between radiation and myeloma is weak (UNSCEAR, 2000). Given that the recorded gamma doses for test participants in the current study are generally much lower than those in the studies cited above, that the numbers of myelomas in the dose trend

analysis are small, and that various sub-groups have been considered, it seems likely that the results for men with a positive gamma dose are due to chance.

Multiple myeloma rates have also been studied in other groups of nuclear weapons test participants. In a study of approximately 70,000 US military personnel who took part in at least one out of five selected US nuclear weapons test series in Nevada or the Pacific in the 1950s (Institute of Medicine, 2000), mortality from multiple myeloma was slightly less than national rates (SMR 80, based on 82 deaths) and was compatible with that in a matched control group (RR 1.10, 95% CI 0.79-1.52). Results have been reported from other studies of US test participants. Among over 38,000 US Navy personnel who took part in Operation Crossroads, held in 1946 at Bikini Atoll in the Pacific (Johnson *et al*, 1996), myeloma mortality was consistent with that in a matched control group (RR 0.89, 95% CI 0.55-1.45). In a study of about 8,500 US Navy veterans who took part in Operation Hardtack I in 1958 in the Pacific (Watanabe *et al*, 1995), myeloma deaths were proportionally not greater than expected from national rates, nor were they higher than expected from a matched control group, although there were only two deaths observed. Among 528 men from New Zealand who participated in UK atmospheric nuclear weapons tests in the Pacific (Pearce *et al*, 1997), there was one myeloma death observed compared with 0.3 expected from national rates; compared to a matched control group, the relative risk was 1.4 (90% CI 0.1-180). The corresponding findings for myeloma incidence among the New Zealand participants were one case observed compared with 0.5 expected from national rates, and a relative risk of 0.7 (90% CI 0.0-5.3) compared to matched controls. Thus, even though some of these studies were small, they do not show raised risks of multiple myeloma.

Various epidemiological studies have been conducted in an attempt to learn more about factors other than radiation that might influence the induction of multiple myeloma. These studies have generally not shown strong associations; there have some suggestions of a link with chemicals, but the data do not always allow specific types of chemicals to be identified (Herrinton *et al*, 1996). Baseline rates of multiple myeloma in England and Wales increased amongst persons aged over 70 years during 1960s-1980s, but were more stable at younger ages over this period, and have been stable at all ages in more recent years (Swerdlow *et al*, 2001); the earlier increase may have reflected improved ascertainment of the disease in the elderly. It should be emphasised that baseline rates of multiple myeloma increase with increasing age and that, as evidenced in the current study, it would be expected that numbers of cases would increase among both test participants and controls as these men get older.

Taken overall, the results from this analysis do not indicate an association between participation in the UK nuclear weapons test programme and the risk of

multiple myeloma. In particular, there is no indication of an increase in myeloma rates among participants in recent years, other than would be expected as men born at the same time reach older ages. Although previous analyses of this cohort reported a raised risk of myeloma in the early years following test participation, compared to rates in the control group, it seems likely - as suggested by Darby *et al* (1993a,b) - that this was a chance finding. Analyses of subgroups with greater potential for exposure provided little evidence of increased risks, although the numbers of men involved were smaller and the statistical power was therefore less.

## 7.3 Leukaemia

The risk of leukaemia has been shown to be increased in various populations exposed to radiation, such as the Japanese atomic bomb survivors and several groups who received exposures for medical reasons. Recent reviews of the relevant literature include those by UNSCEAR (2000) and NRPB (2000). These studies have linked each of the main sub-types of leukaemia with radiation, with the exception of chronic lymphatic leukaemia (CLL). Furthermore, it has been shown that risks tend to start to increase within a few years of exposure and are largely expressed within the period up to around 20-30 years following exposure. Consequently, several of the analyses conducted here have examined leukaemia excluding CLL and the period 2-25 years following first test participation. However, there are some indications that the temporal pattern of radiation-induced leukaemia varies according to age at exposure and to the sub-type of the disease, with longer latency periods for exposure in adulthood than in childhood, and for myeloid leukaemia than for acute lymphocytic leukaemia (which is rare in adults) (Preston *et al*, 1994; Little *et al*, 1999). Consequently, raised risks of leukaemia other than CLL may persist more than 25 years after exposure, although at a lower level than in the earlier period.

Most of the information linking radiation exposure of adults and leukaemia relates to relatively high doses, received either acutely or in fractions. However, analyses of the relationship between radiation dose and leukaemia in the Japanese atomic bomb survivors are consistent with a linear-quadratic dose-response trend down to low doses, such that the risk per unit dose at low doses is smaller than at higher doses (Preston *et al*, 1994; Pierce *et al*, 1996). These data are consistent with the absence of a dose-threshold below which risks are not increased (Little *et al*, 1998). Direct confirmation of raised leukaemia risks from low dose exposures is difficult, owing to problems with low statistical power and the potential for bias or confounding. Nevertheless, studies of radiation workers have indicated an association between occupational radiation exposure and the risk of leukaemia, of a magnitude consistent with that predicted from the Japanese A-bomb data (Cardis *et al*, 1995; Muirhead *et al*, 1999). Furthermore, there has been some suggestion from these worker studies that any link with

radiation is stronger in analyses of leukaemia excluding CLL, rather than of all leukaemias combined.

The doses received by participants in nuclear weapons tests are likely, in the main, to be lower than those received by radiation workers employed for many years in the nuclear industry. In particular, among the 1,716 UK participants with a non-zero recorded radiation dose, the mean dose was about 10 mSv, and only 81 participants were recorded as having received 50 mSv or more, whereas the approximately 125,000 UK radiation workers in the UK National Registry for Radiation Workers had a mean dose of 30 mSv and doses ranging up to over 500 mSv (Muirhead *et al*, 1999). Furthermore, in contrast to studies of radiation workers, only a minority of weapons test participants have recorded radiation doses, so making it harder still to detect raised leukaemia risks related to radiation amongst these men. However, given that any effect of test participation might be due to factors other than radiation, it is important in the context of the current analysis to consider results from other studies of nuclear weapon test participants. In the "Five Series Study" of about 70,000 US military personnel who took part in at least one out of five selected US nuclear weapons test series in Nevada or the Pacific in the 1950s (Institute of Medicine, 2000), leukaemia mortality was less than national rates (SMR 74, based on 185 deaths), with some weak evidence of a raised risk relative to a matched control group (RR 1.15, 95% CI 0.93-1.43); similar results were obtained for leukaemia excluding CLL. Among over 38,000 US Navy personnel who took part in Operation Crossroads, held in 1946 at Bikini Atoll in the Pacific (Johnson *et al*, 1996), leukaemia mortality was similar to that in a matched control group (RR 1.02, 95% CI 0.75-1.39). In a study of about 8,500 US Navy veterans who took part in Operation Hardtack I in 1958 in the Pacific (Watanabe *et al*, 1995), leukaemia deaths were proportionally not greater than expected from national rates, nor were they higher than expected from a matched control group, although only six deaths were observed amongst these participants. In contrast, among 528 men from New Zealand who participated in UK atmospheric nuclear weapons tests in the Pacific (Pearce *et al*, 1997), there were four leukaemia deaths observed compared with 0.8 expected from national rates, whilst the relative risk compared to a matched control group was 5.6 (90% CI 1.0-41.7); the corresponding relative risk for leukaemia incidence among the New Zealand participants was very similar to that for mortality. Thus, although the numbers of leukaemias in some of these studies were small, there are suggestions from the New Zealand study and, to a lesser extent, the US Five Series Study of a raised risk of leukaemia.

The first analysis of the cohort of UK test participants identified a raised risk of leukaemia relative to controls (Darby *et al*, 1988a,b), which is reflected in the results presented in the current report for the period 2-25 years after first test participation. For example, the relative risk for leukaemia mortality over this period was 3.38 (90% CI 1.45-8.25). However, Darby *et al* (1988a,b) drew

attention to the difficulty in interpreting this result, given that mortality rates in participants were only slightly above national levels, whilst control rates were substantially below them. In the current analysis, the SMRs for participants and controls over the period 2-25 years after first test participation were 123 and 32 respectively. Unlike some other types of cancer, it is unclear which factors might give rise such low leukaemia rates in the controls, other than perhaps chance. During the extra follow-up for the second analysis, the relative risk for leukaemia decreased as the SMR for the controls increased (Darby *et al*, 1993a,b). In particular, the SMRs over the period up to the end of 1990 among participants and controls were 100 and 56 respectively (RR 1.75, 90% CI 1.01-3.06), with little indication of a raised risk during the extra follow-up period for the second analysis, ie. 1984-90 (Darby *et al*, 1993a,b).

Over the additional eight years of follow-up for the current analysis, mortality from leukaemia of all types among test participants was similar to that expected from national rates and to that among the controls. However, during this period, there was a greater suggestion of a raised rate among test participants compared with controls when CLL was excluded from the mortality analysis (RR 1.81, 90% CI 0.80-4.18) or when incidence data were studied (RR 1.37, 90% CI 0.86-2.22 for all leukaemias). The difference between the SMRs for all leukaemias over the full follow-up period to the end of 1998 was smaller than that in the periods of the previous analyses (values of 98 in test participants and 68 in controls), although there was still some evidence of a raised rate in participants compared with controls (RR 1.45, 90% CI 0.96-2.17). The evidence for a difference in mortality was stronger after excluding CLL (RR 1.83, 90% CI 1.15-2.93), although this reflected in part a low SMR for controls (ie. 58, compared with 106 for test participants). In addition, the relative risk for leukaemia incidence was similar both to that for leukaemia mortality and for the incidence of leukaemia excluding CLL, with RR values of about 1.3-1.4 that were just short of conventional levels of statistical significance.

Among leukaemia sub-types, the evidence for a higher risk among test participants compared with controls was greatest for CML and, to a lesser extent, AML. Studies of the Japanese atomic bomb survivors and of some medically-exposed groups have shown that both of these leukaemia sub-types and ALL can be induced by radiation (Preston *et al*, 1994; Little *et al*, 1999). It should be noted that the precision of the ALL analysis is more limited than that of the AML and CML analyses, owing to the smaller number of cases of the former sub-type compared with the latter two. In contrast, even though there were more cases of CLL than ALL in the analysis, there was little to suggest a higher rate of CLL among test participants compared with controls. This result should be viewed in the light of findings from various studies of groups exposed to radiation, which have not shown a raised risk of CLL (UNSCEAR, 2000). The comparison of data of haematological neoplasms held by NRPB for the current study with data held by LRF showed generally good agreement in the assessment of leukaemia sub-

types. An exception concerned LRF's classification of some cases coded by the NHSCRs as NHL, which LRF listed as being CLL. However, not only are these diseases similar, but also there is little evidence that either of them can be induced by radiation (UNSCEAR, 2000). Consequently, the analyses of leukaemia excluding CLL that have been presented here as a means of focussing on putative radiation effects should not have affected by disease misclassification.

Leukaemia risks were examined in several sub-groups of test participants. There was no evidence of raised risks among men with a recorded dose, or of an increasing trend in risk with increasing gamma dose among monitored test participants, although the numbers of cases in these analyses were limited. Among men who were in groups identified by MOD as liable to exposure to radiation, employed by AWE, were directly involved in the minor trails at Maralinga and/or had a recorded dose greater than zero, leukaemia rates were not noticeably raised relative to national rates, nor was there clear evidence that risks relative to controls were higher among these men than among test participants overall, although the data were sparse. In contrast, amongst other test participants who – in addition – were not present at a major operation, there was evidence of raised leukaemia risks compared with controls, which was stronger over the period 2-25 years following test participation than over whole follow-up period. This latter finding is similar to that reported by Darby *et al* (1988a,b) for the same group of test participants over the period to the end of 1983; however, Darby *et al* (1988a,b) were unable to highlight any characteristics that distinguished these cases of leukaemia excluding CLL from other test participants. Finally, there was no single test operation at which leukaemia risks were particularly raised, although again the small numbers limited inferences.

It is notable that, even though the relative difference between leukaemia rates in test participants and controls appears to have narrowed with increasing follow-up, there is still some evidence of a raised risk among participants relative to controls. Given that mortality in controls is still low relative to national rates, the possibility of a chance finding cannot be ruled out. Nevertheless, the evidence for a raised risk appeared to be stronger when CLL – which does not appear to be radiation-inducible – was excluded from the analyses. In addition, studies of nuclear test participants in the USA and New Zealand have in some instances indicated a small raised risk of leukaemia. Furthermore, studies of the Japanese atomic bomb survivors and some medically-exposed groups indicate that, whilst risks of radiation-induced leukaemia tend to be concentrated within about the first two or three decades following exposure, risks may persist over a longer period, although the doses in these studies are generally much higher than those to test participants. Taken overall, the current analysis indicates that the possibility that test participation has caused a small risk of leukaemia other than CLL cannot be ruled out and that, whilst the evidence for any risk appears

to have been greatest in the early years after the tests, a small risk might have persisted in more recent years.

## 7.4 Other cancers

It is known from epidemiological studies of the Japanese atomic bomb survivors and studies of patients who received high radiation doses that radiation can induce a wide range of different cancers (UNSCEAR, 2000). Indeed, there are only a few cancer types for which there is little or no evidence of an association with radiation, eg. Hodgkin's disease. There are some indications of differences between cancer types in their sensitivity to induction from radiation exposure, as measured by the relative increase in risk per unit dose (UNSCEAR, 2000). However, particularly for exposures in adulthood, the largest difference appears to arise between leukaemia and solid cancers generally, with smaller differences between different types of solid cancers (Pierce *et al*, 1996; UNSCEAR, 2000). Consequently, in the current analysis, both results for individual cancer types and for all cancers combined have been studied. Analyses were also conducted for all cancers excluding non-melanoma skin cancer, because of the low level of registration of such skin cancers. However, the findings for this grouping were similar to those for all cancers combined.

The interpretation of results for specific cancer types other than leukaemia and multiple myeloma requires some care since, simply by chance, one would expect to find about one or two findings that are significant at the 5% level when analysing data for more than 20 cancer types. Indeed, there were significant differences between the test participants and controls only for bladder cancer (increased among participants) based on mortality data, and for liver and prostate cancer (both increased among participants) plus kidney cancer (increased among controls) based on incidence data. Amongst these findings, only for liver cancer incidence was there evidence of differences in rates between participants and controls in both the earlier period of follow-up and in the additional period. However, the statistical significance of the liver cancer incidence results was slightly weaker when primary liver cancer was analysed, as a means of reducing the impact of metastatic cancers originating in other sites. As background to these results, it should be noted that studies of the Japanese A-bomb survivors and of groups who received high radiation doses for medical reasons have shown raised risks of bladder and liver cancer, whereas the evidence for a link between radiation and prostate cancer is weaker (UNSCEAR, 2000). Also, whilst alcohol can affect rates of liver cancer, possibly via the development of cirrhosis (London and McGlynn, 1996), mortality from cirrhosis and other alcohol-related diseases other than cancer was similar among test participants and controls, although raised relative to national rates.

Mortality for specific cancer types among both test participants and controls was usually less than expected from national rates, sometimes to a statistically significant extent. However, for all cancers combined, mortality among both test participants and controls was closer to national rates during the most recent eight years of follow-up than in the period of the previous analysis. This may reflect a "wearing off" of the healthy worker effect at long periods after the start of employment in the services or at AWE. There was a suggestion that mortality from all cancers combined might be higher among participants than controls in the most recent period (RR 1.07, 90% CI 0.98-1.17, one-sided p=0.09, two-sided p=0.18), but the corresponding incidence data showed similar rates in the two groups (RR 1.01, 90% CI 0.95-1.07). Results for a grouping of cancers related to smoking were fairly similar to those for all cancers combined, suggesting that smoking habits have not biased the comparisons of participants and controls. Among men monitored for radiation exposure or who had potential for exposure, risks of cancers other than leukaemia and multiple myeloma were generally not raised. Consequently, in line with studies of US and New Zealand test participants (Institute of Medicine, 2000; Pearce *et al*, 1997), there is little evidence from the current analysis to indicate that test participation has influenced the induction of cancer generally.

## 7.5 Non-cancer diseases and other causes of death

Most of the evidence relating radiation to health effects occurring years or decades subsequently concerns the induction of cancer. However, in recent years, further follow-up of the Japanese atomic bomb survivors has pointed to raised risks of mortality from non-cancer diseases (Shimizu *et al*, 1999). Whilst the evidence for such an effect is strongest at doses in excess of about 0.5 Sv, it is unclear at present whether risks might persist down to low radiation doses. Furthermore, it would appear than that any risks of non-cancer diseases at low doses would not exceed the corresponding cancer risks (Shimizu *et al*, 1999). Nevertheless, it is worth examining results for non-cancer mortality in the current study.

Both for non-cancer diseases in total and for specific disease groupings, mortality was similar among test participants and controls. In particular, this held for diseases related to smoking, so indicating that smoking habits have not affected comparisons of the two groups. As with cancer overall, SMRs for non-cancer diseases appeared to be higher in the most recent period of follow-up than in the earlier period, again pointing to a wearing-off of the healthy worker effect. However, even during this recent period, mortality from all non-cancer diseases combined was still significantly less than national rates among test participants and controls (SMRs of 86 in both groups).

Mortality from all accidents and violence was also similar among test participants and controls, although here the rates were raised relative to national rates (SMRs of 121 and 116 respectively over the full follow-up period ) and there was more evidence among controls than participants of a decrease in SMRs over time. Among individual causes, there was an excess of mortality among participants relative to controls for a category entitled "other injury and poisoning", in common with the previous analysis (Darby *et al*, 1993a,b). However, since there was no clear pattern among the deaths in this category, this result is likely to be due to chance, associated with analysing data from many different causes of death. A study of UK Gulf War veterans provided some indication of a raised risk of mortality from accidents and violence, relative to a matched control group (Macfarlane *et al*, 2000). Whilst it was suggested by Macfarlane *et al* (2000) that this finding might have reflected differences between Gulf War veterans and controls in their perception of risk or in activities that they undertook subsequently, it should be emphasised that the period following operations covered by the Gulf War study is much shorter than the follow-up in the current study.

Studies of nuclear test participants from US and New Zealand have generally not shown raised risks of deaths from causes other than cancer (Institute of Medicine, 2000; Pearce *et al*, 1997). In common with those results, there is little or no evidence from the current analysis to indicate that test participation has influenced mortality from non-cancer causes.

# 8 CONCLUSIONS

This third analysis of men from the UK who participated in the UK nuclear weapon tests programme has shown that overall levels of mortality and cancer incidence in test participants have continued to be similar to those in a matched control group. Furthermore, overall levels of mortality in both test participants and controls were still lower than expected from national rates, although this difference has narrowed with longer follow-up. There was no evidence of an increased risk of multiple myeloma among test participants in recent years; rates of this disease were similar in test participants and controls, and mortality among participants was consistent with national rates. In view of the equivocal nature of the evidence linking multiple myeloma with radiation exposure, it is concluded – in line with the second analysis – that the possible risk of myeloma among test participants identified in the first analysis is likely to have been a chance finding. Analyses of subgroups with greater potential for exposure provided little evidence of increased risks, although the numbers of men involved were smaller and the statistical power was therefore less.

In common with earlier analyses, there is some evidence of a raised risk of leukaemia among test participants relative to controls, particularly when focussing on leukaemia other than CLL, although the relative difference in rates between the two groups appears to have narrowed with increasing follow-up. Whilst this difference might represent a chance finding, given that mortality in controls was low relative to national rates, some studies of nuclear test participants in the USA and New Zealand have indicated a small raised risk of leukaemia. In addition, studies of the Japanese atomic bomb survivors and of some medically-exposed groups indicate that risks of radiation-induced leukaemia may persist more than two or three decades following exposure, although the doses in these studies are generally much higher than those recorded for test participants. Taken overall, the possibility that test participation caused a small absolute risk of leukaemia other than CLL among men from the UK cannot be ruled out; the evidence for any increased risk appears to have been greatest in the early years after the tests, but a small risk may have persisted in more recent years.

# 9 ACKNOWLEDGEMENTS

The authors gratefully acknowledge the contributions made by the following organisations and individuals to this analysis: Professor Nicholas Wald and other members of the Advisory Group set up to oversee this analysis (a list of members is given in Appendix F); the staff of the Ministry of Defence and the Atomic Weapons Establishment who assisted in the collection of data; the organisations that provided follow-up information, including the Office for National Statistics, the General Register Offices for Scotland and Northern Ireland, the General Register Office of Ireland, the Benefits Agency of the Department of Social Security, the Central Services Agency of the Northern Ireland Department of Health and Social Services, the Northern Ireland Cancer Registry, the Health Departments in Dublin, Guernsey, Jersey and the Isle of Man, MOD Medical Statistics and AEA Technology; Sue Rabbitt Roff (University of Dundee) for taking part and sharing her data in the multiple myeloma intercomparison; Mrs Sheila Gray for representing the British Nuclear Tests Veterans Association on the Advisory Group; the Leukaemia Research Fund Centre for Clinical Epidemiology for their participation in the comparison of haematological diagnoses; Dr Anne Braidwood (Veterans Agency) for facilitating a check on diagnoses and Professor Ray Cartwright (LRF) for reviewing this material; and Dr Andrew Wotherspoon (Royal Marsden), for providing advice on diseases related to multiple myeloma. The substantial contributions made by Professors Sarah Darby and Sir Richard Doll (Cancer Research UK) to the setting up of this study and to conducting the first two analyses are also gratefully acknowledged. The analysis was funded by the Ministry of Defence.

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# 11 ABBREVIATIONS AND ACRONYMS USED

| | |
|---|---|
| ACHRE | (US) Advisory Committee on Human Radiation Experiments |
| AERE | Atomic Energy Research Establishment |
| ALL | Acute Lymphatic Leukaemia |
| AML | Acute Myeloid Leukaemia |
| AWE | Atomic Weapons Establishment (formerly Atomic Weapons Research Establishment) |
| BEIR | (US Committee on the) Biological Effects of Ionizing Radiation |
| BNTVA | British Nuclear Tests Veterans Association |
| CI | Confidence Interval |
| CLL | Chronic Lymphatic Leukaemia |
| CML | Chronic Myeloid Leukaemia |
| CSA | Central Services Agency of Northern Ireland Department of Health and Social Services |
| DSS | Department of Social Security |
| GRO(S) | General Register Office for Scotland |
| ICD | International Classification of Diseases |
| LHA | Local Health Authority |
| LRF | Leukaemia Research Fund |
| MM | Multiple Myeloma |
| MOD | Ministry of Defence |
| NAAFI | Navy, Army and Air Force Institute |
| NHS | National Health Service |
| NHSCR | National Health Service Central Register |
| NRPB | National Radiological Protection Board |
| NWTPS | Nuclear Weapons Test Participants Study |
| ONS | Office for National Statistics (formerly the Office for Population Censuses and Surveys) |
| RAAF | Royal Australian Air Force |
| RAF | Royal Air Force |
| RM | Royal Marines |
| RN | Royal Navy |
| RNVR | Royal Naval Volunteer Reserve |
| RNZN | Royal New Zealand Navy |
| RR | Relative Risk |
| SMR | Standardised Mortality Ratio |
| SRO | Service Record Office |
| Sv, mSv | Sievert, millisievert (units of radiation dose) |
| UNSCEAR | United National Scientific Committee on the Effects of Atomic Radiation |
| WHO | World Health Organisation |

# 12 ANNEX SUMMARY OF CLASSIFICATION OF MULTIPLE MYELOMA CASES IDENTIFIED BY NRPB AND THE UNIVERSITY OF DUNDEE

*NB. A detailed description of the intercomparison between NRPB and the University of Dundee is given in Appendix A.*

There was a total of 73 cases in the intercomparison. Of these, 28 were known to both NRPB and Dundee, 15 were known to NRPB database but were not on the Dundee list, and 30 were on the Dundee list but not on the NRPB list. Details of the first two of these three groups are given in Table A2 (see Appendix A) and also in Figure 1 below. Since NRPB had information for much larger group of participants than did Dundee, it was not surprising that NRPB would know of some myeloma cases that Dundee did not. The categories into which the 30 cases on the Dundee list but not on the NRPB list fall can be summarised as follows (see also Figure 1).

*Do the men fall within the definition of test participants?*

Four men in the Dundee list clearly fell outside the definition of the NRPB cohort because they were not in the Army, Navy, RAF or AWE. The service records for a further five individuals did not confirm test involvement. These nine men constitute category (a) in Figure 1.

*Was there sufficient data to trace the men at the SROs?*

There were two men on the Dundee list who were potential test participants but for whom the Service Record Offices (SROs) were unable to trace their records owing to a lack of information (see category *(b)* in Figure 1). It should be noted that, in the course of constructing the NRPB cohort, Darby *et al* (1988b) reported that 3% of servicemen suspected of being participants could not be traced at the SROs.

*Are they in the NRPB cohort?*

Of the 47 men on the Dundee list who were confirmed test participants traced at the SROs, nine were not included in the main NRPB cohort. Of these nine men, three were independent responders previously known to NRPB, and for whom NRPB had a record of myeloma. Of the remaining six men (see category *(c)* in Figure 1), five were independent responders identified in the course of the intercomparison, and one was an independent responder known to NRPB for whom there was no record of myeloma on the NRPB database and who was stated by Dundee to be a post-1994 case. As pointed out in sections 2.1 and 2.5 of the report, it was not possible to obtain a complete listing of all test participants from MOD records when constructing the NRPB cohort. Consequently, it is not surprising that some of the confirmed test participants on the Dundee list are not in the main NRPB cohort. However, the estimated

coverage of test participants in the NRPB cohort based on the Dundee list is 38/47, ie. 81%, is similar to the value of 85% estimated previously.

*Have myelomas been recorded in the period of follow-up?*

Information on deaths up to the end of 1998 is thought to be complete (see section 4.3). The intercomparison did not identify any additional myeloma deaths in the NRPB cohort during this period.

Cancer incidence data are thought to be largely (of the order of 90%) complete up to the end of 1994. Three men in the NRPB cohort were reported by Dundee as having developed myeloma in the period since 1994, and the date of diagnosis for another man was unknown. At the time of the intercomparison, NRPB did not have registrations for these four men (who are included within category *(d)* in Figure 1).

*Have they been recorded with myeloma whilst resident in the UK?*

One myeloma death identified by Dundee occurred overseas. However, the NRPB follow-up is restricted to the UK, and therefore deaths overseas are not included. ONS had previously informed NRPB that this man had been lost to follow-up (he is included within category (d) in Figure 1).

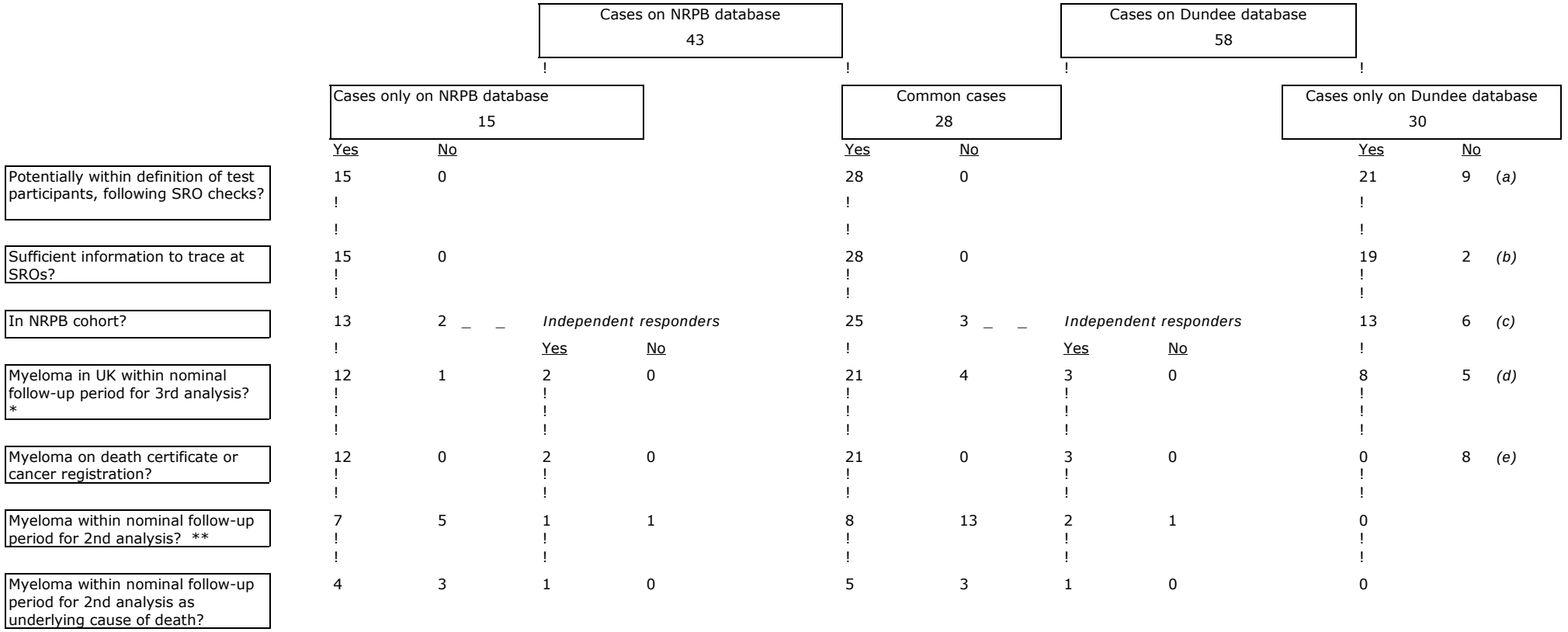
*Is myeloma recorded on the death certificate or on a cancer registration?*

For eight men on the Dundee list, NRPB has death certificates that do not mention myeloma; nor does NRPB have registrations of myeloma for these men. Three of them were recorded on the death certificate as having had the unrelated condition, myeloid dysplasia, and Dundee had a statement (but not a death certificate) relating to myeloma for another three men in this group. Further details are given in Appendix A. The eight men constitute category (e) in Figure 1.

*Conclusions*

This investigation did not bring to light additional death certificates or cancer registrations with multiple myeloma among test participants known to NRPB, during the period for which mortality and cancer data are thought to be largely complete. Furthermore, of the 47 men identified by Dundee who were confirmed test participants, 38 were included in the NRPB cohort; this proportion is similar to that estimated previously based on data for independent responders (ie. 85%). Since corresponding data are not available for the control group, none of the multiple myeloma cases identified by Dundee, but not NRPB, could be added to the NRPB database without leading to bias.

**Figure 1 Classification of multiple myeloma cases identified by NRPB and Dundee** (*Note: Italicised letters are referenced in text of Annex.)*




* *Taken as being the period over which data should be largely complete, ie. to the end of 1998 for mortality and to the end of 1994 for incidence.*

** *Taken as being the period over which data should have been largely complete, ie. to the end of 1990 for mortality and to the end of 1987 for incidence.*

# APPENDIX A

# INTERCOMPARISON OF CASES OF MULTIPLE MYELOMA HELD BY NRPB AND THE UNIVERSITY OF DUNDEE

**J A O'Hagan, C R Muirhead, D Bingham, G L C Berridge and G M Kendall**

## A1 Background

Three epidemiological analyses have now been undertaken of mortality and cancer incidence among over 20,000 UK participants in the UK atmospheric nuclear weapons test programme and a similar number of controls. The first analysis (Darby *et al*, 1988a,b) was based on follow-up to the end of 1983; the second analysis (Darby *et al*, 1993a,b) involved follow-up to the end of 1990; and the current analysis extended the follow-up to the end of 1998. In each instance, information on deaths and cancer registrations was supplied principally by the National Health Service Central Registers (NHSCRs), with validation checks carried out using, for example, data provided by the Department of Social Security (DSS). However, the processing by the NHSCRs of cancer registrations is slower than for deaths. In particular, at the time of the second analysis, data processing by the NHSCRs was finished only for cancers diagnosed up to the end of 1987, and there was some indication that not all of these registrations had been passed to NRPB (Darby *et al*, 1993b). As regards the third analysis, the Office for National Statistics indicated in mid-2000 that the cancer incidence data as of that time appeared to be largely complete up to the end of 1994 (Quinn, 2000).

Based on records for just over 2,000 British servicemen in the British Nuclear Tests Veterans Association (BNTVA), Sue Rabbitt Roff of the University of Dundee reported that she had identified increased numbers of deaths from and cases of multiple myeloma, both prior to 1991 and in more recent years (Rabbitt Roff, 1999).

In order to make a further comparison between myeloma rates among the test participants and the controls, and between these groups and national rates, the Ministry of Defence (MOD) commissioned NRPB in 1999 to conduct the analysis reported here. At its first meeting in November 1999 an Advisory Group - set up for this analysis under the Chairmanship of Professor Nicholas Wald - recommended that attempts should be made to compare the two sets of multiple myeloma data held by Sue Rabbitt Roff and NRPB. This followed an earlier

statement from Professor John Kaldor (a corresponding member of the Advisory Group) who, in a report prepared in 1999 on behalf of the Australian Government (Kaldor, 1999), recommended that:

"Formal contact should be established with the NRPB and Sue Rabbitt Roff to propose that cross-matching of the two sets of multiple myeloma cases be undertaken."

This appendix describes the aims, procedures and findings of the intercomparison between NRPB and the University of Dundee.

## A2 Aims

To investigate quantitatively the reasons for any discrepancy between the multiple myeloma data held by S Rabbitt Roff at the University of Dundee and by NRPB. To examine the implications for the new analysis, particularly regarding the mechanism of follow-up and the assessment of completeness of the study cohort.

## A3 Procedures

A meeting took place at NRPB, Chilton on 14 September 2000, at which data on multiple myeloma held by NRPB and the University of Dundee were compared. The attendees were as follows.

| | |
|---|---|
| *NRPB*: | Dr G M Kendall, Dr C R Muirhead, Dr D Bingham, Mrs J A O'Hagan, Mrs G L C Berridge |
| *BNTVA*: | Mrs S Gray |
| *University of Dundee*: | Ms S Rabbitt Roff |

Sue Rabbitt Roff supplied a listing of 58 men which was compared with NRPB data. NRPB had a listing containing details of 43 men (38 in the study cohort and 5 independent responders) with multiple myeloma on the death certificate, either as the underlying or a contributory cause; or a cancer registration for multiple myeloma. NRPB also had on-line access to their database to check details held for anyone on the Dundee listing.

## A4 Summary of findings

The men on the Dundee list can be categorised as follows.

- Twenty-eight records matched exactly as being on both listings of multiple myeloma.

- In eight cases, the individual was unknown to NRPB and there was no obvious reason why he was not eligible for inclusion in the study – provided that test participation could be confirmed. In the report of the previous analysis (Darby *et al*, 1993b), it was estimated that about 15% of test participants had not been included in the NRPB cohort. *Subsequent checking of MOD records showed that, of the eight individuals, four could be added to the independent responder database as confirmed test participants (ie. men identified on the basis of information supplied independently of MOD, whose participation was confirmed by MOD records); service records for another three individuals showed no indication of test participation; and the remaining individual could not be traced at the Service Record Offices.*

- Four Dundee cases were reported as recent notifications, ie. after 1994. They matched against NRPB records that did not have multiple myeloma recorded on the database. NRPB understands from the Office for National Statistics (ONS) that cancer notification data as of mid-2000 were largely complete only up to 1994 (Quinn, 2000).

- One man was marked 'lost to follow-up' on the NRPB database, as reported by ONS; the Dundee researchers had a death certificate showing that he died overseas, of multiple myeloma. NRPB follow-up is restricted to the UK.

- Eight cases matched with records for which NRPB held death certificates but which did not include multiple myeloma as a cause of death. In addition, no multiple myeloma registrations were held by NRPB for any of these cases. Consequently, these cases are not included in the NRPB analyses of myeloma mortality, which are based on equivalent data held for participants and the control group. For three out of the eight cases, Dundee had statements relating to multiple myeloma. A fourth man, known to have died in 1992, was a recent addition to the Dundee list and details regarding his reason for inclusion on the list were not available at the time of the inter-comparison; his death certificate, held by NRPB, did not include multiple myeloma. In three of the remaining four cases, the death certificate included the unrelated condition, myeloid dysplasia. The fourth was coded for carcinoma of the spine.

- There was one further man in the NRPB cohort where Dundee had a report of myeloma that NRPB did not. NRPB did not hold a death certificate for this man. The date of the diagnosis reported by Dundee is not known.

- Three cases were identified within NRPB's data, but the MOD Service Record Offices (SROs) had been unable to trace the relevant records, because NRPB had been unable to supply sufficient information. *Two of these men were independent responders, ie. they were identified as potential test participants independently of MOD sources. Subsequent checking of MOD records led to*

*two of the three men being traced. One of these men was confirmed as a test participant, while there is no evidence to suggest that the other man was a participant. The man whose participation was confirmed as a consequence of the extra information arising from the intercomparison had already been identified within NRPB's data but was previously untraced at the SROs. Consequently, in line with standard practice for men traced using information from independent sources, this man was added to the list of independent responders.* As background, it was noted in the report of the 1st analysis (Darby *et al*, 1988b) that about 3% of servicemen suspected of being test participants could not be traced at the SROs.

- Four cases fell outside the definition of the NRPB study population:
  - one man had been on HMS Newfoundland, a ship which was not actively involved in tests;
  - one man had been at Woomera and was therefore not actively involved in tests;
  - one man was employed by the Merchant Navy; and
  - one man was employed by the Meteorological Office.
- One record cited by the Dundee researchers matched with an independent responder whose record, supplied by the SRO, did not show test involvement.

Tables A1 and A2 summarise the classification of deaths and cases, according to whether they fell in the period of the previous (ie. second) analysis, the period of the extended follow-up, or subsequently. The cited follow-up periods differ between deaths and cancer registrations, because ONS generally reports registrations later than deaths. In particular, it was mentioned in the report of the second analysis (Darby *et al*, 1993b) that processing of cancer registrations at ONS was complete only for cases up to the end of 1987, whereas deaths were available up to the end of 1990. Nevertheless, all cancer registrations received for the period up to the end of 1990 were included in the second analysis because, whilst this information was not complete for 1988-1990, it was collected in a comparable manner for both the participant and control groups.

Table A1 shows that the number of deaths with myeloma as underlying cause in the NRPB cohort during the period of the previous analysis is the same as that reported in Table 6.1 of Darby *et al* (1993b), ie. a total of nine deaths. Table A2 shows a total of 16 myeloma registrations and deaths (either as underlying or contributory cause) in the NRPB cohort during the period of the previous analysis. Of these 16 men,

- were included in Table 6.4 of Darby *et al* (1993b);

- one was a 1986 registration that was received too late for inclusion in the previous analysis (although a 1988 registration for another man was received in time and was included in Table 6.4 of Darby *et al* (1993b));
- one man had another type of cancer as underlying cause of death and was classified as such in the previous analysis;
- one man was in a group judged to have no more potential for radiation exposure than the general public, for which mortality (but not incidence) findings were reported separately in Appendix A of Darby *et al*, (1993b); and
- Dundee had a report of myeloma for one man whose death certificate – held by NRPB - did not mention myeloma.

## A5 Actions arising from the intercomparison

The following actions were implemented following the intercomparison.

I. NRPB undertook further investigation of the eight men not on the NRPB database, but who would be eligible if test participation were confirmed. NRPB submitted details for all eight men to the MOD SROs. The service records, when traced, confirmed that four of these men could be added to the independent responder database as confirmed test participants. Service records were traced for a further three men, but there was no evidence of test participation. Records for the remaining man could not be traced at the SROs.

II. NRPB performed epidemiological analyses of multiple myeloma and related diagnoses, based on death certificates and cancer registrations, as part of the third analysis. Further details are given in the main part of this report.

III. NRPB included cases of myeloma and lymphoma recorded as contributory cause of death when studying the incidence of these diseases in the third analysis (see main part of the report).

IV. NRPB included results for both mortality and cancer incidence in the group of participants judged to have no more potential for radiation exposure than the general public, within the third analysis report (see Appendix C).

V. With regard to the myeloma cases identified in the intercomparison, the Advisory Group recommended that NRPB's analyses should be restricted to myelomas identified solely via the standard follow-up procedures (see Section 3 of the main report), and that identified cases registered in the period up to and including 1998 should be included. Descriptive information on the cases identified by NRPB only, by Dundee only, and by both NRPB and Dundee is presented in Tables A1 and A2 below.

## A6 Acknowledgements

The authors wish to thank Sue Rabbitt Roff (University of Dundee) and Sheila Gray (British Nuclear Tests Veterans Association) for their cooperation, and the Office for National Statistics, the General Register Offices of Scotland and Northern Ireland, and the Northern Ireland Cancer Registry for giving their approval to the use of their cancer registration data in this comparison.

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**TABLE A1 Classification of deaths in the multiple myeloma intercomparison**

| | | Number on both the Dundee and NRPB lists | Number on NRPB list but not on Dundee list | Number on Dundee list but not on NRPB list | TOTAL |
|---|---|---|---|---|---|
| **1.** | **NRPB cohort** | **16** | **11** | **5** | **32** |
| (i) | in period of previous analysis (up to 31.12.1990) | 4 | 5 [a] | 0 | |
| (ii) | in period of extended follow-up (in period 1.1.1991-31.12.1998) | 10 | 4 | 4 [b] | |
| (iii) | in period after 31.12.1998 | 2 | 2 | 1 [c] | |
| **2** | **Independent responders** | **1** | **1** | **2** | **4** |
| (i) | in period of previous analysis (up to 31.12.1990) | 1 | 1 | 2 [d] | |
| (ii) | in period of extended follow-up (in period 1.1.1991-31.12.1998) | 0 | 0 | 0 | |
| (iii) | in period after 31.12.1998 | 0 | 0 | 0 | |
| **3** | **Other men** | **0** | **0** | **11** | **11** |
| (i) | potentially within definition of test participants | 0 | 0 | 6 [e] | |
| (ii) | outside definition of test participants | 0 | 0 | 5 [f] | |
| *TOTAL* | | ***17*** | ***12*** | ***18*** | ***47*** |

*Notes:*

(a) Includes one man who died within 3 years of his first test participation. He was therefore excluded from the lagged analyses in Darby *et al* (1993b) (eg Table 6.9), but was included in the unlagged analyses (eg Table 6.1).

(b) Four men where NRPB and Dundee hold the same death certificate, and the disease codings do not include multiple myeloma.

(c) One death that occurred overseas, where NRPB had recorded 'lost to follow-up (NRPB follow-up is restricted to the UK)

(d) Two men who were matched amongst NRPB independent responders, but whose records had not been traced previously at the SROs owing to insufficient information for the other record to be traced.

(e) One of these men was identified within NRPB's data, but his record had not been traced previously at the SROs. His participation was confirmed subsequently as a consequence of extra information arising from the intercomparison, and he was added to the list of independent responders. Records for the remaining five men were traced by the SROs, with test participation confirmed in two instances and no evidence of participation found in the other three cases.

(f) Includes one independent responder where no evidence of test participation has been identified.

**NB** The mortality study reported in Darby *et al* (1993b) considered underlying cause of death only and so, to enable comparisons, the NRPB numbers in this table are based on underlying cause only. Table A2, in common with the incidence analysis reported in Darby *et al* (1993b), includes both underlying and contributory cause of death, as well as cancer registrations.

**TABLE A2 Classification of cases and deaths in the multiple myeloma intercomparison**

| | | Number on both the Dundee and NRPB lists. | | | Number on NRPB list but not on Dundee list. | | | Number on Dundee list but not on NRPB list. | | | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Death[a] | Cancer[b,c] | | Death[a] | Cancer[b,c] | | Death[a] | Cancer[b,d] | |
| **1.** | **NRPB cohort** | **25** | | | **13** | | | **13** | | | **51** |
| (i) | in period of previous analysis[e] | | 7[j] | 1[k] | | 5[l] | 2[h,m] | | 0 | 1[q] | |
| (ii) | in extended period[f] | | 10 | 3[*] | | 3 | 2[h,n] | | 4[o] | 3 | |
| (iii) | in subsequent period[g] | | 1 | 3 | | 1 | 0 | | 1[p] | 4[i] | |
| **2** | **Independent responders** | **3** | | | **2** | | | **4** | | | **9** |
| (i) | in period of previous analysis[e] | | 1 | 1[r] | | 1 | 0 | | 2[s] | 0 | |
| (ii) | in extended period[f] | | 0 | 1 | | 0 | 1 | | 0 | 0 | |
| (iii) | in subsequent period[g] | | 0 | 0 | | 0 | 0 | | 0 | 2[i,t] | |
| **3** | **Other men** | **0** | | | **0** | | | **13** | | | **13** |
| (i) | potentially within definition of test participants | | 0 | 0 | | 0 | 0 | | 5[u] | 2[w] | |
| (ii) | outside definition of test participants | | 0 | 0 | | 0 | 0 | | 5[v] | 0 | |
| ***TOTAL*** | | ***28*** | | | ***15*** | | | ***30*** | | | ***73*** |

Notes:

a Included in this period as result of details on death certificate, either as the underlying or a contributory cause.
b Included in this period as result of cancer details. Men reported to have died from myeloma during the same period are excluded from this group.
c Includes only cancer registrations provided by the NHSCRs.
d Includes statements of multiple myeloma obtained by Dundee.
e Includes cases up to 31.12.1987 and deaths up to 31.12.1990.
f Includes cases between 1.1.1988 and 31.12.1994 and deaths between 1.1.1991 and 31.12.1998 (excluding men in category (i)).
g Includes cases since 31.12.1994 and deaths since 31.12.1998 (excluding men in categories (i) and (ii)).

h Includes men (3 in total) whose cancer incidence registrations include them, as multiple myeloma cases, in an earlier analysis than would arise on the basis of their death certificate.

i Includes men (5 in total) reported by Dundee as recent cases. NRPB would not expect to have received all recent registrations by the time of the intercomparison. One of these men had not been traced at SRO due to insufficient data being available. One further man is included in this category, as his date of diagnosis is unknown.

j Includes one man who was not included as a myeloma case in the 2nd analysis, as multiple myeloma was included on his death certificate as a contributory cause to another cancer. The disease coding selection process used for the 2nd analysis is discussed more fully in section 3.2a of Darby *et al* (1993a). It should be noted that for the same reason, two men in the control group were not counted as myeloma cases in the 2nd analysis.

k One man whose multiple myeloma registration falls within the period covered by the 2nd analysis. However, there was an unusually long delay in reporting this 1986 registration, which was not received by NRPB until after the 2nd analysis.

l Includes one man who died within 3 years of his first test participation. He was therefore excluded from the lagged analyses in Darby *et al* (1993b) (eg. Table 6.9), but was included in the unlagged analyses (eg. Table 6.1).

m Includes one man who was excluded from the main analysis in the last report, as he was part of the group judged to have had no more potential for radiation exposure than the general public. This group is discussed in more detail by Darby *et al* (1993b) (section 2.2d and Appendix A). He does not appear in the tables in Appendix A of that report, as his is an incidence case and the tables showed deaths only. Appendix C of the current report does include findings on cancer incidence in this group.

n Includes one man whose cancer incidence registration (in 1988) would have included him in the time period for the 3rd analysis. He died in the period of the 2nd analysis, but his death certificate does not include multiple myeloma. In fact this man was included in the incidence analysis for the last report, as his registration had been notified quickly.

o Four men where NRPB and Dundee hold the same death certificate, and the disease codings do not include multiple myeloma.

p One man who died overseas and therefore falls outside NRPB follow-up. NRPB follow-up is restricted to the UK.

q One man who died within the period of the previous analysis, but without myeloma mentioned on the death certificate.

r One man whose death certificate does not include multiple myeloma.

s Two men who were matched amongst NRPB responders, but whose records had not been traced at the SROs due to insufficient data being available. Subsequently, one record was traced by MOD, but there was no evidence of participation. There was still insufficient information for the other record to be traced.

t Includes a man within NRPB's data who was previously untraced by SROs but whose participation was confirmed as a consequence of extra information arising from the intercomparison. He has been added to the list of independent responders.

u These five men were traced by the SROs, with test participation confirmed in two instances and no evidence of participation found in the other three cases.

v Includes one independent responder where no evidence of test participation has been identified.

w Service records confirming test participation have been traced for both of these men.

# APPENDIX B

# COMPARISON OF DATA ON HAEMATOLOGICAL MALIGNANCIES HELD BY NRPB AND THE LEUKAEMIA RESEARCH FUND

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## B1 Background

Data on mortality and cancer incidence in the NRPB study of UK nuclear weapons test participants and controls (NWTPS) are obtained principally from the National Health Service Central Registers (NHSCRs). The Register offices and regional cancer registries, which supply the NHSCRs with death and cancer data respectively, provide data for all of Great Britain. Certificates for deaths arising since the start of the study (1950s) are available from NHSCRs and the national system of recording cancer registrations was in effective operation from 1971.

The Leukaemia Research Fund (LRF) Data Collection Study (DCS) for haematological neoplasms was set up in 1983 as a source of data on haematological neoplasms independent of the information collected by the regional cancer registries. It covers a population of over eleven million persons in the areas of Yorkshire, Lancashire, Cumbria, Hampshire, Isle of Wight, Dorset and Wiltshire (Cartwright *et al*, 1990). The diagnoses of cancer in the DCS are the subject of detailed review (Cartwright *et al*, 1990, 1997). Consequently, the diagnoses for persons in the DCS should be more accurate than those on death certificates or in details of cancer registrations. However, the temporal and geographical coverage of the DCS means that not it is not possible to cross-check all the haematological neoplasms recorded in the NWTPS.

## B2 Aims

To look for any systematic differences between the data held by NRPB and LRF on haematological neoplasms among test participants and controls. Samples of records without haematological neoplasms would also be sent to LRF to check the completeness of data on the NWTPS. Any differences among the test participants and their controls and the LRF data would be examined, and the

likely impact of any such differences on the analyses using the NRPB data assessed.

## B3 Methods

Data for the following groups of persons were sent to LRF:

(A) All persons in the participant and control cohorts recorded on 1 September 2000 as having a haematological neoplasm, as underlying or contributory cause of death, or with a cancer registration for such a neoplasm, based on data held by NRPB (478 men). Details for 32 independent responders in this category were also sent to LRF. On the NWTPS databases, causes of death and cancer registrations are coded to the 9$^{th}$ or 10$^{th}$ revision of the International Classification of Diseases (ICD). Haematopoietic neoplasms were selected using ICD-9 codes 200 – 208 (malignancies) and 238.4, 238.5, 238.6 and 238.7 (non-malignant neoplasms) and ICD-10 codes C81-C96 (malignancies) and D45, D46 and D47 (non-malignant neoplasms).

(B) A 10% sample of participants and a 10% sample of controls recorded on 1 September 2000 as having another type of cancer, based on underlying or contributory cause of death, or a cancer registration for such a neoplasm, according to data held by NRPB (543 men). LRF were also sent details for 9 independent responders in this category.

(C) A 2% sample of participants and a 2% sample of controls recorded on 1 September 2000 as having died, but without mention of cancer on the death certificate and without a cancer registration (141 men). One independent responder in this category was sent to LRF.

(D) A 2% sample of participants and a 2% sample of controls not recorded on 1 Sep 2000 as having died, and not having a cancer registration (650 men). Details of 7 independent responders in this category were sent to LRF.

Consequently, records were checked for 1,861 men in total. Identifying information included:

- full name,
- date of birth,
- date of death (where applicable),
- NHS number (old and new),

- address(es) (with dates, although the latest address was not always available).

Information on participant/control status and on the NRPB follow-up was not provided to LRF, in order that the comparison could be performed blind.

For each person, LRF was asked:

(a) whether they held a registration of a haematological malignancy, and;

(b) if so, the corresponding diagnosis, ICD-9 or ICD-10 site code and date.

Based on the replies provided by LRF, NRPB analysed the number of registrations among each of the groups (A) to (D) specified above.

NWTPS and LRF cancer details were initially compared on the basis of ICD site coding and the resulting cancer diagnosis that would used in the NWTPS incidence analysis. For NWTPS records, cancer registration data was taken in preference to mentions of cancer on the death certificate, as in the analysis (see Section 3.3). The ICD-9 groupings used to select haematopoietic cancers in the NWTPS analysis are given in Table B1. In cases where ICD-10 codes were provided, these were translated to ICD-9 codes using tables supplied by the World Health Organisation.

A comparison of LRF and NWTPS cancer data was also made on the basis of the diagnosis supplied by LRF and the diagnosis from NWTPS records. LRF diagnoses are based on the latest internationally accepted classifications of haematological malignancy (Cartwright *et al*, 1990) and so differ from the ICD classifications used to categorise cancers for the NWTPS analysis (Table B1).

## B4 Results

### B4.1 Matching of Submitted Study Members to LRF Registry

A total of 1861 records were submitted to LRF, who matched 75 records to persons on the LRF register (Table B2). Proportionally more controls were matched to the LRF registry than either participants ($p = 0.002$, $\chi^2$ test) or independent responders ($p = 0.03$, $\chi^2$ test) (Table B2). All the matching cases were part of Group A, i.e. had been reported as having a haematological neoplasm as a cancer registration or cause of death according to NWTPS records. Of the 75 men matched, 66 had a cancer registration for a haematological neoplasm on the NWTPS and 55 of the men had died.

### B4.2 Comparison, by ICD Site Code, of NWTPS and LRF Cancer Data

For the 66 men with cancer registrations on the NWTPS, the NWTPS cancer site code matched exactly with the site code according to LRF for 36 men. For the 9 men with only death certificate data, the ICD site code on the certificate matched the LRF cancer site code in 5 cases. Thus there were 34 cases where NWTPS and LRF site codes differed. However, when the cancer diagnoses derived from the ICD codes, using the classifications in Table B1, were compared there were only 15 differences between the NWTPS and LRF (Table B3). Thus many of the 34 differences in ICD coding did not affect the cancer that would be ascribed in the analysis.

### B4.3 Comparison, by Diagnosis, of NWTPS and LRF Data

Results of the comparison of diagnoses supplied by LRF and those used in NWTPS are shown in Table B4. Comparisons of diagnoses provided by LRF with those on NWTPS were complicated because the diagnostic categories used by the LRF did not exactly match with those used in the NWTPS analysis. Further examination of differences (Table B4) between LRF diagnoses, taken as the reference diagnoses, and NWTPS diagnoses is made below:

| LRF diagnosis | NWTPS diagnosis, where different |
|---|---|
| acute lymphatic leukaemia (ALL) | - no differences on NWTPS |
| acute myeloid leukaemia (AML) | - 1 man diagnosed with chronic myeloid leukaemia on the NWTPS. The NWTPS diagnosis was derived from the death certificate, as a cancer registration had not yet been received by NWTPS. |
| chronic lymphatic leukaemia (CLL) | - 1 man diagnosed with unspecified leukaemia (UL) on the NWTPS, according to cancer registration. The death certificate for this man had CLL recorded.<br>- 1 man diagnosed with usnpecified lymphatic leukaemia (ULL) on NWTPS. The NWTPS diagnosis of ULL is closely related to CLL.<br>- 4 men diagnosed with NHL on NWTPS, from cancer registrations. In 2 of these cases, CLL was recorded as a cause of death on the death certificate. |
| chronic myeloproliferative disorder (CMD) | - this category can be taken to include the NWTPS diagnoses of chronic myeloid leukaemia (CML), polycythaemia vera (PV) and the 3 cases categorised as 'other specified neoplasms' (ICD-9 code 238.7 – haematopoietic and lymphatic neoplasms of unknown behaviour). On this basis, LRF and NWTPS diagnoses agreed. |

| LRF diagnosis | NWTPS diagnosis, where different |
|---|---|
| Hodgkin's disease (HD) | - no differences on NWTPS. |
| myelodysplastic syndrome (MDS) | - this category comes underneath 'other diseases' on the NWTPS as these syndromes are not neoplastic diseases. For 1 man on the NWTPS a lymphoproliferative disease (CMD) was diagnosed rather than a myelodysplastic syndrome. |
| multiple myeloma (MM) | - no differences on NWTPS. |
| mycosis fungoides (MF) | - this disease can be classified under NHL. On this basis, LRF and NWTPS diagnoses agreed. |
| non-Hodgkin's lymphoma | - 2 men diagnosed with NHL on LRF were diagnosed with AML on NWTPS. One of these cases is due to hairy cell leukaemia (ICD-9 code 202.4) being classed as an NHL by LRF but a leukaemia by NWTPS<br>- LRF has one extra case of NHL (Waldenström's macroglobulinaemia), that was diagnosed as MM on NWTPS. |

From the examination of difference in LRF and NWTPS diagnoses given above, it can be seen that the number of differences in diagnoses held by LRF and NWTPS is dependent upon the categories of haematopoietic diseases used in the NWTPS and the sources of NWTPS information (cancer registration, death certificates, alone or in combination) used in the comparison. In order to make the diagnoses held by the LRF and NWTPS more comparable, the haematological neoplasms on the NWTPS can be categorised as follows:

a) acute myeloid leukaemias (excluding hairy cell leukaemia, ICD-9 code 202.4),

b) acute lymphatic leukaemias

c) chronic lymphatic leukaemias (including unspecified lymphatic leukaemias)

d) chronic myeloproliferative disorders (including chronic myeloid leukaemias, polycythaemia vera and lymphatic and haematopoietic neoplasms of unknown behaviour)

e) Hodgkin's disease

f) multiple myeloma

g) myelodysplastic syndromes

h) non-Hodgkin's lymphomas (including hairy cell leukaemia, mycosis fungoides)

Using these categories for diagnoses on the NWTPS, the LRF and NWTPS diagnoses agree in 66 cases (see Figure 4.2). There are 9 unresolved differences between LRF and NWTPS diagnoses, which are as follows:

Test participants:

- 1 man diagnosed with AML by LRF but CML by NWTPS

Controls:

- 4 men diagnosed with CLL on LRF and NHL on NWTPS
- 1 man diagnosed with NHL by LRF and AML by NWTPS
- 1 man diagnosed with NHL by LRF but multiple myeloma by NWTPS
- 1 man diagnosed with MDS by LRF but CMD by NWTPS
- 1 man diagnosed with CLL on LRF and UL on NWTPS

## B5 Discussion

LRF did not identify any new haematological neoplasms among groups of men without these diseases who were submitted by NRPB. This provides reassurance that cases of haematological cancer are not missing from the NWTPS databases. The overall success rate (15%) of matching NWTPS members with haematological neoplasms to the LRF Registry is not unexpected, considering the smaller population and time covered by LRF compared to the NHSCRs (see Background).

There does seem to be a higher ascertainment at LRF of haematological neoplasms among controls compared to participants or independent responders. Many factors could influence the success in matching of study members including geographical location, completeness of personal information and date of occurrence of cancer. A different geographical distribution of participants and controls appears unlikely to be responsible for the different matching rate at LRF, as there is a similar distribution of participants and controls among cancer registries (see Section 4.4) and this is likely to extend to areas covered by the LRF. Whilst reasons for the different rates of matching of participants and controls at LRF are unclear, if the results are taken at face value then, at LRF,

test participants are not being recorded with greater numbers of haematopoietic neoplasms than controls.

There were a substantial number of cases overall (20%) where the diagnosis derived from the ICD codes supplied by LRF differed from the diagnosis assigned at NRPB (Table B4). Better matching between LRF and NWTPS diagnoses was obtained when cancer categories used by the LRF and NWTPS were made more comparable. On this basis, differences between LRF and NWTPS data only occurred in 9 out of 75 cases (12%), suggesting good agreement between LRF and NWTPS diagnoses. Four of the discrepancies are between diagnoses for NHL and CLL. These are closely related diseases and mis-diagnoses between these diseases can occur relatively easily (Cartwright *et al*, 1990). There was good agreement between LRF and NWTPS in the diagnosis of multiple myeloma, which is of special interest to the analysis. The one discrepancy for a man diagnosed with multiple myeloma on the NWTPS but Waldenström's macroglobulinaemia, a type of NHL, by the LRF. There was also good agreement between diagnosis of acute myeloid leukaemia, which is of interest in radiation-induced leukaemia, on the LRF and NWTPS, with seven agreements in diagnoses and two differences. In one of the differences, the NWTPS diagnosis for chronic myeloid leukaemia is taken from the death certificate and it is possible that when the cancer registration is received this may have a different diagnosis, reflecting the symptoms at the time of the cancer registration.

Given the different rates of matching at LRF among participants and controls, replacement of NWTPS cancer data with LRF data could only be unequally and incompletely done on the control and test participant cohorts. Consequently, the NWTPS data have been retained in the analyses in the main part of the report. However, some estimates can be made of the impact of using the LRF diagnoses in preference to the NWTPS diagnoses on the cancers of interest in the analysis. The greatest change in numbers of cancers is for CLL, which increases by five among controls and decreases by one among participants. CLL is perhaps the subtype of leukaemia of least interest in the analysis because it is not thought to be radiation inducible (UNSCEAR, 2000). Thus changes of the numbers of CLLs in the NWTPS should not heavily influence the conclusions drawn from the analysis. The number of cases of AML would be increased by one in participants, which would slightly strengthen the evidence for an increased relative risk of AML among participants compared to controls in the main analysis. For MM, which is of special interest to this analysis, the reduction in the number of cases of MM among controls by one would produce a small increase in the relative risks of MM among participants compared to controls. This small change would not alter the overall conclusions regarding multiple myeloma in the analysis.

## B6 Acknowledgement

The authors wish to thank the Office for National Statistics for giving its approval to the use of their cancer registration data in this comparison.

## B7 References

Cartwright R A, Alexander F E, McKinney P A and Ricketts T J. *Leukaemia and Lymphoma: An Atlas of Distribution within Areas of England and Wales 1984-1988*. London, Leukaemia Research Fund (1990).

Cartwright R A, McNally R J, Rowland D J and Thomas J. *The Descriptive Epidemiology of Leukaemia and Related Conditions in Parts of the UK 1984-1993*. London, Leukaemia Research Fund (1997).

UNSCEAR. *Sources and Effects of Ionizing Radiation. Vol II Effects.* New York, United Nations (2000).

**Table B1 Selection of haematological cancers in NWTPS analysis by ICD-9 codes**

| Type of Haematological Cancer | ICD-9 codes |
|---|---|
| Hodgkin's disease (HD) | 201 |
| Non-Hodgkin's lymphoma (NHL) | 200, 202.0 – 202.3, 202.5 – 202.9 |
| Multiple myeloma (MM) | 203.0, 203.8, 238.6 |
| Polycythaemia vera (PV) | 238.4 |
| Leukaemia – all subtypes | 202.4, 203.1, 204 – 208 |
| Acute lymphatic leukaemia (ALL) | 204.0, 204.2 |
| Acute myeloid leukaemia (AML) | 202.4, 205.0, 205.2, 206.0, 206.2, 207.0 |
| Chronic lymphatic leukaemia (CLL) | 204.1, 207.8 |
| Chronic myeloid leukaemia (CML) | 205.1, 205.3, 206.1 |
| Unspecified acute leukaemia (UAL) | 203.1, 208.0, 208.2 |
| Unspecified lymphatic leukaemia (ULL) | 204.9 |
| Unspecified leukaemia (UL) | 208.8, 208.9 |

**Table B2 Number of Records sent to LRF and matched to the LRF Registry**

| | Test Participants | | Controls | | Independent Responders | |
|---|---|---|---|---|---|---|
| | No. of records sent | No. of records matched (% of sent) | No. of records sent | No. of records matched (% of sent) | No. of records sent | No. of records matched (% of sent) |
| Group A | 249 | 26 (10%) | 229 | 48 (21%) | 32 | 1 (3%) |
| Group B | 265 | 0 | 278 | 0 | 9 | 0 |
| Group C | 71 | 0 | 70 | 0 | 1 | 0 |
| Group D | 328 | 0 | 322 | 0 | 7 | 0 |

**Table B3 Comparison of NWTPS and LRF cancer data by ICD site codes**

| Type of Cancer | No. of men reported by NWTPS with this cancer [a] | No. of cases where LRF agree with NWTPS cancer type/sub-type [a] | Details of cases where LRF provided a different cancer type/sub-type (ICD code) [a] |
|---|---|---|---|
| Hodgkin's disease | 2 | 2 | |
| NHL | 30 | 25 | 1 x AML (202.4) |
| | | | 4 x CLL (204.1) |
| Multiple myeloma | 16 | 15 | 1 x Waldenström's macroglobulinaemia[b] (C88.0) |
| PV | 3 | 0 | 3 x haematopoietic neoplasms of uncertain behaviour[c] (238.7) |
| ALL | 2 | 2 | |
| AML | 9 | 8 | 1 x NHL (200) |
| CLL | 3 | 3 | |
| CML | 3 | 2 | 1 x AML (205.0) |
| UL | 1 | 0 | 1 x CLL (204.1) |
| ULL | 1 | 0 | 1 x CLL (204.1) |
| All leukaemia subtypes | 19 | 15[d] | see details above |
| Haematopoietic neoplasms of uncertain behaviour[c] (238.7) | 4 | 3 | 1 x myelodysplastic syndrome[e] (D46.0) |
| Myelodysplastic syndrome[e] (D46.4) | 1 | 0 | 1 x UAL (208.0) |
| Total | 75 | 60 | |

*Notes*

a Diagnosis derived ICD codes using NWTPS categories (Table B1).

b Waldenström's macroglobulinaemia is not classed as a neoplasm in the main NWTPS analysis.

c Haematopoietic neoplasms of uncertain behaviour (ICD-9 code 238.7) are classed as 'Other specified neoplasms' in the NWTPS analysis.

d Two of the changes for leukaemias are from one leukaemia sub-type to another.

e Myelodysplastic syndromes (ICD-10 code D46) are not classed as neoplasms in the NWTPS analysis.

**Table B4 Comparison of NWTPS and LRF Cancer Data by Diagnosis**

| | NWTPS diagnosis | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ALL | AML | CLL | UL | ULL | CML | OSN | PV | HD | MM | NHL | OTH | Total |
| LRF diagnosis | | | | | | | | | | | | | |
| ALL | 2 | | | | | | | | | | | | 2 |
| AML | | 7 | | | | 1 | | | | | | | 8 |
| CLL | | | 3 | 1 | 1 | | | | | | 4 | | 9 |
| CMD | | | | | | 2 | 3 | 3 | | | | | 8 |
| HD | | | | | | | | | 2 | | | | 2 |
| MDS | | | | | | | 1 | | | | | 1 | 2 |
| MM | | | | | | | | | | 15 | | | 15 |
| MF | | | | | | | | | | | 2 | | 2 |
| NHL | | 2 | | | | | | | | 1 | 24 | | 27 |
| Total | 2 | 9 | 3 | 1 | 1 | 3 | 4 | 3 | 2 | 16 | 30 | 1 | 75 |

*Notes*

CMD = chronic myeloproliferative disease

MDS = myelodysplastic syndrome

MF = mycosis fungoides

OSN = other specified neoplasms

OTH = other diseases (non-neoplastic)

# APPENDIX C

# MORTALITY AND CANCER INCIDENCE IN TEST PARTICIPANTS WITH NO MORE POTENTIAL FOR RADIATION EXPOSURE THAN THE GENERAL PUBLIC

Whilst assembling the cohort of test participants for this study, groups of men were identified who satisfied the criteria for inclusion in the study, but who appeared to have no more potential for radiation exposure from the weapons test programme than the general public. These groups comprised men whose test participation was restricted solely to the following categories:

(a) RAAF Edinburgh Field or RAAF Pearce, but who were not members of the squadron involved in cloud sampling;

(b) Monte Bello Islands, but departing before 3 October 1952, the date of Operation Hurricane;

(c) Christmas Island, but departing before 15 May 1957, the date of the first explosion of Operation Grapple;

(d) the crew of HMS Comus or HMS Concord, both of which visited the Monte Bello Islands briefly in March or April 1956 before the first explosion of Operation Mosaic.

These men were included as test participants in the first analysis (Darby *et al*, 1988a,b). However, they have been excluded from the main tables in both the second analysis (Darby *et al*, 1993a,b) and the current analysis. This Appendix presents the results from continued follow-up of these men, who number 1520 in total. Details of the breakdown by Service and rank are given in Appendix A of Darby *et al* (1993b).

Table C1 shows mortality by broad cause among these men up to the end of 1998. Both the SMR for all causes of death and that for all cancers was slightly below 100, whereas the SMR for all accidents and violence was greater than 100; however, in none of these instances was there a statistically significant difference relative to national rates. In contrast, mortality from all diseases other than cancer was significantly lower than national rates (SMR 83). For each of these groupings, mortality rates amongst these men were similar to those in the group group, with relative risks close to 1.

Table C2 presents mortality and incidence findings for specific types of cancer among this group of participants. These results are based on the full period after first test participation. Mortality rates were generally consistent with national rates and both mortality and incident rates were mostly compatible with the corresponding rates among controls, although small numbers for many individual

cancer types restricted inferences. One exception to this pattern arose for stomach cancer, for which mortality rates in participants were significantly greater than both national rates (SMR 180) and those in the controls (RR 2.42, 90% CI 1.43-4.04); the corresponding relative risk for stomach cancer incidence was 1.63 (90% CI 0.95-2.73). The other cancer type for which participants and controls differed in their rates was the incidence of cancer of connective and soft tissue (RR 9.44, 90% CI 3.61-23.8, based on six cases in participants); there was no significant difference in the corresponding mortality rates, although the numbers were very small. Given that 27 distinct cancer categories were considered in Table C2, it is not surprising that findings significant at the 1 in 20 level would be found for one or two of these categories. There was only one death from multiple myeloma in these participants and one further case in the incidence analysis; no further cases were added using the wider definition of the disease. Rates of myeloma were compatible with values expected from national rates of mortality and from rates of mortality and incidence in the controls. Mortality from leukaemia and leukaemia excluding CLL was consistent with national rates, both over the full follow-up period and during the period 2-25 years after first test participation. In contrast, leukaemia risks were raised relative to controls (although not to a statistically significant extent), mainly reflecting the low rates among controls compared with national rates.

## C1 References

Darby S C, Kendall G M, Fell T P, O'Hagan J A, Muirhead C R, Ennis J R, Ball A M, Dennis J A and Doll R. A summary of mortality and incidence of cancer in men from the United Kingdom who participated in the United Kingdom's atmospheric nuclear weapon tests and experimental programmes. *Br Med J*, 296, 332-338 (1988a).

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Darby S C, Kendall G M, Fell T P, Doll R, Goodill A A, Conquest A J, Jackson D A and Haylock R G E. Mortality and cancer incidence 1952-1990 in UK participants in the UK atmospheric nuclear weapon tests and experimental programmes. Chilton, NRPB-R266 (London, HMSO) (1993b).

**TABLE C1 Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) among test participants with no more potential for radiation exposure than the general public, and relative risks (RR) compared with controls, by broad cause of death.**

| Cause of death | Test participants with no potential for radiation exposure | | | | Mortality rate relative to controls | | | |
|---|---|---|---|---|---|---|---|---|
| | O | E | SMR | Prob[a] | RR | 90% CI[d] | Prob[b] one-sided | Prob[c] two-sided |
| All neoplasms | 112 | 116.44 | 96 | 0.71 | 1.03 | 0.87, 1.22 | 0.40 | 0.80 |
| Other diseases | 197 | 237.18 | 83 | 0.0078 | 1.02 | 0.90, 1.16 | 0.40 | 0.81 |
| Accidents and violence | 32 | 25.68 | 125 | 0.23 | 1.17 | 0.84, 1.62 | 0.23 | 0.46 |
| Unknown | 7 | | | | | | | |
| All causes | 348 | 379.60 | 92 | 0.11 | 1.03 | 0.94, 1.13 | 0.32 | 0.63 |

*Notes*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR $\leq$ 1.00).

(c) Two-sided test that the RR is different from unity.

(d) Confidence interval.

**TABLE C2 (a) Observed deaths (O), deaths expected from national rates (E) and standardised mortality ratios (SMR) among test participants and controls, and relative risks (RR) of mortality in test participants compared with controls, for 27 distinct types of cancer**

| | Test participants with no potential for radiation exposure | | | | Mortality rate relative to controls | | | |
|---|---|---|---|---|---|---|---|---|
| Type of cancer | O | E | SMR | Prob[a] | RR | 90%CI[d] | Prob[b] one-sided | Prob[c] Two-sided |
| Tongue, mouth, pharynx | 4 | 1.93 | 207 | 0.13 | 1.64 | 0.58, 4.17 | 0.27 | 0.31 |
| Oesophagus | 9 | 5.24 | 172 | 0.12 | 1.48 | 0.77, 2.77 | 0.18 | 0.36 |
| Stomach | 14 | 8.11 | 173 | 0.05 | 2.36 | 1.39, 3.95 | 0.0024 | 0.0048 |
| Large intestine & rectum | 9 | 13.3 | 68 | 0.27 | 0.73 | 0.39, 1.33 | 0.22 | 0.44 |
| Liver | 3 | 1.53 | 196 | 0.20 | 2.69 | 0.74, 8.39 | 0.12 | 0.13 |
| Primary liver cancer | 1 | 0.89 | 113 | 1.00 | 1.08 | 0.07, 6.45 | 0.68 | 1.00 |
| Gallbladder | 0 | 0.47 | 0 | 1.00 | 2.69 | 0.00, 71.16 | 0.93 | 1.00 |
| Pancreas | 7 | 5.02 | 139 | 0.36 | 1.37 | 0.65, 2.78 | 0.28 | 0.49 |
| Larynx | 2 | 1.16 | 173 | 0.64 | 1.32 | 0.26, 4.83 | 0.51 | 0.66 |
| Lung | 31 | 38.85 | 80 | 0.23 | 0.87 | 0.63, 1.19 | 0.25 | 0.49 |
| Bone | 1 | 0.33 | 300 | 0.28 | 9.73 | 0.15, 619.1 | 0.38 | 0.38 |
| Connective and soft tissue | 1 | 0.53 | 187 | 0.41 | 5.02 | 0.27, 42.26 | 0.22 | 0.22 |
| Malignant melanoma | 0 | 1.27 | 0 | 0.41 | 0 | 0.00, 2.22 | 0.18 | 0.26 |
| Other skin cancer | 0 | 0.27 | 0 | 1.00 | -[e] | | | |
| Prostate | 3 | 6.16 | 49 | 0.23 | 0.52 | 0.16, 1.48 | 0.19 | 0.37 |
| Testis | 0 | 0.62 | 0 | 0.66 | 0 | 0.00, 5.76 | 0.37 | 0.57 |
| Bladder | 2 | 3.72 | 54 | 0.45 | 0.92 | 0.19, 3.30 | 0.59 | 1.00 |
| Kidney | 1 | 2.92 | 34 | 0.38 | 0.25 | 0.02, 1.36 | 0.11 | 0.18 |
| Tumours of central nervous system | 6 | 4.97 | 121 | 0.65 | 1.22 | 0.54, 2.61 | 0.41 | 0.64 |
| Thyroid | 1 | 0.21 | 481 | 0.19 | 15.08 | 0.55, 414.1 | 0.12 | 0.12 |
| Adrenals | 0 | 0.08 | 0 | 1.00 | 0 | 0.00, 47.69 | 0.87 | 1.00 |
| Hodgkin's disease | 0 | 1.09 | 0 | 0.43 | 0 | 0.00, 4.58 | 0.36 | 0.62 |
| Non-Hodgkin's lymphoma | 1 | 3.35 | 30 | 0.28 | 0.27 | 0.02, 1.51 | 0.14 | 0.24 |
| Multiple myeloma [f] | 1 | 1.63 | 61 | 0.74 | 0.80 | 0.05, 4.64 | 0.60 | 1.00 |
| Leukaemia | 4 | 3.28 | 122 | 0.78 | 1.99 | 0.69, 5.15 | 0.17 | 0.27 |
| Leukaemia excluding CLL | 3 | 2.69 | 112 | 1.00 | 2.23 | 0.63, 6.72 | 0.18 | 0.18 |
| Polycythaemia vera | 0 | 0.08 | 0 | 1.00 | 0 | 0.00, 207.1 | 0.94 | 1.00 |
| Other specified neoplasms | 4 | 2.41 | 166 | 0.31 | 2.28 | 0.78, 6.03 | 0.12 | 0.12 |
| Unspecified neoplasms | 8 | 7.92 | 101 | 1.00 | 0.91 | 0.46, 1.74 | 0.47 | 0.95 |
| All neoplasms | 112 | 116.44 | 96 | 0.71 | 1.03 | 0.87, 1.22 | 0.40 | 0.80 |

*Notes for Table C2(a)*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).

(c) Two-sided test that the RR is different from unity.

(d) Confidence interval

(e) The RR cannot be calculated, because there were no deaths observed among the controls.

(f) The observed number of deaths and the relative risk are unchanged for the wider definition of multiple myeloma (ICD 9$^{th}$ revision codes 203.0, 203.1, 238.6 and 273.1).

**TABLE C2 (b) Numbers of incident cancers (I) among test participants and relative risks (RR) of incident cancer in test participants compared with controls for 27 distinct types of cancer**

| | Test participants with no potential for radiation exposure | Incidence rate in test participants relative to controls | | | |
|---|---|---|---|---|---|
| Type of cancer | I | RR | 90% CI[c] | Prob[a] one-sided | Prob[b] two-sided |
| Tongue, mouth, pharynx | 4 | 0.89 | 0.32, 2.21 | 0.51 | 1.00 |
| Oesophagus | 7 | 1.15 | 0.55, 2.31 | 0.44 | 0.83 |
| Stomach | 13 | 1.59 | 0.93, 2.66 | 0.082 | 0.16 |
| Large intestine & rectum | 15 | 0.67 | 0.41, 1.06 | 0.077 | 0.15 |
| Liver | 3 | 2.93 | 0.81, 9.18 | 0.098 | 0.11 |
| Primary liver cancer | 1 | 1.26 | 0.08, 7.67 | 0.64 | 0.72 |
| Gallbladder | 1 | 2.59 | 0.15, 17.62 | 0.45 | 0.35 |
| Pancreas | 7 | 1.33 | 0.63, 2.70 | 0.31 | 0.62 |
| Larynx | 7 | 1.76 | 0.82, 3.60 | 0.12 | 0.19 |
| Lung | 35 | 0.84 | 0.62, 1.13 | 0.18 | 0.35 |
| Bone | 1 | 2.38 | 0.10, 24.37 | 0.52 | 0.45 |
| Connective and soft tissue | 6 | 9.44 | 3.61, 23.79 | <0.001 | <0.001 |
| Malignant melanoma | 2 | 0.54 | 0.11, 1.89 | 0.27 | 0.43 |
| Other skin cancer | 27 | 0.99 | 0.70, 1.40 | 0.52 | 0.95 |
| Prostate | 19 | 1.40 | 0.91, 2.14 | 0.10 | 0.20 |
| Testis | 1 | 0.48 | 0.03, 2.85 | 0.37 | 0.71 |
| Bladder | 12 | 1.13 | 0.65, 1.92 | 0.41 | 0.81 |
| Kidney | 4 | 0.60 | 0.22, 1.47 | 0.21 | 0.41 |
| Tumours of central nervous system | 6 | 1.13 | 0.50, 2.39 | 0.48 | 0.96 |
| Thyroid | 1 | 4.24 | 0.22, 36.66 | 0.35 | 0.26 |
| Adrenals | 0 | 0 | 0.00, 47.74 | 0.88 | 1.00 |
| Hodgkin's disease | 1 | 0.57 | 0.04, 3.26 | 0.44 | 0.72 |
| Non-Hodgkin's lymphoma | 7 | 1.19 | 0.56, 2.40 | 0.41 | 0.83 |
| Multiple myeloma | 2 | 0.89 | 0.18, 3.20 | 0.57 | 1.00 |
| Multiple myeloma (wider definition)[d] | 2 | 0.89 | 0.18, 3.20 | 0.57 | 1.00 |
| Leukaemia | 6 | 1.94 | 0.85, 4.20 | 0.10 | 0.14 |
| Leukaemia excluding CLL | 4 | 1.99 | 0.69, 5.14 | 0.17 | 0.27 |
| Polycythaemia vera | 0 | 0 | 0.00, 6.12 | 0.53 | 1.00 |
| Other specified neoplasms | 10 | 1.14 | 0.62, 2.03 | 0.41 | 0.83 |
| Unspecified neoplasms | 6 | 0.86 | 0.39, 1.82 | 0.44 | 0.88 |
| All neoplasms excluding non-melanoma skin cancer | 176 | 1.06 | 0.93, 1.21 | 0.25 | 0.50 |
| All neoplasms | 203 | 1.05 | 0.93, 1.19 | 0.27 | 0.54 |

*Notes*

(a) One-sided test that the RR is greater than unity (RR ≥ 1.00), or less than unity (RR < 1.00).

(b) Two-sided test that the RR is different from unity.

(c) Confidence interval.

(d) ICD 9th revision codes 203.0, 203.1, 238.6 and 273.1.

# APPENDIX D

# MORTALITY AND CANCER INCIDENCE IN TEST PARTICIPANTS OVER THE ENTIRE PERIOD OF THE FOLLOW-UP

**TABLE D1 Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) among test participants and controls for officers and other ranks, together with relative risks (RR) of mortality in test participants compared with controls, by broad cause of death**

| | | Test participants | | | | Controls | | | | Mortality rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cause of death | Status | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] | RR | 90%CI[d] | Prob[b] one-sided | Prob[c] two-sided |
| All neoplasms | Officers | 315 | 455.16 | 69 | <0.001 | 335 | 501.17 | 67 | <0.001 | 1.06 | 0.92, 1.21 | 0.25 | 0.51 |
| | Other ranks | 1231 | 1211.26 | 102 | 0.58 | 1310 | 1288.65 | 102 | 0.56 | 1.00 | 0.94, 1.07 | 0.47 | 0.95 |
| Other diseases | Officers | 559 | 1020.62 | 55 | <0.001 | 611 | 1131.78 | 54 | <0.001 | 1.02 | 0.92, 1.13 | 0.37 | 0.75 |
| | Other ranks | 2210 | 2432.82 | 91 | <0.001 | 2349 | 2602.43 | 90 | <0.001 | 1.01 | 0.96, 1.06 | 0.36 | 0.73 |
| Accidents and violence | Officers | 80 | 52.20 | 153 | <0.001 | 110 | 59.57 | 185 | <0.001 | 0.87 | 0.67, 1.12 | 0.19 | 0.38 |
| | Other ranks | 356 | 306.67 | 116 | 0.0061 | 307 | 59.57 | 102 | 0.69 | 1.14 | 1.00, 1.30 | 0.054 | 0.11 |
| Unknown | Officers | 21 | | | | 27 | | | | | | | |
| | Other ranks | 85 | | | | 112 | | | | | | | |
| All causes | Officers | 975 | 1528.75 | 64 | <0.001 | 1083 | 1693.38 | 64 | <0.001 | 1.02 | 0.94. 1.09 | 0.38 | 0.75 |
| | Other ranks | 3882 | 3954.37 | 98 | 0.25 | 4078 | 4194.85 | 97 | 0.071 | 1.01 | 0.98, 1.05 | 0.29 | 0.58 |

*Notes*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

(b) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).

(c) Two-sided test that the RR is different from unity.

(d) Confidence interval.

**TABLE D2 (a) Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) among test participants and controls by Service and broad cause of death**

| | | Test participants | | | | Controls | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cause of death | Service | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] |
| All neoplasms | RN | 548 | 505.58 | 108 | 0.062 | 635 | 572.26 | 111 | 0.010 |
| | Army | 312 | 353.51 | 88 | 0.026 | 292 | 329.52 | 89 | 0.036 |
| | RAF | 604 | 686.43 | 88 | 0.0014 | 634 | 761.25 | 83 | <0.001 |
| | AWE | 82 | 120.89 | 68 | <0.001 | 84 | 126.80 | 66 | <0.001 |
| Other diseases | RN | 956 | 1033.80 | 92 | 0.015 | 1088 | 1167.69 | 93 | 0.019 |
| | Army | 630 | 712.41 | 88 | 0.0018 | 554 | 647.52 | 86 | <0.001 |
| | RAF | 993 | 1437.19 | 69 | <0.001 | 1145 | 1622.18 | 71 | <0.001 |
| | AWE | 190 | 270.26 | 70 | <0.001 | 173 | 296.82 | 58 | <0.001 |
| Accidents and violence | RN | 146 | 107.86 | 135 | <0.001 | 170 | 126.21 | 135 | <0.001 |
| | Army | 122 | 96.51 | 126 | 0.0125 | 68 | 70.00 | 97 | 0.81 |
| | RAF | 157 | 140.00 | 112 | 0.16 | 171 | 148.89 | 115 | 0.078 |
| | AWE | 11 | 14.49 | 76 | 0.43 | 8 | 14.44 | 55 | 0.088 |
| Unknown | RN | 30 | - | - | - | 55 | - | - | - |
| | Army | 27 | - | - | - | 23 | - | - | - |
| | RAF | 45 | - | - | - | 55 | - | - | - |
| | AWE | 4 | - | - | - | 6 | - | - | - |
| All causes | RN | 1680 | 1648.32 | 102 | 0.44 | 1948 | 1867.64 | 104 | 0.066 |
| | Army | 1091 | 1163.56 | 94 | 0.032 | 937 | 1048.17 | 89 | <0.001 |
| | RAF | 1799 | 2265.38 | 79 | <0.001 | 2005 | 2534.14 | 79 | <0.001 |
| | AWE | 287 | 405.85 | 71 | <0.001 | 271 | 438.26 | 62 | <0.001 |

*Note*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

**TABLE D2 (b) Observed deaths (O), deaths expected from social class specific national rates ($E_S$), and standardised mortality ratios corrected for social class ($SMR_S$) together with relative risks (RR) of mortality in test participants compared with controls, by Service and broad cause of death**

| | | Test participants | | | Mortality rate in test participants relative to controls | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cause of death | Service | O | $E_S$ | $SMR_S$ | Probability[a] | RR | 90% CI[d] | Prob[b] one-sided | Prob[c] two-sided |
| All neoplasms | RN | 548 | 555.91 | 99 | 0.75 | 0.98 | 0.89, 1.08 | 0.36 | 0.72 |
| | Army | 312 | 368.46 | 85 | 0.0027 | 1.01 | 0.88, 1.16 | 0.46 | 0.91 |
| | RAF | 604 | 700.83 | 86 | <0.001 | 1.04 | 0.94, 1.14 | 0.26 | 0.51 |
| | AWE | 82 | 114.64 | 72 | 0.0015 | 1.10 | 0.84, 1.46 | 0.30 | 0.72 |
| Other diseases | RN | 956 | 955.00 | 100 | 0.97 | 0.99 | 0.92, 1.07 | 0.46 | 0.92 |
| | Army | 630 | 654.10 | 96 | 0.35 | 1.05 | 0.95, 1.16 | 0.22 | 0.44 |
| | RAF | 993 | 1302.84 | 76 | <0.001 | 0.97 | 0.90, 1.04 | 0.24 | 0.49 |
| | AWE | 190 | 239.31 | 79 | 0.0011 | 1.32 | 1.10, 1.59 | 0.0057 | 0.92 |
| Accidents and violence | RN | 146 | 98.45 | 148 | <0.001 | 1.01 | 0.83, 1.22 | 0.50 | 0.99 |
| | Army | 122 | 88.44 | 138 | <0.001 | 1.38 | 1.05, 1.82 | 0.027 | 0.05 |
| | RAF | 157 | 126.26 | 124 | 0.0086 | 0.99 | 0.82, 1.20 | 0.50 | 0.99 |
| | AWE | 11 | 12.56 | 88 | 0.68 | 1.46 | 0.62, 3.51 | 0.29 | 0.99 |
| Unknown | RN | 30 | - | - | - | - | - | - | - |
| | Army | 27 | - | - | - | - | - | - | - |
| | RAF | 45 | - | - | - | - | - | - | - |
| | AWE | 4 | - | - | - | - | - | - | - |
| All causes | RN | 1680 | 1718.54 | 98 | 0.35 | 0.98 | 0.93, 1.04 | 0.28 | 0.55 |
| | Army | 1091 | 1141.72 | 96 | 0.14 | 1.06 | 0.99, 1.15 | 0.093 | 0.18 |
| | RAF | 1799 | 2190.32 | 82 | <0.001 | 0.99 | 0.94, 1.05 | 0.41 | 0.82 |
| | AWE | 287 | 367.30 | 78 | <0.001 | 1.24 | 1.07, 1.44 | 0.0073 | 0.55 |

*Notes for Table D2(b)*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.
(b) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).
(c) Two-sided test that the RR is different from unity.
(d) Confidence interval.

**TABLE D3 Observed deaths (O), deaths expected from national rates (E) and standardised mortality ratios (SMR) among test participants and controls, and relative risks (RR) of mortality in test participants compared with controls, for 27 distinct types of cancer**

| | Test participants | | | | Controls | | | | Mortality rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Type of cancer (ICD Codes 9th Revision) | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] | RR | 90%CI[d] | Prob[b] 1-sided | Prob[c] 2-sided |
| Cancer of the tongue, mouth, pharynx (141, 143-149) | 32 | 27.05 | 118 | 0.39 | 40 | 28.84 | 139 | 0.0495 | 0.88 | 0.58, 1.33 | 0.34 | 0.63 |
| Cancer of the oesophagus (150) | 74 | 73.61 | 101 | 0.95 | 86 | 78.84 | 109 | 0.43 | 0.93 | 0.71, 1.22 | 0.35 | 0.70 |
| Cancer of stomach (151) | 92 | 118.45 | 78 | 0.013 | 92 | 128.40 | 72 | 0.0008 | 1.08 | 0.83, 1.39 | 0.34 | 0.68 |
| Cancer of large intestine and rectum (153, 154 excl. 154.3, 159.0) | 175 | 188.81 | 93 | 0.33 | 183 | 203.08 | 90 | 0.16 | 1.03 | 0.86, 1.23 | 0.42 | 0.84 |
| Cancer of liver (155) | 24 | 21.26 | 113 | 0.59 | 17 | 22.67 | 75 | 0.25 | 1.54 | 0.88, 2.73 | 0.11 | 0.21 |
| Primary liver cancer (155.0) | 12 | 12.26 | 98 | 1.00 | 13 | 13.06 | 100 | 1.00 | 0.99 | 0.47, 2.05 | 0.57 | 1.00 |
| Cancer of gallbladder (156) | 2 | 6.80 | 29 | 0.057 | 5 | 7.35 | 68 | 0.47 | 0.38 | 0.06, 1.83 | 0.21 | 0.28 |
| Cancer of pancreas (157) | 73 | 71.42 | 102 | 0.86 | 75 | 76.78 | 98 | 0.86 | 1.02 | 0.77, 1.36 | 0.48 | 0.96 |
| Cancer of larynx (161) | 19 | 16.37 | 116 | 0.53 | 24 | 17.58 | 137 | 0.15 | 0.87 | 0.50, 1.50 | 0.38 | 0.76 |
| Cancer of lung (162, 163) | 480 | 562.00 | 85 | <0.001 | 535 | 606.46 | 88 | 0.0032 | 0.97 | 0.88, 1.08 | 0.36 | 0.71 |
| Cancer of bone (170) | 2 | 4.60 | 43 | 0.26 | 1 | 4.71 | 21 | 0.10 | 2.11 | 0.19, 44.14 | 0.48 | 0.61 |
| Cancer of connective and soft tissue (171) | 5 | 7.47 | 67 | 0.46 | 4 | 7.88 | 51 | 0.21 | 1.36 | 0.38, 5.02 | 0.45 | 0.75 |
| Malignant melanoma (172) | 29 | 17.63 | 165 | 0.012 | 27 | 18.52 | 146 | 0.061 | 1.14 | 0.71, 1.83 | 0.36 | 0.69 |
| Other skin cancer (173) | 2 | 3.96 | 51 | 0.45 | 0 | 4.27 | 0 | 0.026 | ∞ | 0.46, ∞ | 0.17 | 0.17 |
| Cancer of prostate (185) | 106 | 92.20 | 115 | 0.16 | 97 | 100.91 | 96 | 0.73 | 1.20 | 0.94, 1.53 | 0.11 | 0.22 |
| Cancer of testis (186) | 10 | 8.75 | 114 | 0.73 | 9 | 8.48 | 106 | 0.86 | 1.15 | 0.48, 2.76 | 0.48 | 0.82 |
| Cancer of bladder (188, 189.3-189.9) | 52 | 54.46 | 95 | 0.79 | 34 | 59.15 | 57 | <0.001 | 1.69 | 1.15, 2.49 | 0.011 | 0.02 |
| Cancer of kidney (189.0-189-2) | 43 | 40.53 | 106 | 0.70 | 63 | 43.32 | 145 | 0.0048 | 0.74 | 0.52, 1.04 | 0.073 | 0.14 |
| Tumours of central nervous system (191-192, 224-225, 239.6) | 70 | 68.94 | 102 | 0.90 | 71 | 72.53 | 98 | 0.86 | 1.04 | 0.78, 1.40 | 0.43 | 0.87 |
| Cancer of thyroid (193) | 1 | 2.90 | 34 | 0.38 | 1 | 3.11 | 32 | 0.28 | 1.00 | 0.04,27.44 | 0.76 | 1.00 |
| Cancer of adrenals (194.0)[e] | 2 | 1.10 | 181 | 0.30 | 2 | 1.16 | 172 | 0.64 | 1.12 | 0.14, 8.75 | 0.65 | 1.00 |
| Hodgkin's disease (201) | 10 | 14.84 | 67 | 0.24 | 12 | 14.86 | 81 | 0.52 | 0.82 | 0.37, 1.81 | 0.41 | 0.67 |
| Non-Hodgkin's lymphoma (200, 202.0-202.3, 202.5-202.9) | 45 | 46.97 | 96 | 0.83 | 51 | 49.72 | 103 | 0.89 | 0.84 | 0.58, 1.21 | 0.23 | 0.46 |
| Multiple myeloma[f] (203 excl. 203.1, 238.6) | 22 | 23.01 | 96 | 0.84 | 18 | 24.73 | 73 | 0.19 | 1.43 | 0.81, 2.54 | 0.17 | 0.27 |
| Leukaemia (202.4, 203.1, 204-208) | 45 | 46.11 | 98 | 0.88 | 33 | 48.61 | 68 | 0.022 | 1.45 | 0.96, 2.17 | 0.069 | 0.14 |
| Leukaemia excluding CLL | 40 | 37.6 | 106 | 0.68 | 23 | 39.40 | 58 | 0.0066 | 1.83 | 1.15, 2.93 | 0.015 | 0.027 |
| Polycythaemia vera (238.4)[g] | 1 | 1.10 | 91 | 1.00 | 2 | 1.19 | 169 | 0.64 | 0.54 | 0.03, 5.84 | 0.52 | 1.00 |
| Other specified neoplasms (140-239 excl. above, 196-199 and 239) | 27 | 34.03 | 79 | 0.23 | 29 | 36.30 | 80 | 0.25 | 1.04 | 0.65, 1.67 | 0.50 | 1.00 |
| Unspecified neoplasms (196-199, 239, excl. 239.6) | 103 | 112.17 | 92 | 0.40 | 134 | 120.50 | 111 | 0.24 | 0.85 | 0.68, 1.07 | 0.12 | 0.25 |
| All neoplasms excluding non-melanoma skin cancer (140-172, 174-239) | 1544 | 1662.47 | 93 | 0.0034 | 1645 | 1785.57 | 92 | <0.001 | 1.01 | 0.95, 1.07 | 0.37 | 0.74 |
| All neoplasms (140-239) | 1546 | 1666.42 | 93 | 0.0029 | 1645 | 1789.82 | 92 | <0.001 | 1.01 | 0.96, 1.08 | 0.35 | 0.71 |

*Notes for Table D3*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.
(b) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).
(c) Two-sided test that the RR is different from unity.
(d) Confidence interval.
(e) Cancers of the adrenal glands are included only from 1958 in the comparison with national rates, no deaths in participants and none in controls have occurred before this.
(f) The observed numbers of deaths and relative risk are unchanged for the wider definition of multiple myeloma (ie. ICD 9$^{th}$ revision codes 203.0, 203.1, 238.6 and 273.1).
(g) Polycythaemia vera is included only from 1968 in the comparison with national rates, no deaths in participants and none in controls occurred before this.

**TABLE D4 Observed deaths (O), deaths expected from national rates (E), and standardised mortality ratios (SMR) among test participants and controls, and relative risks (RR) of mortality in test participants compared with controls for causes of death other than neoplasms**

| Cause of death (ICD Codes 9th Revision) | Test participants | | | | Controls | | | | Mortality rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | O | E | SMR | Prob[a] | O | E | SMR | Prob[a] | RR | 90%CI[d] | Prob[b] one-sided | Prob[c] two-sided |
| **A. Diseases related to smoking** | | | | | | | | | | | | |
| Coronary heart disease (410-414) | 1442 | 1785.06 | 81 | <0.001 | 1576 | 1925.4 | 82 | <0.001 | 0.99 | 0.93, 1.05 | 0.36 | 0.73 |
| Bronchitis, emphysema and chronic obstructive lung disease (491, 492, 496, 519)[e] | 164 | 241.45 | 68 | <0.001 | 176 | 265.63 | 66 | <0.001 | 1.00 | 0.83, 1.21 | 0.51 | 0.97 |
| Aortic aneurysm (441) | 83 | 84.16 | 99 | 0.91 | 86 | 91.24 | 94 | 0.60 | 1.05 | 0.80, 1.37 | 0.41 | 0.81 |
| **B. Diseases related to alcohol** | | | | | | | | | | | | |
| Cirrhosis of liver, alcoholism and alcoholic psychosis (303, 305.0, 291, 571) | 90 | 61.39 | 147 | <0.001 | 103 | 64.93 | 159 | <0.001 | 0.97 | 0.75, 1.24 | 0.43 | 0.86 |
| **C. Other diseases** | | | | | | | | | | | | |
| Infectious and parasitic diseases (1-139) | 22 | 38.94 | 56 | 0.0039 | 34 | 41.61 | 82 | 0.25 | 0.71 | 0.44, 1.15 | 0.13 | 0.23 |
| Diseases of nervous system (320-389) | 64 | 85.97 | 74 | 0.015 | 57 | 91.21 | 62 | <0.001 | 1.24 | 0.90, 1.70 | 0.14 | 0.28 |
| *Motor neurone disease (335.2)* | *16* | *16.39* | *98* | *1.00* | *15* | *17.50* | *86* | *0.56* | *1.12* | *0.58, 2.15* | *0.45* | *0.86* |
| Other diseases of circulatory system (390-459 excl. 410-414, 441) | 532 | 627.26 | 85 | <0.001 | 529 | 682.62 | 77 | <0.001 | 1.09 | 0.99, 1.21 | 0.080 | 0.16 |
| Other diseases of respiratory system (460-519 excl. 491-2, 496, 519) | 148 | 226.41 | 65 | <0.001 | 167 | 247.34 | 68 | <0.001 | 0.97 | 0.80, 1.18 | 0.42 | 0.84 |
| Other diseases of digestive system (520-579 excl. 571) | 98 | 112.04 | 87 | 0.19 | 93 | 120.61 | 77 | 0.0095 | 1.14 | 0.89, 1.47 | 0.20 | 0.39 |
| Remaining diseases other than neoplasms (001-799.8 excl. above diseases and 140-239) | 126 | 199.80 | 63 | <0.001 | 140 | 213.52 | 66 | <0.001 | 0.98 | 0.79, 1.21 | 0.47 | 0.93 |
| **D. Accidents and violence** | | | | | | | | | | | | |
| Motor traffic accidents (E810-E819) | 103 | 109.46 | 94 | 0.57 | 101 | 105.26 | 96 | 0.70 | 0.96 | 0.75, 1.23 | 0.42 | 0.83 |
| Drowning and water transport accidents (E830-E838, E910, E984) | 24 | 18.09 | 133 | 0.19 | 23 | 17.99 | 128 | 0.29 | 0.94 | 0.54, 1.63 | 0.49 | 0.88 |
| Air and space transport accidents (E840-E845) | 41 | 3.62 | 1133 | <0.001 | 57 | 3.55 | 1605 | <0.001 | 0.83 | 0.57, 1.19 | 0.21 | 0.40 |
| Suicide E950-E959 | 102 | 100.03 | 102 | 0.84 | 94 | 102.18 | 92 | 0.43 | 1.16 | 0.90, 1.48 | 0.17 | 0.35 |
| Other injury and poisoning (E800-E999 excl. above) | 166 | 127.66 | 130 | 0.0012 | 142 | 130.53 | 109 | 0.34 | 1.22 | 1.00, 1.48 | 0.053 | 0.11 |
| All known causes, other than neoplasms | 3205 | 3822.45 | 84 | <0.001 | 3378 | 4104.99 | 82 | <0.001 | 1.02 | 0.98, 1.06 | 0.21 | 0.42 |

*Notes for Table D4*

(a) Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.
(b) One-sided test that the RR is greater than unity (RR $\geq$ 1.00), or less than unity (RR < 1.00).
(c) Two-sided test that the RR is different from unity.
(d) Confidence interval.
(e) ICD code 519 (other diseases of respiratory system) is included as it is impossible to separate deaths attributed to this cause from those attributed to ICD code 496 (chronic airways obstruction, not elsewhere classified) in calculating expected deaths prior to 1979.

**TABLE D5 Numbers of incident cancers (I) among test participants and controls, and relative risks (RR) of incident cancer in test participants compared with controls for 27 distinct types of cancer**

| | Test Participants | Controls | Incidence rate in test participants relative to controls | | | |
|---|---|---|---|---|---|---|
| Type of cancer | I | I | RR | 90% CI[c] | Prob[a] 1-sided | Prob[b] 2-sided |
| Tongue, mouth, pharynx | 60 | 76 | 0.86 | 0.64, 1.16 | 0.21 | 0.43 |
| Oesophagus | 73 | 86 | 0.90 | 0.69, 1.19 | 0.29 | 0.58 |
| Stomach | 119 | 123 | 1.04 | 0.83, 1.29 | 0.42 | 0.84 |
| Large intestine and rectum | 319 | 336 | 1.01 | 0.88, 1.15 | 0.47 | 0.93 |
| Liver | 33 | 18 | 2.03 | 1.21, 3.43 | 0.010 | 0.017 |
| Primary liver cancer | 22 | 13 | 1.83 | 0.98, 3.47 | 0.057 | 0.089 |
| Gallbladder | 3 | 7 | 0.44 | 0.11, 1.59 | 0.19 | 0.34 |
| Pancreas | 78 | 78 | 1.06 | 0.80, 1.39 | 0.40 | 0.79 |
| Larynx | 49 | 58 | 0.92 | 0.65, 1.28 | 0.36 | 0.72 |
| Lung | 542 | 615 | 0.95 | 0.86, 1.04 | 0.18 | 0.36 |
| Bone | 5 | 5 | 1.16 | 0.35, 3.86 | 0.53 | 1.00 |
| Connective and soft tissue | 9 | 13 | 0.71 | 0.32, 1.56 | 0.28 | 0.52 |
| Malignant melanoma | 56 | 56 | 1.09 | 0.78, 1.51 | 0.36 | 0.72 |
| Other skin cancer | 333 | 402 | 0.88 | 0.78, 1.00 | 0.049 | 0.098 |
| Prostate | 244 | 216 | 1.22 | 1.04, 1.44 | 0.018 | 0.036 |
| Testis | 24 | 27 | 0.91 | 0.55, 1.51 | 0.43 | 0.77 |
| Bladder | 158 | 153 | 1.10 | 0.91, 1.34 | 0.21 | 0.42 |
| Kidney | 71 | 107 | 0.71 | 0.54, 0.92 | 0.014 | 0.028 |
| Tumours of central nervous system | 90 | 82 | 1.17 | 0.90, 1.52 | 0.18 | 0.35 |
| Thyroid | 6 | 3 | 2.00 | 0.54, 8.29 | 0.25 | 0.50 |
| Adrenals | 3 | 2 | 1.64 | 0.28,11.13 | 0.46 | 0.68 |
| Hodgkin's disease | 19 | 21 | 0.89 | 0.50, 1.57 | 0.41 | 0.75 |
| Non-Hodgkin's lymphoma | 85 | 87 | 0.99 | 0.76, 1.29 | 0.50 | 0.99 |
| Multiple myeloma | 35 | 35 | 1.14 | 0.74, 1.74 | 0.34 | 0.62 |
| Multiple myeloma (wider definition)[d] | 36 | 35 | 1.17 | 0.77, 1.78 | 0.30 | 0.55 |
| Leukaemia | 67 | 53 | 1.33 | 0.97, 1.84 | 0.072 | 0.14 |
| Leukaemia excluding CLL | 49 | 36 | 1.41 | 0.96, 2.09 | 0.073 | 0.14 |
| Polycythaemia vera | 12 | 13 | 0.99 | 0.47, 2.05 | 0.57 | 1.00 |
| Other specified neoplasms | 123 | 143 | 0.93 | 0.75, 1.15 | 0.30 | 0.59 |
| Unspecified neoplasms | 79 | 103 | 0.85 | 0.65, 1.09 | 0.15 | 0.30 |
| All neoplasms excluding non-melanoma skin cancer | 2362 | 2516 | 1.00 | 0.96, 1.05 | 0.44 | 0.88 |
| All neoplasms | 2695 | 2918 | 0.99 | 0.94, 1.03 | 0.33 | 0.65 |

*Notes*

(a) One-sided test that the RR is greater than unity (RR ≥ 1.00), or less than unity (RR < 1.00).

(b) Two-sided test that the RR is different from unity.

(c) Confidence interval.

(d) ICD 9th revision codes 203.0, 203.1, 238.6 and 273.1.

# APPENDIX E

# MORTALITY FROM LEUKAEMIA, MULTIPLE MYELOMA AND OTHER CANCERS AMONG TEST PARTICIPANTS, BY OPERATION

**TABLE E1 Observed deaths (O), deaths expected from national rates (E) and standardised mortality ratios (SMR) among test participants present at UK atmospheric nuclear weapons tests. For leukaemia, the whole follow-up period and the period 2-25 years after first test participation are considered. For multiple myeloma and for other neoplasms, the period more than 10 years after first test participation is considered.**

(NB. The observed numbers of deaths based on the wider definition of multiple myeloma, ie. ICD 9th revision codes 203.0, 203.1, 238.6 and 273.1, are identical to those given here for the standard definition of this disease.)

**(a) Operation Hurricane**

| Cause of death | O | E | SMR | Prob[a] |
|---|---|---|---|---|
| Leukaemia: whole follow-up period | 4 | 4.41 | 91 | 1.00 |
| Leukaemia: 2-25 years | 1 | 1.14 | 87 | 1.00 |
| Leukaemia excluding CLL: whole follow-up period | 2 | 3.46 | 58 | 0.60 |
| Leukaemia excluding CLL: 2-25 years | 0 | 1.02 | 0 | 0.44 |
| Multiple Myeloma: 10+ years | 2 | 2.36 | 85 | 1.00 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 164 | 166.4 | 99 | 0.88 |

### (b) Operation Totem

| Cause of death | O | E | SMR | Prob[a] |
|---|---|---|---|---|
| Leukaemia: whole follow-up period | 0 | 0.52 | 0 | 0.69 |
| Leukaemia: 2-25 years | 0 | 0.14 | 0 | 1.00 |
| Leukaemia excluding CLL: whole follow-up period | 0 | 0.39 | 0 | 1.00 |
| Leukaemia excluding CLL: 2-25 years | 0 | 0.11 | 0 | 1.00 |
| Multiple Myeloma: 10+ years | 0 | 0.29 | 0 | 1.00 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 20 | 21.32 | 94 | 0.83 |

### (c) Operation Mosaic

| Cause of death | O | E | SMR | Prob[a] |
|---|---|---|---|---|
| Leukaemia: whole follow-up period | 3 | 3.21 | 94 | 1.00 |
| Leukaemia: 2-25 years | 0 | 0.99 | 0 | 0.63 |
| Leukaemia excluding CLL: whole follow-up period | 3 | 2.62 | 115 | 0.75 |
| Leukaemia excluding CLL: 2-25 years | 0 | 0.91 | 0 | 0.63 |
| Multiple Myeloma: 10+ years | 2 | 1.60 | 125 | 0.68 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 94 | 108.5 | 87 | 0.16 |

### (d) Operation Buffalo

| Cause of death | O | E | SMR | Prob[a] |
|---|---|---|---|---|
| Leukaemia: whole follow-up period | 2 | 3.37 | 59 | 0.60 |
| Leukaemia: 2-25 years | 0 | 1.10 | 0 | 0.43 |
| Leukaemia excluding CLL: whole follow-up period | 2 | 2.65 | 75 | 0.78 |
| Leukaemia excluding CLL: 2-25 years | 0 | 0.95 | 0 | 0.63 |
| Multiple Myeloma: 10+ years | 1 | 1.75 | 57 | 0.74 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 103 | 123.6 | 83 | 0.065 |

### (e) Operation Antler

| Cause of death | O | E | SMR | Prob[a] |
|---|---|---|---|---|
| Leukaemia: whole follow-up period | 1 | 2.92 | 34 | 0.38 |
| Leukaemia: 2-25 years | 0 | 1.19 | 0 | 0.42 |
| Leukaemia excluding CLL: whole follow-up period | 1 | 2.35 | 43 | 0.53 |
| Leukaemia excluding CLL: 2-25 years | 0 | 1.07 | 0 | 0.44 |
| Multiple Myeloma: 10+ years | 3 | 1.73 | 174 | 0.43 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 95 | 119.1 | 80 | 0.025 |

### (f) Maralinga Experimental Programme

| Cause of death | O | E | SMR | Prob[a] |
|---|---|---|---|---|
| Leukaemia: whole follow-up period | 2 | 1.45 | 138 | 0.66 |
| Leukaemia: 2-25 years | 1 | 0.56 | 180 | 0.43 |
| Leukaemia excluding CLL: whole follow-up period | 2 | 1.14 | 175 | 0.32 |
| Leukaemia excluding CLL: 2-25 years | 1 | 0.48 | 210 | 0.38 |
| Multiple Myeloma: 10+ years | 2 | 0.76 | 264 | 0.18 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 49 | 52.99 | 92 | 0.63 |

### (g) Operation Grapple

| Cause of death | O | E | SMR | Prob[a] |
|---|---|---|---|---|
| Leukaemia: whole follow-up period | 7 | 7.84 | 89 | 0.86 |
| Leukaemia: 2-25 years | 4 | 2.61 | 153 | 0.53 |
| Leukaemia excluding CLL: whole follow-up period | 6 | 6.40 | 94 | 1.00 |
| Leukaemia excluding CLL: 2-25 years | 4 | 2.38 | 168 | 0.31 |
| Multiple Myeloma: 10+ years | 3 | 3.86 | 78 | 0.81 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 240 | 262.1 | 92 | 0.17 |

### (h) Operation Grapple X

| Cause of death | O | E | SMR | Prob[a] |
|---|---|---|---|---|
| Leukaemia: whole follow-up period | 8 | 5.16 | 155 | 0.26 |
| Leukaemia: 2-25 years | 2 | 1.76 | 114 | 1.00 |
| Leukaemia excluding CLL: whole follow-up period | 7 | 4.21 | 166 | 0.21 |
| Leukaemia excluding CLL: 2-25 years | 2 | 1.59 | 126 | 0.68 |
| Multiple Myeloma: 10+ years | 3 | 2.52 | 119 | 0.74 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 151 | 172.2 | 88 | 0.11 |

### (i) Operation Grapple Y

| Cause of death | O | E | SMR | Prob[a] |
|---|---|---|---|---|
| Leukaemia: whole follow-up period | 7 | 7.54 | 93 | 0.86 |
| Leukaemia: 2-25 years | 2 | 2.65 | 76 | 0.78 |
| Leukaemia excluding CLL: whole follow-up period | 7 | 6.22 | 112 | 0.84 |
| Leukaemia excluding CLL: 2-25 years | 2 | 2.43 | 82 | 1.00 |
| Multiple Myeloma: 10+ years | 3 | 3.59 | 84 | 0.81 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 226 | 242.8 | 93 | 0.29 |

### (j) Operation Grapple Z

| Cause of death | O | E | SMR | Prob[a] |
|---|---|---|---|---|
| Leukaemia: whole follow-up period | 10 | 8.99 | 111 | 0.74 |
| Leukaemia: 2-25 years | 4 | 3.20 | 125 | 0.78 |
| Leukaemia excluding CLL: whole follow-up period | 10 | 7.40 | 135 | 0.35 |
| Leukaemia excluding CLL: 2-25 years | 4 | 2.91 | 137 | 0.55 |
| Multiple Myeloma: 10+ years | 5 | 4.30 | 116 | 0.81 |
| All neoplasms except leukaemia and multiple myeloma: 10+ years | 248 | 292.1 | 85 | 0.0085 |

*Note (a)* Two-sided test that the difference between the number of deaths observed and that expected could have occurred by chance.

# APPENDIX F

# MEMBERSHIP OF ADVISORY GROUP

*Chairman:* Professor N J Wald (Wolfson Institute of Preventive Medicine, University of London)

*Members:* Professor D Goodhead (MRC Radiation and Genome Stability Unit, Chilton)*

Dr D J Hole (West of Scotland Cancer Registry, University of Glasgow)

Professor J Kaldor (National Centre in HIV Epidemiology and Clinical Research, Sydney, Australia)#

Professor J Little (University of Aberdeen)

Professor T Sorahan (Institute of Occupational Health, University of Birmingham)

Professor K R Trott (St Barts and Royal London School of Dentistry, University of London)

*Observers:* Lt Col D Baker (MOD)

Miss F A Fry (NRPB)

Mrs S Gray (British Nuclear Tests Veterans Association)+

*Secretariat (NRPB):* Dr G M Kendall, Dr D Bingham, Dr C R Muirhead

**Terms of Reference**

1. To advise on the conduct of an epidemiological analysis based on extended follow-up of mortality and incidence of multiple myeloma and other diseases in the established cohorts of test veterans and controls.
2. To oversee the conduct of the study.
3. To receive and review the draft report before publication.

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* Resigned March 2001.

\# Corresponding member.

\+ From 2000.